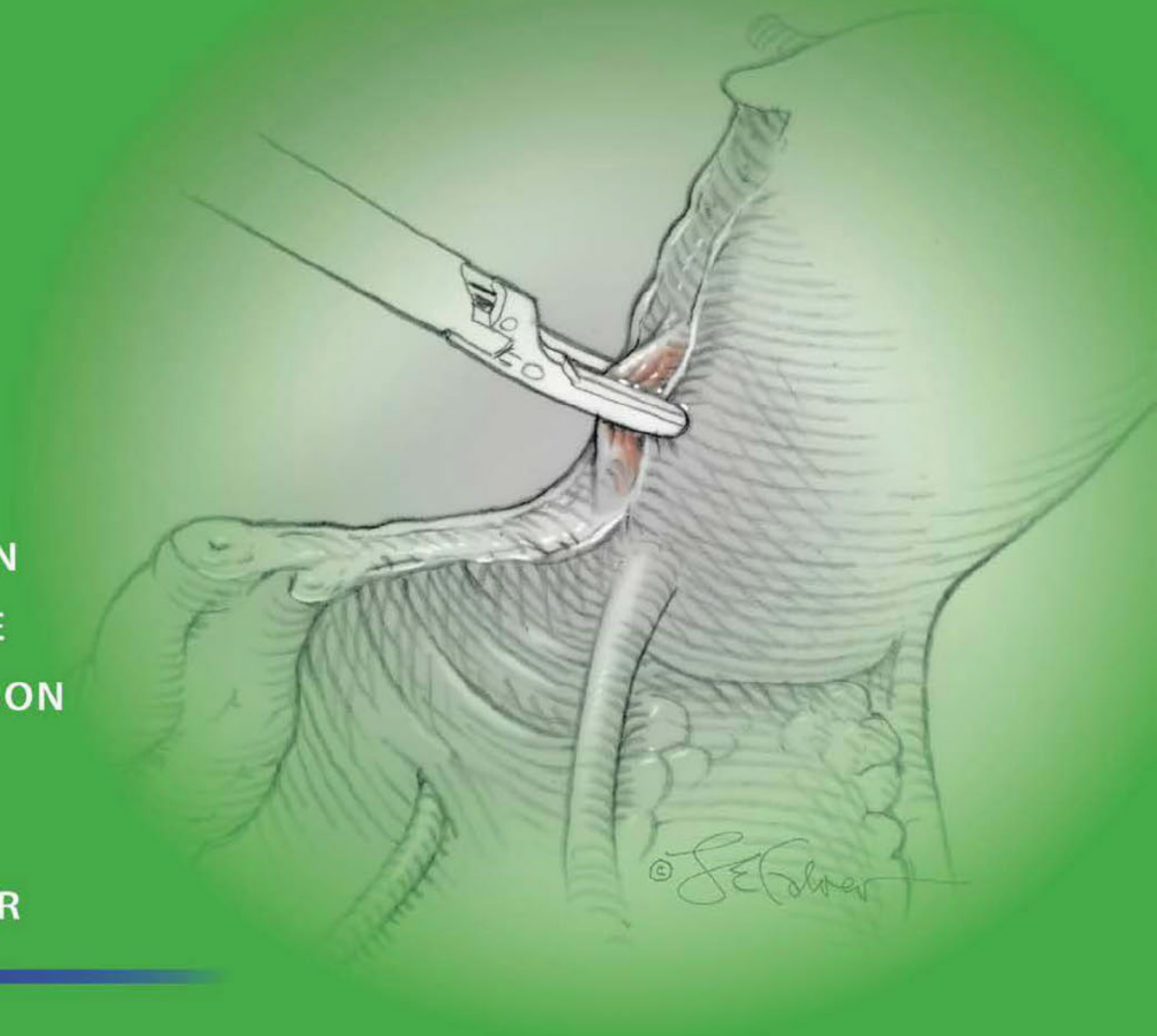
FOURTH EDITION

Williams GYNECOLOGY



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Williams GYNECOLOGY

FOURTH EDITION

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IN MEMORIAM

Kristin Paulson Landon

Early in production of this edition, our *Williams* family lost a dedicated member of the team in Ms. Kristin Landon. We knew her as our valued copyeditor for many editions of both *William Obstetrics* and *Williams Gynecology*. However, Kristin's life was multifaceted, with talents that included analytic chemist, musician, cooking enthusiast, and writer. Indeed, her published science fiction novels include the *Hidden Worlds* trilogy and *Windhome*. We knew Kristin as an integral member of our textbook team. Her precision added clarity to our efforts and made our textbooks better.

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DEDICATION

This edition of Williams Gynecology is dedicated to Dr. Karen Bradshaw, who has served as an Editor of Williams Gynecology since its inaugural edition. We are especially grateful for her tenacity during the formative years of our project and her academic support to bring our first edition to print. Our text's content has benefited greatly from her clinical acumen coupled with a mastery of the evidence-based literature. Her clear, concise chapters distilled challenging reproductive endocrinology tenets into easily understood concepts that translate to the bedside. Indeed, her many teaching awards throughout her career attest to this gift.

Dr. Bradshaw's roots at the University of Texas Southwestern run deep and include her medical school years, residency training, and fellowship study in Reproductive Endocrinology and Infertility. Early in her career as a faculty member at UTSW, she became Director of the Assisted Reproductive Technologies Program. Subsequently, she helped develop the Pediatric Gynecology Service at Children's Hospital, which was a first for Dallas and continues to this day. This was the first of many collaborative and multidisciplinary projects that typify her career. As another example, she was instrumental in expanding the field of minimally invasive surgery (MIS) at our institution and initiated the Laparoscopy Teaching Service. She partnered with the Department of Surgery and was provided a joint appointment to foster MIS development. She served on the Southwestern Minimally Invasive Surgery Executive Committee from its inception in 1997 until her retirement in 2019.

In addition to academics, Dr. Bradshaw was clinically and administratively active in our expanding private practice on campus. As an advocate of health for women as they entered and advanced through menopause, she was the first holder of the Helen J. and Robert S. Strauss and Diana L. and Richard C. Strauss Distinguished Professorship in Women's Health. Her vision led to development of a single, multidisciplinary site to care for the various health aspects of mature women. This was subsequently endowed and became the Lowe Foundation Center for Women's Preventative Health Care.

During her academic career, Dr. Bradshaw promoted academic excellence at UTSW. She served administratively on numerous academic committees involved with medical school, residency, and specialty training. Moreover, Karen was a passionate advocate for the advancement of women in academia at our institution. She was also a voice on the national academic stage. Karen served on the Board of the American Society of Reproductive Endocrinology and Infertility and extensively participated in their postgraduate training efforts. She filled prominent leadership roles in the Society for Reproductive Endocrinology and Infertility, including president. In both organizations, she actively advanced both residency and fellowship training in the specialty.

For us in the Department of Obstetrics and Gynecology, Dr. Bradshaw has played an important role as mentor and colleague. Her experience and clinical expertise have been invaluable, and she has provided guidance for challenging gynecology cases. On so many levels, we have benefitted greatly from her academic and clinical contributions.

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PREFACE

Williams Gynecology provides a thorough, evidence-based presentation of gynecology's depth and breadth. In Section 1, general gynecology topics are covered. Section 2 provides chapters covering reproductive endocrinology and infertility. The developing field of female pelvic medicine and reconstructive surgery is presented in Section 3. In Section 4, gynecologic oncology is discussed.

Traditionally, gynecologic information has been offered either as a didactic text or a surgical atlas. Instead, because the day-to-day activity of a gynecologist blends these two, we did the same with our text. The initial four sections of our book describe the evaluation and medical treatment of gynecologic problems. The remaining two sections focus on the surgical patient. Section 5 offers detailed anatomy and a discussion of perioperative considerations. Our final section presents an illustrated atlas for the surgical correction of conditions described in Sections 1 through 4. In addition, chapters are extensively complemented by illustrations, photographs, diagnostic algorithms, and treatment tables. To interconnect this content, readers will find page references within one chapter that will direct them to complementary content in another.

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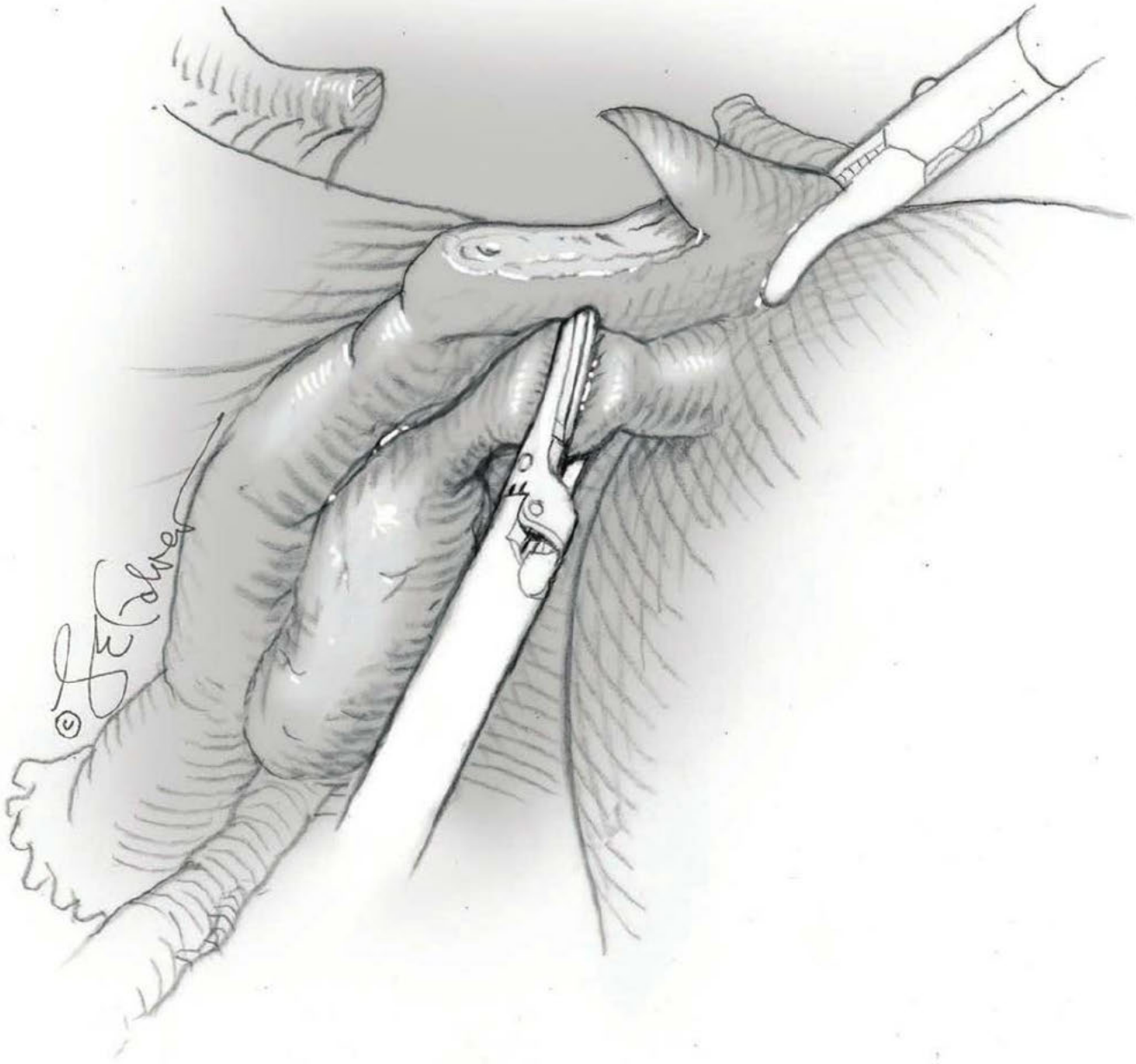
SECTION 1

GENERAL GYNECOLOGY



CHAPTER 1

Well Woman Care

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Serving as both specialist and primary care provider, gynecologists provide patient screening, emphasize ideal health behaviors, and coordinate appropriate consultation for care beyond their scope of practice. Various organizations provide regularly updated preventive care recommendations. Guidelines commonly accessed are those from the American College of Obstetricians and Gynecologists (ACOG), Centers for Disease Control and Prevention (CDC), U.S. Preventive Services Task Force (USPSTF), and American Cancer Society.

MEDICAL HISTORY

During a comprehensive well woman visit, patients are first queried regarding new or ongoing illness. To assist with evaluation, complete medical, social, surgical, and family histories are obtained. Specific gynecologic topics usually cover current and prior contraceptives; results from prior sexually transmitted disease (STD) testing, cervical cancer screening, or other gynecologic tests; sexual history, described in Chapter 3 (p. 63); and menstrual history, outlined in Chapter 8 (p. 182). Obstetric questions chronicle circumstances around deliveries, losses, or complications. Screening for intimate partner violence (p. 24) or depression is also completed (p. 19). Discussion might also assess the patient's support system and any cultural or spiritual beliefs that might affect her general health care. Last, a review of systems, whether performed by the clinician or office staff, can add clarity to new patient problems.

PHYSICAL EXAMINATION

Breast Examination

Many women present to their gynecologist with complaints specific to the breast or pelvis. Accordingly, these are often areas of increased focus, and their evaluation is described here.

Self breast examination (SBE) is an examination performed by the patient herself to detect abnormalities. In contrast, clinical breast examination (CBE) is completed by a health care professional and may identify a small portion of breast malignancies not detected with mammography. In addition, CBE may identify cancer in young women, who are not typical candidates for mammography (McDonald, 2004). Overall, however, studies show that SBE and CBE raise diagnostic testing rates for ultimately benign breast disease and are ineffective in lowering breast cancer mortality rates (Kösters, 2008; Thomas, 2002). Accordingly, several organizations have removed SBE and CBE from their recommended screening practices (Oeffinger, 2015; Siu, 2016). However, the American College of Obstetricians and Gynecologists (2017b) encourages breast self-awareness, which focuses on breast appearance and architecture and may include SBE. It also recommends that women receive a CBE every 1 to 3 years between ages 20 and 39. At age 40, CBE is completed annually. Specific mammography guidelines are listed in Chapter 13 (p. 293).

During CBE, the breasts are initially viewed as a woman sits on the table's edge with hands placed at her hips and with pectoralis muscles flexed. Alone, this position enhances asymmetry. Additional arm positions, such as placing arms above the head, do not add vital information. Breast skin is inspected for breast erythema; retraction; scaling, especially over the nipple; and edema, which is termed peau d'orange change. The breast and axilla are also observed for contour symmetry.

Following inspection, axillary, supraclavicular, and infraclavicular lymph nodes are palpated most easily with a woman seated and her arm supported by the examiner (Fig. 1-1). The axilla is bounded by the pectoralis major muscle ventrally and the latissimus dorsi muscle dorsally. Lymph nodes are detected as the examiner's hand glides from high to low in the axilla and momentarily compresses nodes against the lateral chest wall. In a thin patient, one or more normal, mobile lymph nodes less

FIGURE 1-1 One method of axillary lymph node palpation. Finger tips extend to the axillary apex and compress tissue against the chest wall in the rolling fashion shown in Figure 1-2. The patient's arm is supported by the examiner.

than 1 cm in diameter may commonly be appreciated. The first lymph node to become involved with breast cancer metastasis (the sentinel node) is nearly always located just behind the midportion of the pectoralis major muscle belly.

Breast palpation is completed with a woman supine and with one hand above her head to stretch breast tissue across the chest wall. Examination includes breast tissue bounded by the clavicle, sternal border, inframammary crease, and midaxillary line. Breast palpation within this pentagonal area is approached in a linear fashion. Technique uses the finger pads in a continuous rolling, gliding, circular motion (Fig. 1-2). At each palpation point, tissue is assessed both superficially and deeply.

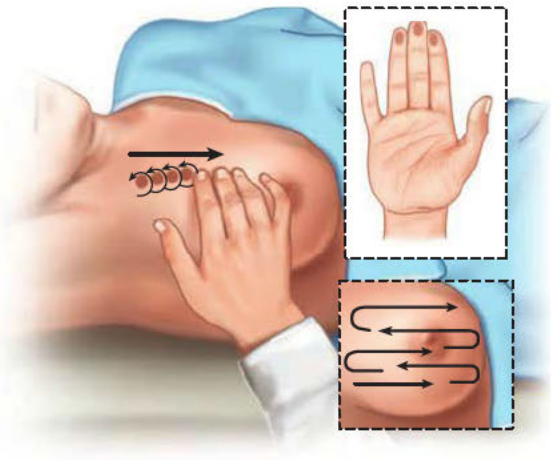

FIGURE 1-2 Recommended patient positioning and palpation technique. One inset shows the path of palpation. The other illustrates use of finger pads and a circular rolling motion to palpate the entire breast.

During CBE, intentional attempts at nipple discharge expression are not required unless a *spontaneous* discharge has been described by the patient.

If abnormal breast findings are noted, they are described by their location in the right or left breast, clock position, distance from the areola, and size. Evaluation and treatment of breast and nipple diseases are described in Chapter 13 (p. 280).

During examination, patients are educated that new axillary or breast masses, noncyclic breast pain, spontaneous nipple discharge, new nipple inversion, and breast skin changes such as dimpling, scaling, ulceration, edema, or erythema should prompt evaluation. This constitutes breast self-awareness. Patients who desire to perform SBE are counseled on its benefits, limitations, and potential harms and instructed to complete SBE the week after menses.

Pelvic Examination

Pelvic examination is typically performed with a patient supine, legs in dorsal lithotomy position, and feet resting in stirrups. The head of the bed is elevated 30 degrees to relax abdominal wall muscles for bimanual examination. A woman is assured that she may stop or pause the examination at any time. Moreover, each part of the evaluation is announced or described before its performance. Recommended STD screening is discussed prior to examination, and necessary samplers are assembled (Table 1-1).

Inguinal Lymph Nodes and Perineal Inspection

Pelvic cancers and infections may drain to the inguinal lymph nodes, and these are palpated during examination. Following this, a methodical inspection of the perineum extends from the mons pubis ventrally, to the labiocrural folds laterally, and to the anus. Notably, infections and neoplasms that involve the vulva can also involve perianal skin. Some clinicians additionally palpate for Bartholin and paraurethral gland pathology. However, in most cases, patient symptoms and asymmetry in these areas will dictate the need for this specific evaluation.

Speculum Examination

Both metal and plastic specula are available for this examination, each in various sizes to accommodate vaginal length and laxity. The plastic speculum may be equipped with a small light that provides illumination, whereas metal specula require an external light source. Preference between these two types is provider dependent.

The vagina and cervix are typically viewed after placement of either a Graves or Pederson speculum (Fig. 1-3). Prior to insertion, a speculum may be warmed with running water or by warming lights built into some examination tables. In addition, lubrication may add comfort to insertion. Gel lubricants do not raise unsatisfactory Pap smear cytology rates or decrease *Chlamydia trachomatis* detection rates compared with water (Griffith, 2005). If gel lubrication is used, a dime-sized aliquot is applied sparingly to the outer surface of the speculum blades.

Immediately before insertion, the labia minora are gently separated, and the urethra is identified. Because of urethral sensitivity, the speculum is inserted well below the meatus. Alternatively, prior to speculum placement, an index finger may be placed in the vagina, and pressure exerted against the

TABLE 1-1. Sexually Transmitted Disease Screening Guidelines for Nonpregnant, Sexually Active Asymptomatic Women

Infectious Agent	Screening Recommendations	Risk Factors
C trachomatis + *N gonorrhoeae*	All ≤24 yr; those older with risks Timing: annually or if new or persistent factors since last negative result	New or multiple partners; partner with STD or multiple partners; inconsistent condom use; sex work; current or prior STD
T pallidum	Those with risks	Sex work; incarceration; HIV; high local prevalence
HIV virus	All aged 13–64 yrs: one time[a] Those with risks: periodically	Multiple partners; injection drug use; sex work; concurrent STD; MSM; at-risk partners; initial TB diagnosis
HCV	All aged 18–79 yrs: one time Those with risk factors: periodically	Injection/intranasal drug use; dialysis; infected mother; blood products before 1992; unregulated tattoo; high-risk sexual behavior
HBV	Those with risk factors	HIV; injection drug use; affected family or partner; multiple partners; high-prevalence country of origin[b]
HSV	No routine screening	

[a]Centers for Disease Control and Prevention (2015) and American College of Obstetricians and Gynecologists (2017d) recommend one-time screening between ages 13 and 64 years. The U.S. Preventive Services Task Force uses a 15–65 yr age range.
[b]Regions of the world with high or intermediate prevalence of include much of Eastern Europe, Asia, Africa, the Middle East, and the Pacific Islands.
C trachomatis = *Chlamydia trachomatis*; HBV = hepatitis B virus; HCV = hepatitis C virus; HIV = human immunodeficiency virus; HSV = herpes simplex virus; MSM = men having sex with men; *N gonorrhoeae* = *Neisseria gonorrhoeae*; STD = sexually transmitted disease; TB = tuberculosis; *T pallidum* = *Treponema pallidum*.
Compiled from those above and Centers for Disease Control and Prevention, 2015; LeFevre, 2014a,b; Moyer, 2013a,b; U.S. Preventive Services Task Force, 2016c,d, 2019.

posterior wall. A woman is then encouraged to relax this wall to improve comfort with speculum insertion. This practice may prove especially helpful for women undergoing their first examination and for those with infrequent coitus, dyspareunia, or heightened anxiety.

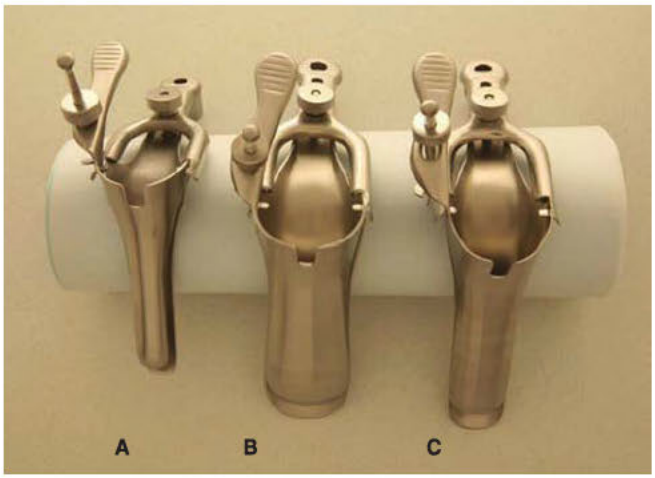

FIGURE 1-3 Vaginal specula. **A.** Pediatric Pederson speculum. This may be selected for child, adolescent, or virginal adult examination. **B.** Graves speculum. This may be selected for examination of parous women with relaxed or collapsing vaginal walls. **C.** Pederson speculum. This may be selected for sexually active women with adequate vaginal wall tone. (Reproduced with permission from US Surgitech, Inc.)

With speculum insertion, the vagina commonly contracts, and a woman may note pressure or discomfort. A pause at this point typically is followed by vaginal muscle relaxation. As the speculum bill is completely inserted, it is angled approximately 30 degrees downward to reach the cervix. Commonly, the uterus is anteverted, and the ectocervix lies against the posterior vaginal wall.

As the speculum is opened, the ectocervix can be identified. Vaginal walls and cervix are inspected for masses, ulceration, or unusual discharge. As outlined in Chapter 29 (p. 630), cervical cancer screening is often completed. Additional swabs for STD screening, culture, or microscopic evaluation can be collected as needed.

Bimanual Examination

Most often, the bimanual examination is performed after the speculum evaluation. Some clinicians prefer to complete the bimanual portion first to better identify cervical location prior to speculum insertion. Either process is appropriate. Uterine and adnexal size, mobility, and tenderness can be assessed during this examination. For women with prior hysterectomy and adnexectomy, bimanual examination is still valuable and can be used to exclude other pelvic pathology.

To begin, a gloved index and middle finger are inserted together into the vagina until the cervix is reached. To ease insertion, a water-based lubricant can be initially applied to these gloved fingers. Once the cervix is reached, uterine orientation can be quickly assessed by sweeping the index finger inward along the

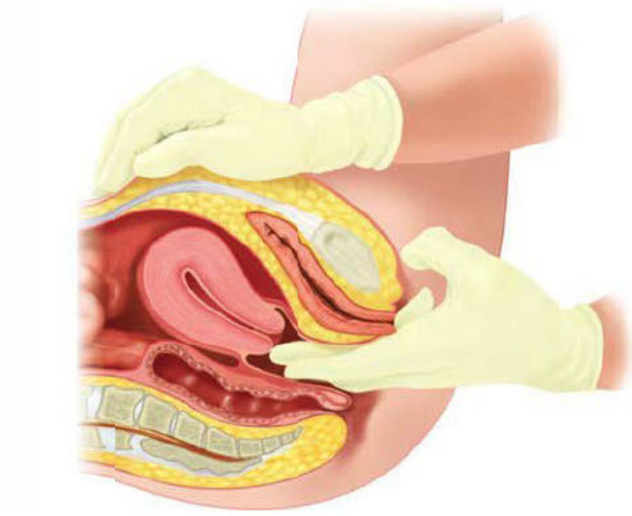

FIGURE 1-4 Bimanual examination. Fingers beneath the cervix lift the uterus toward the anterior abdominal wall. A hand placed on the abdomen detects upward pressure from the uterine fundus. Examination allows assessment of uterine size, mobility, and tenderness.

anterior surface of the cervix. In those with an anteverted position, the uterine isthmus is noted to sweep upward, whereas in those with a retroverted position, a soft bladder is palpated. However, in those with a retroverted uterus, if a finger is swept along the cervix's posterior aspect, the isthmus is felt to sweep downward. With a retroverted uterus, this same finger is continued posteriorly to the fundus and then side-to-side to assess uterine size and tenderness.

To determine the size of an anteverted uterus, fingers are placed beneath the cervix, and upward pressure tilts the fundus toward the anterior abdominal wall. A clinician's opposite hand is placed against the abdominal wall to locate the upward fundal pressure (Fig. 1-4).

To assess adnexa, the clinician uses two vaginal fingers to lift the adnexa from the posterior cul-de-sac or from the ovarian fossa toward the anterior abdominal wall. The adnexum is trapped between these vaginal fingers and the clinician's other hand, which is exerting downward pressure against the lower abdomen. For those with a normal-sized uterus, this abdominal hand is typically best placed just above the inguinal ligament.

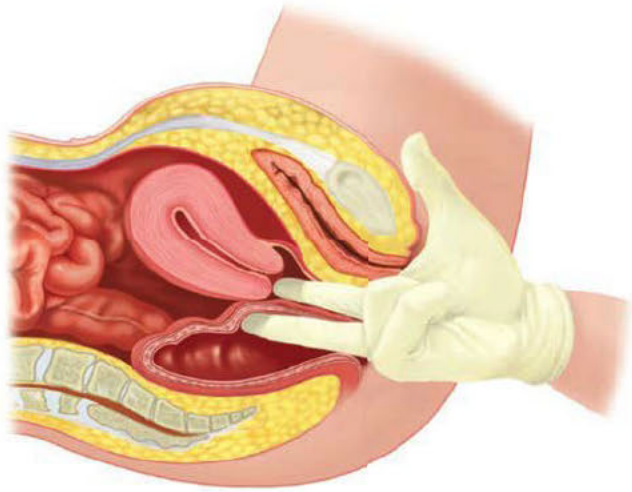

FIGURE 1-5 Rectovaginal examination.

Rectovaginal Examination

The decision to perform rectovaginal evaluation varies among providers. Some prefer to complete this evaluation on all adults, whereas others elect to perform rectovaginal examination for those with specific indications. These may include pelvic pain, an identified pelvic mass, rectal symptoms, or risks for colon cancer.

Gloves are changed between bimanual and rectovaginal examinations to avoid contamination of the rectum with potential vaginal pathogens. Initially, an index finger is placed into the vagina and a middle finger into the rectum (Fig. 1-5). These fingers are swept against one another in a scissoring fashion to assess the rectovaginal septum for scarring or peritoneal studding. The index finger is removed, and the middle finger completes a circular sweep of the rectal vault to exclude masses. If immediate diagnostic fecal occult blood testing is indicated, it may be performed with a sample from this portion of the examination. As noted later, this single fecal occult blood testing does not constitute adequate colorectal cancer screening.

Examination Interval

An initial reproductive health visit is recommended between ages 13 and 15 years (American College of Obstetricians and Gynecologists, 2016b). This visit initiates discussion between an adolescent and health care provider on issues of puberty, menstruation, contraception, and STD protection. Although not mandated, a pelvic examination may be necessary if gynecologic symptoms are described.

For women older than 21, the American College of Obstetricians and Gynecologists (2016c) recommends annual well woman visits for examination, screening, counseling, and immunizations based on age and risk factors. In many cases, physical examination includes a pelvic examination to assess specific symptoms or to complete cervical cancer or STD screening. However, outside these indications, the American College of Physicians, the American Academy of Family Physicians (2017), and USPSTF (2017) recommend against screening pelvic examination for asymptomatic, nonpregnant, adult women. They cite potential harms that include discomfort, anxiety, and overtreatment (Qaseem, 2014). In contrast, potential benefits are early detection of dermatologic changes or of vulvar or vaginal cancer. Thus, the American College of Obstetricians and Gynecologists (2018b) recommends a patient-provider discussion of the benefits and risks of pelvic examination in the asymptomatic, nonpregnant, adult woman who does not require genital screening.

Care of the Transgender Patient

"Transgender" refers to individuals whose gender identity, expression, and behavior differ from those typically associated with their gender assigned at birth (World Professional

TABLE 1-2. Gender Terminology

Transgender: Individuals whose gender identity, expression and behavior differ to varying degrees from those typically ascribed to their sex at birth
Cisgender: Individuals whose gender identity aligns with their sex at birth
Gender dysphoria: Distress that is caused by a discrepancy between a person's assigned gender at birth and the person's gender identity
Gender identity: An individual's intrinsic sense of being male, female, or an alternative gender (gender variant) that is independent of the gender assigned at birth
Sexual orientation: An individual's attraction to members of the same sex and/or a different sex (i.e., lesbian, gay, bisexual, heterosexual, or asexual)
Gender expression: The manner used by individuals to present themselves socially that may or may not be congruent with their gender identity
Gender variance/gender nonconformity: Expression of gender identity that that does not fully adhere to either male or female gender norms
Female-to-male (trans men): Individuals assigned female gender at birth who are changing to a more masculine body/gender role
Male-to-female (trans women): Individuals assigned male gender at birth who are changing to a more feminine body/gender role

Data from World Professional Association for Transgender Health, 2012.

Association for Transgender Health, 2012). Also, an individual's gender identity is independent of their sexual orientation or gender expression (Table 1-2). Despite agreement on these concepts, no definition of "transgender" is universally accepted.

In 2016 in the United States, an estimated 0.6 percent of adults, which approximates 1.4 million, identified as transgender (Flores, 2016). However, global prevalence rates of transgender populations have not been established. In part, differing behavioral expression of gender likely affects rates across cultures.

Despite growing awareness of transgender issues within the medical community, individuals continue to face significant barriers to both medical and mental health care (American College of Obstetricians and Gynecologists, 2011). For example, transgender adolescents compose up to 40 percent of homeless youth, and this can limit health care access (Ray, 2006). Further, medical schools teach little about sexuality in general and even less about the unique aspects of transgender health. This knowledge gap prepares few providers to address specific transgender needs (Mayer, 2008).

In 2017, the Endocrine Society updated clinical practice guidelines to provide an evidence-based standard for the care of transgender persons (Hembree, 2017). The American College of Obstetricians and Gynecologists (2011) urges obstetrician-gynecologists to be willing and able either to provide care for these individuals or to refer them for routine care or gender-affirming treatment. Thus, an understanding of current practices and long-term health risks is essential.

One first step in eliminating barriers is creation of a welcoming and inclusive clinical environment for transgender persons. Intake forms ideally incorporate sexual minorities in the gender field and use terms such as "relationship status" instead of "marital status." Providers begin the visit with an open dialogue that asks for a preferred name and pronoun.

A history of their gender experience ideally uses open-ended questions to ascertain the age at their initial transition, prior supplement or hormone use, and its duration. Importantly, not all transgender patients have undergone surgical transition, and many opt for medical therapy alone. Clarifying prior gender-affirming and sexual practices allows adequate assessment of an individual's medical risks and reproductive needs. Assumptions regarding a patient's sexual orientation or practices are best avoided (Gay and Lesbian Medical Association, 2006).

Prior to physical examination, each patient's individual comfort level with being examined is assessed. A problem-oriented examination usually suffices, and a genital examination is not indicated unless needed for a specific complaint or routine screening.

Medical Management of Gender Dysphoria

Gender dysphoria is the condition commonly ascribed to transgender individuals seeking medical care (see Table 1-2). The *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5) defines it as the distress experienced by persons whose gender identity is incongruent to the gender they were assigned at birth (American Psychiatric Association, 2013). This diagnosis is best made by a qualified mental health provider. Following diagnosis, initiation of proper gender-affirming hormone therapy improves health outcomes and quality of life in these individuals (Gorin-Lazard, 2012). Those with gender dysphoria often have concurrent psychosocial or psychiatric issues. Thus, patients receiving hormone therapy are recommended to receive continuing psychotherapy (Spack, 2013).

In female-to-male transgender persons, the primary goals of testosterone therapy are cessation of menses and virilization. An increase in muscle mass and decline in fat mass are other effects. Testosterone is typically administered intramuscularly (IM) or subcutaneously every 1 to 2 weeks. To induce puberty in adolescents, initial testosterone doses may begin at 25 mg weekly. Doses increase incrementally every 3 to 6 months to reach the typical adult maintenance dose, which is 50 to 100 mg weekly (Hembree, 2017). Creams and patches are not

TABLE 1-3. Medical Management of Gender Dysphoria

	Puberty Suppression	FTM	MTF
Medications	Provide GnRH analogues: Implant (histrelin) Intramuscular (leuprolide)	Testosterone Parenteral (IM or SC) Oral Transdermal	Estrogen Oral Transdermal Parenteral Antiandrogens Spironolactone
Anticipated effects	Prevent secondary sexual characteristics of the assigned gender	Deepened voice Facial/body hair growth ↑ libido Amenorrhea Clitoral enlargement ↑ percentage muscle mass compared to body fat	Breast growth ↓ testicle size ↓ percentage muscle mass compared to body fat Antiandrogens may reduce effects of endogenous testosterone
Anticipated risks	May decrease BMD (may theoretically be reversed with sex hormone therapy)	Polycythemia Weight gain Acne Androgenic hair loss Sleep apnea	VTE Gallstones ↑ liver enzyme levels Weight gain Hypertriglyceridemia
No risk increase/ data inconclusive		BMD loss Breast cancer Cervical cancer Ovarian cancer Uterine cancer	Breast cancer

BMD = bone mineral density; FTM = female to male; GnRH = gonadotropin-releasing hormone; IM = intramuscular; MTF = male to female; SC = subcutaneous; VTE = venous thromboembolism.

as widely prescribed as data are limited regarding their use for puberty induction.

Serum testosterone levels are measured every 2 to 3 months to ensure that levels are in the normal physiologic range for males (320 to 1000 ng/dL). Importantly, the most common adverse effects of exogenous testosterone are erythrocytosis and more atherogenic lipid levels (Bhasin, 2006). Accordingly, patients undergo periodic laboratory testing while receiving treatment. Panels include a complete blood count (CBC), liver function tests (LFTs), and lipid and hemoglobin A_{1c} levels (Spack, 2013).

In male-to-female transgender individuals, feminizing therapy is often begun to promote breast growth, redistribute body fat, and reduce body hair growth. Estrogen, either conjugated equine estrogens or 17β-estradiol, is typically administered orally, transdermally, or parenterally (estrogen esters). Puberty induction with 17β-estradiol may begin with a 1-mg oral daily dose that is incrementally increased every 3 to 6 months to reach the typical adult maintenance doses of 4 to 6 mg daily. Similarly, transdermal estrogen may begin with a patch that delivers 0.1 mg/d estradiol daily and is changed once or twice weekly depending on brand. Dosing can then be incrementally raised to a daily 0.4 mg/d dose, which is achieved by wearing multiple 0.1 mg/d patches (Deutsch, 2018). As with any patient undergoing chronic estrogen replacement therapy, transgender women are screened and counseled regarding the higher risk for thromboembolic disease, liver dysfunction, and hypertension (Spack, 2013). Effects of hormone therapy and different methods of administration are summarized in Table 1-3.

Concurrently, testosterone is ideally lowered to premenopausal levels (<50 ng/dL). For this degree of suppression, treatment with estrogen alone is insufficient. Thus, adjuncts, such as progestins with antiandrogen activity or GnRH agonists, are options. Another is spironolactone, which directly blocks androgen receptor binding.

With therapy, serum testosterone and estradiol levels are measured every 3 months to ensure that serum estradiol levels do not exceed the peak physiologic range for premenopausal females. The preferred range is 100 to 200 pg/mL (Spack, 2013). Estrogen therapy can promote pituitary lactotroph cell growth. And, several reports describe prolactinomas occurring after long-term, high-dose estrogen therapy. Accordingly, periodic serum prolactin level testing is recommended (Hembree, 2017).

Surgical Management of Gender Dysphoria

Most, but not all, transgender individuals consider gender-affirming surgeries necessary to complete their transition. These procedures are classified as those that directly impair fertility and those that do not. The former include hysterectomy and gonadectomy, and in minors, performance of these is typically controlled by governing laws (Hembree, 2017). However, less-legislated procedures may be considered in both minors and

adults who have been living in their new gender role and have been receiving hormonal therapy for approximately 12 months. Such surgeries include mastectomy and breast reconstruction and other procedures meant to feminize or masculinize the face and body. Consensus among the patient, physician, and the mental health provider is advisable.

Female-to-male transgender individuals commonly choose total hysterectomy, and both vaginal and laparoscopic approaches are options. Of these, the vaginal approach appears to be more cost-effective and amenable to subsequent phalloplasty, which is creation of a phallus, if elected (O'Hanlan, 2007). The gynecologist also provides essential counseling regarding retention or removal of ovaries. This decision is made with utmost respect for the patient's autonomy and is directed by their desire for removal of their female gonads and their plans for future fertility. Gynecologic considerations also include comorbid pathology, such as endometriosis or positive *BRCA* gene mutation status, which may favor oophorectomy. As another counseling point, future disruption of their testosterone therapy due to financial constraints could pose osteoporosis risks from lack of exogenous steroid hormones. Primary ovarian retention may mitigate this risk.

During female-to-male transition, mastectomy is also often undertaken, as testosterone therapy has little effect on breast regression. In adults, discussion regarding mastectomy usually takes place after androgen therapy has begun. Other procedures available to transgender males have been less satisfactory and not as widely sought. Surgical creation of a neopenis is still cost-prohibitive and typically requires multiple stages. That said, newer surgical techniques are yielding improved cosmetic results (Monstrey, 2007).

Male-to-female transgender surgery can involve penile and testicular excision and creation of a neovagina. Postoperatively, significant risks for vaginal and urethral stenosis persist, and lifelong vaginal dilation is required to maintain neovagina patency. Other cosmetic procedures include breast augmentation and facial feminizing surgery. These reconstructive procedures are best performed by urologists, gynecologists, or plastic surgeons with experience and specialized training in this field.

Adolescent Care

The effects of gender dysphoria in adolescents are potentiated by the unwanted physical changes that accompany puberty. Medical treatment of gender dysphoria during puberty improves psychological functioning in this group (de Vries, 2011). The Endocrine Society suggests suppression of pubertal development in adolescents who meet criteria for gender dysphoria (Hembree, 2017).

Puberty suppression is commonly accomplished with gonadotropin-releasing hormone (GnRH) analogues in the form of the histrelin implant (Supprelin LA) or depot leuprolide acetate (Lupron). Histrelin is a single subcutaneous implant that delivers the GnRH agonist over 12 months. Depot leuprolide acetate is administered IM in distinct doses that supply activity for 1 month or for 3 months. With these agents, gonadotropin suppression is profound (Chap. 9, p. 208).

Suppression is considered once Tanner stage 2 development is reached (Fig. 15-3, p. 322), that is, before the physical signs of puberty have significantly progressed. GnRH agonists offer the advantage of complete reversibility. However, their overall effect on bone density is not well studied. Accordingly, the Endocrine Society recommends that bone mineral density testing be completed annually (Hembree, 2017). They also support initiation of gender-affirming hormones in adolescents by age 16, although use in 14-year-old adolescents has been described (de Vries, 2014).

Long-Term Considerations

Transgender aging is an underexplored field (Fredriksen-Goldsen, 2014). The American College of Obstetricians and Gynecologists (2018a) advocates against routine discontinuation of systemic hormone therapy in postmenopausal women if used for the management of persistent vasomotor symptoms. However, no such recommendations exist for gender-affirming hormones in transgender persons receiving long-term therapy.

Both testosterone and estrogen therapy pose many of the same medical risks in both trans- and cisgender populations. However, their use in transgender persons is complicated by prolonged exposure to exogenous high-dose hormones and the potential negative secondary effects of early gonadectomy. In addition to monitoring weight and blood pressure and directed physical examination, routine health evaluation should seek lifestyle risk factors (such as smoking) and concurrent use of medications that can heighten the risks of long-term gender-affirming hormone therapy. Laboratory testing described earlier is standard for transgender adults (p. 7).

For transgender males, age-appropriate screening for breast cancer is continued as recommended by the American Cancer Society (Smith, 2018a). Long-term estrogen use does not raise the breast cancer risk in this group. But, breast cancer has been reported in transgender males even following mastectomy and highlights the need for continued screening (Shao, 2011). No cases of endometrial cancer have been reported in transgender males following long-term testosterone treatment. That said, individuals who maintain their uterus and ovaries are counseled regarding the potential risk of endometrial hyperplasia resulting from the aromatization of testosterone to estradiol (Futterweit, 1998; Moore, 2003). Thus, transgender males who present with abnormal uterine bleeding (AUB) following prolonged amenorrhea may benefit from evaluation similar to that in cisgender women with AUB. Evaluation for AUB may be considered if bleeding persists despite 6 to 12 months of suppressed luteinizing hormone and follicle-stimulating hormone levels and a testosterone level in the male range. If cervical tissue is still present, cervical cancer screening is performed as recommended by the American College of Obstetricians and Gynecologists (Chap. 29, p. 630).

Transgender women should continue routine screening for prostate and breast cancer. Breast cancer has been reported in transgender females undergoing long-term estrogen therapy. That said, no long-term studies have determined the actual risk of breast cancer in this population (Ganly, 1995). Although the overall benefit of screening mammography for transgender females has not been established, breast cancer screening as in the general population is reasonable (Hembree, 2017).

Prolonged use of gender-affirming hormones has potentially negative effects on ovarian and testicular function. Thus, a discussion regarding plans for future childbearing is essential (Mayer, 2008). These discussions ideally take place prior to initiation of hormone therapy. Fertility preservation options offered to transgender individuals mirror those suitable to their cisgender counterparts (Chap. 21, p. 466). Conversely, unintended pregnancies have occurred in transgender men receiving testosterone. Thus, contraceptive needs are addressed in patients who have maintained their uterus (Light, 2014). Contraceptive options for transgender men do not differ from those for cisgender women (Chap. 5, p. 111). Testosterone is not a form of contraception, and this should be emphasized during patient discussion.

PREVENTIVE CARE

Gynecologists have an opportunity to evaluate their patients for leading causes of female morbidity and mortality and intervene accordingly. In 2016, screening recommendations by the American College of Obstetricians and Gynecologists (2016c) were updated. The USPSTF regularly revises its screening guidelines, which can be accessed at www.USPreventiveServicesTaskForce.org. Many of these topics are covered in other text chapters. Some remaining important subjects are presented in the following sections.

Immunization

The need for new or repeat administration of vaccines is best reviewed periodically. Table 1-4 summarizes recommended schedules, precautions, and contraindications for these adult vaccines, and as of 2019, a link is provided to the full schedules at: http://www.cdc.gov/vaccines/schedules. In general, any vaccine may be coadministered with another type at the same visit.

Cancer Screening

Colon Cancer

In the United States, colon cancer is the third leading cause of cancer death in women, behind lung and breast cancer (Siegel, 2019). Incidence and mortality rates from this cancer have declined during the past two decades, largely due to improved screening tools. No trials have directly compared any of the screening tools. Instead, identifying an acceptable screening strategy for an individual patient may improve overall compliance and screening completion rates (U.S. Preventive Services Task Force, 2016a).

Guidelines recommend screening average-risk patients for colorectal cancer from age 50 to 75 with any of the methods shown in Table 1-5 (Smith, 2018a). Black women in the United States have a higher incidence of colorectal cancer, and the U.S. Multi-Society Task Force on Colorectal Cancer recommends discussing initial screening at age 45 (Rex, 2017). Health care disparities related to race and colon cancer are complex, and patient-oriented outcome studies are lacking to strongly support this earlier screening. Other organization guidelines, including those of the USPSTF (2016a), have not yet supported this earlier screening age.

Direct visualization methods can detect cancer *and* precancerous lesions. Of these, colonoscopy visualizes the entire colon, and biopsy can be performed simultaneously if needed. Stool-based tests include fecal occult blood test, fecal immunochemical test, and stool DNA tests.

Because colonoscopy allows for both screening and simultaneous diagnostic evaluation, it is often the preferred colorectal cancer screening test. For the patient with average risk and normal findings, testing is repeated every 10 years. In the United States, the direct visualization method offered may depend on a patient's insurance plan coverage.

Fecal occult blood testing (gFOBT) is an adequate *annual* screening method when two or three stool samples are

TABLE 1-4. Summary of Recommendations for Adult Immunization

Vaccine and Route	Reason to Vaccinate	Vaccine Administration	Contraindications and Precautions[a,b]
Influenza[c] **IIV** *or* **RIV** *Give SC*	• All adults	• Yearly • October is ideal, or as long as virus is circulating	**Precaution** • GBS within 6 wk of prior vaccine • IIV: egg allergy
Pneumococcal **PCV13** *Give IM* **PPSV23** *Give IM or SC*	• All ≥65 yr • Chronic illness[d]; asplenia; immunocompromise; smokers	• Age ≥65 yr without health issues: PCV13, then PPSV23 after 1 yr ***or*** PPSV23, then PCV13 after 1 yr • Variant regimens for other indications[d]	
Hepatitis A *Give IM*	• Desires immunity • Contact or travel risk[e]; other health indications[d]	• Two doses: 0 and 6 months	
Hepatitis B *Give IM*	• Desires immunity • Contact or travel risks[e]; other health indications[d]	• Three doses: 0, 1, and 6 months	

(Continued)

TABLE 1-4. Summary of Recommendations for Adult Immunization *(Continued)*

Vaccine and Route	Reason to Vaccinate	Vaccine Administration	Contraindications and Precautions[a,b]
Combined Hepatitis A + B *Give IM*	• Indications for hepatitis A or B	• Three doses: 0, 1, and 6 months	
Tdap **Td** *Give IM*	• All adults • Pregnancy	• No prior vaccine: 1 dose Tdap • Td booster every 10 yr • At-risk wounds: booster Td dose if ≥5 yr since prior dose • Pregnancy: Tdap dose at 27–36 wk regardless of prior dosing	**Contraindication** • Tdap: encephalopathy after prior vaccine **Precaution** • GBS within 6 wk of prior vaccine • Tdap: unstable neurologic condition
Varicella *Give SC*	• Lacks immunity	• Two doses: 0 and 1 month • Nonimmune gravida: give series postpartum	**Contraindications** • Pregnancy • Immunocompromise **Precaution** • Recent antibody-containing blood products • Hold "-cyclovir" antivirals[f] 14 days after vaccine
Zoster **RZV** *Give IM* **ZVL** *Give SC*	• RZV: ≥50 yr ***or*** • ZVL: ≥60 yr	• Two doses: 0, 2–6 months • One dose	**ZVL Contraindications** • Immunocompromise • Pregnancy **Precaution** • Hold "-cyclovir" antivirals[f] 14 days after vaccine
MMR *Give SC*	• Lacks immunity	• One dose • Nonimmune gravida: give postpartum	**Contraindications** • Immunocompromise • Pregnancy **Precaution** • Prior thrombocytopenia • Recent antibody-containing blood products
HPV *Give IM*	• Desires immunity • Ages 9 to 45 yr	• Three doses: 0, 1, and 6 months	**Precaution** • Pregnancy

[a]Previous anaphylactic reaction to any of a vaccine's components serves as a contraindication for any vaccine.
[b]Moderate to severe illness is a precaution to vaccination. Mild illness is not a contraindication.
[c]Several influenza vaccines are available and listed at: https://www.cdc.gov/flu/protect/vaccine/vaccines.htm.
[d]Full guidelines found at http://www.cdc.gov/vaccines/schedules/downloads/adult/adult-combined-schedule.pdf.
[e]A list is found at https://wwwnc.cdc.gov/travel/page/yellowbook-home.
[f]These include acyclovir, famciclovir, valacyclovir.
GBS = Guillain-Barré syndrome; HPV = human papillomavirus; IIV = inactivated influenza vaccine; IM = intramuscular; MMR = measles, mumps, rubella; PCV = pneumococcal conjugate vaccine; PPSV = pneumococcal polysaccharide vaccine; RIV = recombinant influenza vaccine; RZV = recombinant zoster vaccine; SC = subcutaneous; Td = tetanus, diphtheria; Tdap = tetanus, diphtheria, activated pertussis; ZVL = zoster vaccine live.
From Dooling, 2018; Food and Drug Administration, 2018; Kim, 2019.

TABLE 1-5. Screening Guidelines for the Early Detection of Colorectal Cancer and Adenomas for Average-Risk Women Aged 50 to 75 years[a]

Direct Visualization Tests		
Test	**Interval**	**Key Issues for Informed Decisions**
Colonoscopy	10 years	Bowel prep required; conscious sedation provided
FSIG	5 years	Bowel prep required, sedation usually not provided Positive findings usually merit colonoscopy
CT Colonography	5 years	Bowel prep required, polyps ≥6 mm merit colonoscopy; incidental extracolonic findings are common and can result in unnecessary diagnostic testing
Stool-based Tests		
Test	**Interval**	**Key Issues for Informed Decisions**
gFOBT	Annually	Two to three stool samples *collected at home* (a single sample gathered during an office examination is insufficient); positive results merit colonoscopy
FIT	Annually	Single specimen *collected at home*; positive results merit colonoscopy
FIT-DNA	3 years	Lower specificity/higher sensitivity than FIT; positive results merit colonoscopy

[a]One method is selected.
FIT = fecal immunochemical test; FSIG = flexible sigmoidoscopy; gFOBT = guaiac-based fecal occult blood test.
Adapted from Rex, 2017; Smith, 2018a; U.S. Preventive Services Task Force, 2016a.

self-collected by the patient and the cards are returned for analysis. This method relies on a chemical oxidation reaction between the heme moiety of blood and alpha guaiaconic acid, a component of guaiac paper. However, gFOBT is not specific for human blood, and some factors can yield false-positive results. Ingestion of red meat or iron is an example. In contrast, vitamin C may preemptively react with the reagents and lead to false-negative results (Park, 2010). All of these must be eliminated for 3 days before testing. In addition, women should avoid nonsteroidal antiinflammatory drugs (NSAIDs) 7 days prior to testing to limit risks of gastric irritation and bleeding. These restrictions are cumbersome for some patients and lead to noncompliance.

Alternatively, the fecal immunochemical test (FIT) relies on an immune reaction to human hemoglobin. Similar to gFOBT, the FIT test is performed for annual screening on patient-collected stool samples but does not require pretesting dietary limitations. Advantages to FIT include greater specificity for human blood, and thus fewer false-positive results and improved accuracy for detecting colorectal cancer (U.S. Preventive Services Task Force, 2016a). An emerging screening strategy combines FIT with testing for altered DNA biomarkers in cells shed into the stool (FIT-DNA). One Food and Drug Administration (FDA)-approved test, Cologuard, screens stool for both DNA and hemoglobin biomarkers that are associated with colorectal cancer (Imperiale, 2014). Positive test results from any of these three stool tests warrant further evaluation by colonoscopy.

During patient evaluation of pelvic complaints such as pain, a gynecologist not uncommonly performs gFOBT testing for diagnostic purposes on a single stool sample obtained during digital rectal examination. As noted, this single stool sample is not adequate colorectal cancer screening.

These guidelines are appropriate for those with average risk. High-risk factors include a personal history of colorectal cancer or adenomatous polyps, a first-degree relative with colon cancer or adenomas, chronic inflammatory bowel disease, prior cancer-related abdominopelvic radiation, or known or suspected hereditary syndrome such as hereditary nonpolyposis colon cancer (Lynch syndrome) or familial adenomatous polyposis (Smith, 2018a).

Lung Cancer

In the United States, this cancer is estimated to account for 13 percent of all new cancers diagnosed in women in 2019 (Siegel, 2019). It is now the leading cause of cancer-related death in both men and women. Cumulative exposure to tobacco smoke is an important risk factor for lung cancer; thus all smokers should be advised of tobacco-use risks and encouraged to stop. A list of potential aids is found on page 13.

Lung cancer screening with low-dose computed tomography (CT) scanning is recommended for individuals aged 55 to 74, who have a 30-pack-year or longer history, who actively smoke or quit within the past 15 years, and who lack life-limiting comorbidities (Tanoue, 2015). One remembers that pack-year determination is calculated by multiplying the number of packs smoked per day by the number of years the person has smoked. By convention, one pack contains 20 cigarettes. Although a common diagnostic test, chest radiography is not recommended as a lung cancer screening tool.

Skin Cancer

The incidence of skin cancers (melanoma and non-melanomas) has risen in the United States during the past three decades. In 2019, melanoma was expected to account for 1 percent of all cancer deaths in women (Siegel, 2019). Skin cancer risks

include fair complexion, use of indoor tanning beds, history of sunburns, family or personal history of skin cancer, and personal history of numerous moles (>100). The USPSTF (2016b) notes insufficient evidence to recommend whole body screening by physician or patient for skin cancer in the general adult population. It does advise clinicians to use the "ABCDE" system—asymmetry, border irregularity, color, diameter (>6 mm), and evolving over time—to evaluate skin lesions of concern and refer appropriately.

Lifestyle Changes

Smoking

Tobacco use is the leading preventable cause of disease, disability, and death in the United States and has been linked with certain cancers, cardiovascular disease, chronic lung diseases, and stroke (Barboza, 2016). Moreover, specific to women's health, smoking is linked to diminished fertility, pregnancy complications, and postoperative complications.

Almost 70 percent of adults who smoke daily are interested in quitting, and approximately half attempted to quit in the previous year. Guidelines from the USPSTF recommend that clinicians ask all patients about tobacco use, advise them to stop, and provide brief behavioral interventions (Siu, 2015a).

Behavioral interventions can be effective for any health-related lifestyle change. The five A's framework is a useful strategy for engaging patients and is tailored for smoking cessation in this example.

- Ask: every patient about tobacco use
- Advise: all users to quit
- Assess: her willingness to quit and decide if she is in a (1) precontemplation, (2) contemplation, (3) preparation, or (4) action phase. Her stage of readiness guides further discussion
- Assist: her attempts to quit (develop plan together)
- Arrange: for follow-up

Many behavioral interventions are available including local or community group programs, brief in-person behavioral counseling sessions, or even telephone counseling interventions. Patients can be referred to the National Cancer Institute's smoking cessation website: www.smokefree.gov or toll-free quit line: 1-800-QUIT-NOW. These supports provide free, evidence-based information, professional assistance, and in some cases free or discounted cessation medications.

Pharmacotherapy interventions approved by the FDA are bupropion SR, varenicline, and nicotine replacement therapy. These can be used in combination with behavioral interventions, and their use together can improve cessation rates. If appropriate, pharmacologic treatments to aid smoking cessation can be offered to all interested women and are listed in Table 1-6. Gynecologists who are proficient in the use of these therapies may prescribe. Referral is also appropriate (American College of Obstetricians and Gynecologists, 2014).

Exercise

Exercise is known to help prevent coronary artery disease, diabetes, osteoporosis, obesity, depression, insomnia, and multiple types of cancer (Piercy, 2018). Many of these associations result from the effects of exercise to help lower blood pressure, improve blood sugar control, reduce weight, and decrease low-density lipoprotein (LDL) cholesterol levels (Eckel, 2014).

In 2018, an estimated 10 percent of the premature mortality rate was associated with inadequate physical activity (Piercy, 2018). Recommendations from the U.S. Department of Health and Human Services (2018) include moderate-intensity activity for at least 150 minutes each week *or* vigorous-intensity activities for 75 minutes each week. When counseling patients on physical activity, the "talk test" is helpful to determine activity intensity. Generally, a woman doing moderate-intensity aerobic exercise can talk, but not sing, during the activity. A person doing vigorous-intensity activity generally cannot say more than a few words without pausing for a breath. Current evidence also supports raising routine daily physical activity levels, such as taking the stairs rather than the elevator (Piercy, 2018).

Research supports biweekly muscle-strengthening exercise that involves all the major muscle groups. Sedentary behavior, specifically time spent sitting, has also become of interest. Guidelines are beginning to address risks, but no recommendations are currently available.

Obesity

Associated Risks and Diagnosis

In 2016, 40 percent of women in the United States were obese, and this reflects a steady rise over the previous decade (Hales, 2018). Possible consequences include diabetes mellitus, nonalcoholic fatty liver disease, hypertension, hyperlipidemia, heart disease, osteoarthritis, and obstructive sleep apnea. Gynecologic issues related to obesity include abnormal menstruation, risks for endometrial neoplasia, and worsening polycystic ovary syndrome. Some hormonal contraceptives and emergency contraceptives may have lower efficacy in obese women. And, during pregnancy, obese women suffer higher rates of cesarean delivery, gestational diabetes, preeclampsia, and postpartum hemorrhage, among others (Hawkins, 2018). Even if not trained as weight management specialists, clinicians ideally screen for obesity, provide initial obesity evaluation and management, and refer as needed.

Screening is accomplished with calculation of body mass index (BMI). BMI, although not a direct measure of body fat content, is valuable in assessing the risk for weight-related complications. Several online calculators can be found. For adolescents (and children), BMI is adjusted for age and gender and calculated as a percentile. A BMI calculator for adolescents can be found at http://apps.nccd.cdc.gov/dnpabmi/.calculator.aspx. Table 1-7 reflects the definitions for underweight, overweight, and obesity for adolescents and adults. Adult obesity is further divided. Class 1 is a BMI 30 to 34.9 kg/m^2, class 2 is 35 to 39.9 kg/m^2, and class 3 is $\geq$40 kg/m^2. Class 3 obesity is often referred to as extreme obesity.

No standard single or panel laboratory test is indicated for an obese woman. Evaluation for comorbidities is tailored and factors her family and social histories. Blood pressure measurement, fasting lipid and glucose level screening, and thyroid function testing can all be considered for these patients during initial evaluation.

TABLE 1-6. Drugs Used for Smoking Cessation

Agent	Brand Name	Initial Dosing	Maintenance	Therapy Duration	Additional Considerations
Nicotine Replacement					
Patch[d]	Habitrol Nicoderm CQ	If >10 CPD: a 21-mg patch is reapplied daily wk 1–6 If <10 CPD: 14-mg patch for wk 1–6	14-mg patch is used wk 7–8	8–12 wk	
Gum[d]	Nicorette 2 mg 4 mg (if ≥25 CPD)	1 piece every 1–2 hr for wk 1–6 (maximum 24 pieces/d)	1 piece every 2–4 hr for wk 7–9	12 wk	Not chewed like regular gum, "chew and park" Not for those with extensive dental work
Lozenge[b]	Commit 2 mg 4 mg (if smokes <30 min after waking)	1 piece every 1–2 hr for wk 1–6 (maximum 20 pieces/d)	1 piece every 2–4 hr for wk 7–9	12 wk	Do not eat 15 min prior
Inhaler[d]	Nicotrol		6 (average use) to 16 cartridges puffed qd for 12 wk	12–24 wk	More expensive
Nasal spray[d]	Nicotrol		1 dose = 1 spray to each nostril per hr (maximum 5 doses/hr & 40/d)	12–24 wk	More expensive
Nicotine Agonists					
Varenicline[c]	Chantix	0.5 mg PO qd for 3 d, then 0.5 mg PO bid for next 4 d	1 mg PO bid	12 wk	Start 1 wk before quit date Avoid if history of suicide ideation or attempt; nausea is common
CNS Agents					
Bupropion[c]	Wellbutrin SR Zyban	1–2 wk prior to cessation: 150 mg PO qd for 3 d	150 mg PO bid	7–12 wk; may use for 6 mo.	Start 1 wk before quit date Avoid in patients with disordered eating, seizures, insomnia
Nortriptyline[a,d]		25 mg PO qd with gradual increase	75–100 mg PO qd	12 wk; may use for 6 mo.	Start at least 10 d before quit date
Clonidine[a,c]	Catapres-TTS	0.1-mg transdermal patch is changed weekly	0.1- to 0.2-mg transdermal patch weekly		Use limited by: dry mouth, sedation, postural hypotension

[a]Recommended as second-line agents by U.S. Department of Health and Human Services (Fiori, 2008).
[b]Has not been evaluated by the Food and Drug Administration (FDA) for pregnancy.
[c]Considered an FDA pregnancy category C drug.
[d]Considered an FDA pregnancy category D drug.
bid = twice daily; CNS = central nervous system; CPD = cigarettes per day; PO = orally; qd = daily.

TABLE 1-7. Definitions of Abnormal Weight for Adults and Adolescents Using Body Mass Index

Age Group	Underweight	Overweight	Obese	Extreme Obesity
Adolescent	<5th percentile for age	85th to 95th percentile for age	>95th percentile for age	
Adult	<18.5	25–29.9	Class I: 30–34.9 Class 2: 35–39.9	Class 3: ≥40

For a woman with an elevated BMI, a clinician assesses her readiness for change and thereby, provides appropriate guidance, support, or referral. In addition, questions regarding previous attempts at weight loss, social hurdles that impede diet and exercise change, and detrimental eating habits are discussed.

Treatment

Effective weight loss is best achieved by assisting patients in making healthier dietary, physical activity, and behavioral choices that will lead to a net negative caloric balance. The initial goal is to achieve a 5 to 10 percent weight loss over the initial 6 months of treatment (Jensen, 2014; National Heart, Lung, and Blood Institute, 2013). Caloric reduction is the most important component, whereas increased and sustained physical activity is particularly important in maintenance. Table 1-8 illustrates recommended guidelines to direct therapy for overweight or obese women. Several clinician and patient aids can be found in *Managing Overweight or Obesity in Adults*, available at: www.nhlbi.nih.gov/health-topics/managing-overweight-obesity-in-adults.

One of the most effective strategies encourages self-monitoring with a diet/activity calorie tracker. Many free versions are accessible either online or through smartphone applications. One sponsored by the U.S. Department of Agriculture is available at: www.choosemyplate.gov. Women are encouraged to follow a low-calorie diet that yields a 500 kcal/d deficit. This is an intake of 1200 to 1500 kcal/d (Jensen, 2014; National Heart, Lung, and Blood Institute, 2013). Specific daily calorie requirements by gender and age from the Institute of Medicine (2002) are listed at: www.health.gov/dietaryguidelines/2015/guidelines/appendix-2/.

In addition to diet and exercise, pharmacologic or surgical options may be advised for selected obese patients. Table 1-9 outlines specifics of weight loss medications. Orlistat (Xenical) is a reversible inhibitor of gastric and pancreatic lipases and blocks the digestion and absorption of approximately 30 percent of dietary fat (Kushner, 2018). This drug is approved for over-the-counter use at half the prescription strength (Allī). Because of its action, fatty stools and increased defecation are common side effects. Severe liver injury has been reported rarely, and labeling reflects this risk (Food and Drug Administration, 2010). Orlistat can reduce the absorption of fat-soluble vitamins, and patients are advised to take a daily oral multivitamin (Bray, 2013). Combination oral contraceptive action is not reduced by orlistat (Hartmann, 1996). This agent is not recommended during pregnancy but does not appear teratogenic (Källén, 2014). Orlistat is poorly absorbed, and thus theoretically is unlikely to reach significant breast milk levels (Briggs, 2017).

Four medications have been approved by the FDA since 2012: lorcaserin, phentermine-topiramate, naltrexone-bupropion, and liraglutide. Each suppresses appetite, and all are approved in conjunction with a reduced-calorie diet. These medications have met stringent FDA requirements, which included predetermined measures of effectiveness (5 percent mean weight loss after 1 year) and postmarketing long-term cardiovascular disease outcome trials (Kushner, 2018). The FDA recommends evaluation of weight loss after 3 to 4 months. This is based on observations that those who fail to lose weight early are less successful at 1 year. Choice of a specific agent is individualized and may be driven by comorbidities. For example, liraglutide might be more appropriate for a woman with diabetes (Khera, 2016). None of these are recommended during pregnancy or lactation.

Lorcaserin is a serotonin-receptor agonist used to suppress appetite. Naltrexone SR-bupropion SR (Contrave) is a combination of naltrexone, which is FDA approved for the treatment of alcohol dependence and opioid blockade, and bupropion, an antidepressant and smoking cessation aid.

Phentermine-topiramate (Qsymia) is a combination medication and is gradually titrated upward as needed. This drug has fetotoxicity potential and prescribing providers must participate in a Risk Evaluation and Mitigation Strategy (REMS) program. REMS are safety strategies mandated by the FDA to help manage known risks associated with a medicine yet still allow patients to have access to the benefits of a given drug.

Liraglutide is a glucagon-like peptide-1 receptor agonist delivered by self-administered subcutaneous injection. In studies, mean

TABLE 1-8. Treatment Recommendations According to BMI

Treatment	BMI 25–26.9	BMI 27–29.9	BMI 30–34.9	BMI 35–39.9	BMI ≥ 40
Diet, activity, behavioral therapy	WCM	WCM	+	+	+
Pharmacotherapy	—	WCM	+	+	+
Surgery	—	—	—	WCM	+

+ represents the use of indicated treatment regardless of comorbidities; BMI = body mass index; WCM = with comorbidities (type 2 DM, hypertension, obstructive sleep apnea, heart disease).

TABLE 1-9. Drugs Used for Weight Loss

Agent (Brand Name)	Oral[a] Daily Dosing	Mechanism	Placebo-subtracted Wt. Loss at 1 Year (%)	Adverse Effects
Gastrointestinal Fat Blocker				
Orlistat (Xenical, Alli)	120 mg three times	Blocks digestion and absorption of fat	n/a (6.2 kg avg. wt. loss)	Oily stools, fecal urgency or fecal incontinence
Appetite Suppressant				
Lorcaserin (Belviq)	10 mg twice	Serotonin receptor agonist	3.2	Headache, dizziness, increased heart rate or blood pressure
Phentermine/ topiramate (Qsymia)	3.75 mg/23 mg once for 2 wks, then 7.5 mg/46 mg once for 12 wks	Similar to amphetamines, appetite suppressed and satiety enhanced	8.4	Paraesthesia, dizziness, dysgeusia, insomnia, constipation, dry mouth
Naltrexone/bupropion (Contrave)	8 mg/90 mg (1 tab); titrate up by 1 tab each wk to reach 2 tabs twice daily	Opioid antagonist, antidepressant	4.0	Headache, GI side effects, insomnia, dry mouth
Liraglutide (Saxenda)	0.6 mg SC; titrate up by 0.6 mg SC each wk to reach 3 mg SC once daily	GLP-1 agonist, slows gastric emptying, decreases food intake	5.0	GI side effects

[a]Except for liraglutide.
GI = gastrointestinal; GLP-1 = glucagon-like peptide-1 receptor agonist; n/a = not available; SC = subcutaneously; Wt. = weight.

weight loss averages 6 to 8 percent (Davies, 2015; Pi-Sunyer, 2015). Liraglutide has an associated risk for pancreatitis. Because of this and an unclear risk of medullary thyroid carcinoma, the FDA requires participation in a REMS program. This drug is contraindicated for women with a family or personal history of medullary thyroid carcinoma or multiple endocrine neoplasia (Novo Nordisk, 2017).

Bariatric surgery is an important consideration for women with BMIs ≥40 or with BMIs ≥35 if other comorbid conditions are present (Garber, 2018). Of available laparoscopic procedures, three are more commonly performed and fall into two categories: restrictive (gastric banding, gastric sleeve) or malabsorptive (gastric bypass). Gastric banding places an adjustable plastic ring around the stomach to limit food intake. Sleeve gastrectomy removes 80 percent of the body of the stomach, creating a tubular sleeve appearance. Restrictive procedures produce modest weight loss and carry low surgical complication rates (Wolfe, 2016).

The Roux-en-Y gastric bypass creates a small stomach pouch that is connected directly to the jejunum to bypass the duodenum. This reduces calorie and nutrient absorption and can lead to substantial weight loss in individuals with morbid obesity. Gastric bypass has been linked with improvement in comorbid risk factors and decreased mortality rates. However, common long-term problems can include malabsorption of micronutrients such as iron, folate, calcium/vitamin D, and vitamin B_{12} (Abdeen, 2016).

Following bariatric surgery, patients are advised to delay pregnancy for 12 to 24 months (American College of Obstetricians and Gynecologists, 2017a). Rapid weight loss during this time poses theoretical risks for intrauterine fetal-growth restriction and nutritional deprivation. However, as weight is lost, fertility rates overall appear to improve, and risks for pregnancy rise (Merhi, 2009). Thus, effective contraception is needed. Most contraceptive methods appear to be as effective in women with elevated BMIs compared with normal-weight controls. However, the contraceptive patch (OrthoEvra) is less effective in those weighing more than 90 kg (Zieman, 2002). Specific to those with malabsorptive bariatric surgery types, oral contraception efficacy may be lower due to poor absorption (Curtis, 2016). Last, due to its risk for associated weight gain, depot medroxyprogesterone acetate (Depo-Provera) may be an unpopular choice in women trying to lose weight.

Cardiovascular Disease

This is the leading cause of death in the United States. In 2011 to 2014, 36 percent of women were affected by cardiovascular disease (CVD), and more than 410,000 women died from its complications (Benjamin, 2018). Stratification of CVD predispositions can identify vulnerable patients for management or referral (Table 1-10). Ideal goals for exercise, glucose and lipid levels, blood pressure, and smoking cessation are discussed in other sections of this chapter.

TABLE 1-10. Classification of Cardiovascular Disease (CVD) in Women

≥1 assigns high-risk status	Known CHD or CVD Peripheral arterial disease Abdominal aortic aneurysm End-stage renal disease Diabetes mellitus
≥1 assigns at-risk status	Smoking SBP ≥120 or DBP ≥80 mm Hg, or treated hypertension Total cholesterol ≥200 mg/dL, HDL <50 mg/dL, or treated dyslipidemia Obesity Poor diet Physical inactivity Family history of premature CVD Metabolic syndrome Autoimmune collagen-vascular disease Prior PIH or gestational DM

CHD = coronary heart disease; CVD = cardiovascular disease; DBP = diastolic blood pressure; DM = diabetes mellitus; HDL = high-density lipoprotein; PIH = pregnancy-induced hypertension; SBP = systolic blood pressure.
Abbreviated from Mosca, 2011.

Chronic Hypertension

Nearly 45 million American women are hypertensive, and this accounted for 33 percent of U.S. women from 2011 to 2014. The risk of hypertension rises with age and is higher for black women compared with those of other races (Benjamin, 2018). Chronic hypertension raises the risks for myocardial infarction, stroke, congestive heart failure, renal disease, and peripheral vascular disease. Moreover, chronic hypertension and its potential therapies may limit contraception choices for some women. Thus, gynecologists ideally are familiar with criteria used to diagnose hypertension. Although many may choose to refer patients for hypertension treatment, gynecologists should be aware of target goals and long-term risks associated with this disease.

For adult screening, the American Heart Association (2017) recommends blood pressure assessment starting at age 20 and repeated evaluation every 2 years if initially normal (Table 1-11). For patients with elevated pressures, assessment is at least annually.

With screening, blood pressures are best taken with a woman seated in a chair with the tested arm resting on a table, at the level of the heart. Ideally, the patient has been able to rest quietly for a few minutes prior to measurement and to have refrained from tobacco and caffeine use immediately prior to testing. An appropriately sized cuff is selected, and the cuff bladder should encircle at least 80 percent of the arm. Hypertension is diagnosed if readings are elevated on at least two separate office visits over one or more weeks.

With the diagnosis of chronic hypertension, assessment then follows for both modifiable and nonmodifiable CVD risk factors. Thus, routine laboratory tests recommended before initiating therapy include an electrocardiogram, urinalysis, blood glucose level, complete blood count, lipid profile, thyroid testing, and serum potassium and creatinine level measurement. A more extensive search for identifiable underlying causes is not generally indicated unless hypertension is not controlled with initial treatment (Table 1-12) (Whelton, 2018).

TABLE 1-11. Blood Pressure Categories in Women

BP Category	SBP (mm Hg)		DBP (mm Hg)
Normal	<120	and	<80
Elevated	120–129	and	<80
Stage 1 HTN	130–139	or	80–89
Stage 2 HTN	>140	or	>90

DBP = diastolic blood pressure; HTN = hypertension; SBP = systolic blood pressure.
Adapted from Whelton, 2018, with permission.

For treatment, lifestyle changes that mirror those for CVD are encouraged. However, if blood pressure is significantly elevated or resistant to lifestyle modification alone, then pharmacologic treatment may be needed to decrease long-term complications. Recommendations are shown in Table 1-13, and the target blood pressure with treatment is <130/80 mm Hg.

Stroke

This is the fifth leading cause of death in the United States, and in 2014, approximately 425,000 American women suffered a new or recurrent stroke (Benjamin, 2018). Gender-specific risk

TABLE 1-12. Identifiable Causes of Hypertension

Common	Renal parenchymal disease Renovascular disease Primary aldosteronism Obstructive sleep apnea Drug/alcohol Caffeine Smoking Alcohol NSAIDs Oral contraceptives Cyclosporine Decongestant/anorectics Herbal medicines (ephedra, ma huang) Cocaine and amphetamines Adrenal steroids
Uncommon	Pheochromocytoma Thyroid or parathyroid disease Cushing syndrome Coarctation of the aorta Congenital adrenal hyperplasia

NSAIDs = nonsteroidal antiinflammatory drugs.

TABLE 1-13. Initial Drug Therapy for Adults with Hypertension

Health Status	Treatment
General	Nonblack: thiazide-type diuretic, ACEI, ARB, or CCB Black: thiazide-type diuretic or CCB
Renal disease	ACEI or ARB

ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin-receptor blocker; BP = blood pressure; CCB = calcium-channel blocker.

factors for stroke in women include hypertension, atrial fibrillation, migraines with aura, and combination oral contraceptives. Low-dose aspirin use for the primary prevention of CVD is recommended only in women aged 50 to 59 years who have a ≥10 percent CVD risk (using the risk calculator outlined next) and are not at increased risk for bleeding (Bibbins-Domingo, 2016). No consensus describes the optimal dose or frequency of aspirin for stroke prevention. For women aged ≥60, the conversation balances risks of bleeding complications from aspirin against the benefits of stroke prevention for a given patient.

Dyslipidemia

Hypercholesterolemia

Serum cholesterol is known to be related to atherosclerotic CVD (ASCVD). The lipoprotein carriers are LDL, high-density lipoprotein (HDL), and very low-density lipoprotein (VLDL), and LDL is the dominant atherogenic form (Grundy, 2019). Other ASCVD risk factors include smoking, hypertension, dysglycemia, and advancing age. Using these, prediction models can estimate the risk of developing ASCVD. One tool is available through a smartphone application or accessible online at www.tools.acc.org/ASCVD-Risk-Estimator-Plus.

Preventively, adults aged ≥20 years ideally have lipids measured (either fasting or nonfasting) every 5 years. This profile includes measurement of total, LDL, and HDL cholesterol levels and triglyceride concentrations. If the initial nonfasting lipid profile reveals a triglycerides level ≥400 mg/dL, a fasting lipid is then performed (Grundy, 2019).

Lowering LDL levels is associated with reduced rates of ASCVD. Initial management usually begins with lifestyle and dietary changes. Lipid-lowering treatment for primary prevention is added for: (1) those with persisting LDL levels ≥190 mg/dL, (2) those aged 40 to 75 years with diabetes and LDL levels ≥70 mg/dL, and (3) those aged 40 to 75 years with an estimated 10-year risk of a cardiovascular event that is at least 7.5 percent (Stone, 2014). The risk estimator referenced above can help guide providers through recommendations and offer therapeutic advice.

Hypertriglyceridemia

Triglycerides are not directly atherogenic. Instead, they represent an important biomarker of CVD risk because of their association with proinflammatory, proatherogenic proteins found on all classes of the plasma lipoproteins. Because hypertriglyceridemia is associated with many other unique CVD risk factors, the benefit of lowering triglycerides directly remains uncertain (Jellinger, 2017). Triglycerides are particularly responsive to dietary adjustments, specifically restricting fat and carbohydrates. Omega-3 supplementation can also help lower levels. Medication therapy is reserved for those with triglyceride levels ≥500 mg/dL and is implemented to lower these levels to prevent pancreatitis.

Diabetes Mellitus

Diabetes is common, and approximately 14.9 million adult women in the United States are diabetic (Centers for Disease Control and Prevention, 2017a). The long-term consequences of this endocrine disorder are serious and include coronary heart disease, stroke, peripheral vascular disease, nephropathy, neuropathy, and retinopathy.

The USPSTF recommends screening of all adults aged 40 to 70 who are overweight or obese (Siu, 2015b). However, the American Diabetes Association (2019) recommends that screening be considered at 3-year intervals in those aged ≥45 or in those with a BMI ≥25 and one other risk factor (Table 1-14).

Diabetes and prediabetes may be diagnosed by various laboratory tests listed in Table 1-15. Measurement of plasma glucose concentration is performed on venous samples, and the aforementioned values are based on the use of such methods. Capillary blood glucose testing using a blood glucometer is an effective monitoring tool but is not recommended for diagnostic use.

For those diagnosed with diabetes, referral to an internist is usually indicated. Control of blood glucose levels reduces microvascular complications such as CVD, neuropathy, and nephropathy. Lifestyle optimization is essential for all patients with diabetes, and weight loss is recommended for overweight or obese patients with prediabetes or diabetes mellitus type 2. If lifestyle modification is insufficient for glucose control, many therapeutic options are available for patients in lieu of insulin. To lower diabetic morbidity, therapy goals for otherwise normal patients include hemoglobin A_{1c} levels below

TABLE 1-14. Adult Risk Factors for Diabetes

Age ≥45 years
Body mass index ≥25
Affected first-degree relative
Physical inactivity
Ethnicity: African-, Hispanic-, Native-, and Asian-Americans; Pacific Islanders
Prior prediabetes-range test values
Prior gestational diabetes mellitus
Hypertension (≥140/90 mm Hg or on therapy)
HDL cholesterol <35 mg/dL and/or triglyceride level >250 mg/dL
Polycystic ovary syndrome
Acanthosis nigricans
Cardiovascular disease

HDL = high-density lipoprotein.

TABLE 1-15. Diagnostic Criteria for Diabetes Mellitus

HbA_{1C} ≥6.5%
or
Fasting plasma glucose ≥126 mg/dL. Fasting is no caloric intake for at least 8 hr
or
2-hr plasma glucose ≥200 mg/dL during an OGTT
or
Symptoms of diabetes plus random plasma glucose concentration ≥200 mg/dL. Classic symptoms of diabetes include polyuria, polydipsia, and unexplained weight loss

Criteria for Increased Diabetes Risk (prediabetes)
Fasting plasma glucose: 100–125 mg/dL
or
2-hr plasma glucose during 75-g OGTT: 140–199 mg/dL
or
HbA_{1C}: 5.7–6.4%

FPG = fasting plasma glucose; HbA_{1c} = hemoglobin A_{1c}; OGTT = oral glucose tolerance test.

6.5 percent, blood pressure readings <130/80 mm Hg, LDL levels <100 mg/dL, triglyceride levels <150 mg/dL, weight control, and smoking cessation (Garber, 2018).

Patients with prediabetes, that is, impaired fasting glucose or impaired glucose tolerance, have an elevated risk for developing diabetes. To avert or delay this, management includes greater physical activity and weight loss, drugs such as metformin, nutritional counseling, and yearly diabetes screening. Medications, including weight loss medications discussed earlier, can be considered for those meeting criteria (p. 14).

Metabolic Syndrome

The metabolic syndrome refers to a clustering of specific CVD risk factors with the underlying pathophysiology thought to be related to insulin resistance (Grundy, 2005; Kahn, 2005). The components include insulin resistance, visceral obesity, hypertension, and low HDL but high triglyceride levels.

When the metabolic syndrome was initially identified, it served as a useful paradigm to draw attention to the fact that CVD risk factors often clustered in patients. Over time, as risk assessments and screening guidelines have advanced, the clinical usefulness of the metabolic syndrome has waned. If identified, management of the syndrome does not differ from management of individual risk factors and focuses on lifestyle modification discussed in earlier sections.

Thyroid Disease

The risk of thyroid disease accrues with age, and dysfunction is more common in women. Expert panels disagree regarding thyroid screening of the general population. Only the American Thyroid Association recommends that adults, especially women, be screened for thyroid dysfunction by measurement of a serum thyroid-stimulating hormone (TSH) concentration, beginning at age 35 and then again every 5 years. Other organizations' guidelines recommend screening in older women or those with risk factors for thyroid disease (LeFevre, 2015). People at higher risk include the elderly and those with prior head or neck radiation, thyroid surgery, autoimmune disease, type 1 diabetes mellitus, affected first-degree relative, pituitary disease, or lithium use.

Geriatric Screening

Women are now living longer, and the current life expectancy for women in the United States is 81 years (Arias, 2017). As a woman moves past menopause, many of her health care needs may not be gynecologic.

Of these, functional status is a patient's ability to perform both basic and complex activities for independent living. Basic activities are grooming and toileting, whereas bill paying and housekeeping are more complex instrumental activities of daily living (Katz, 1963; Lawton, 1969). Declines in functional status are linked to higher risks of hospitalization, institutionalization, and death. Identifying this status loss may permit early intervention.

Loss of cognitive function may present as short- and long-term memory loss, difficulty with problem solving, or inattention to personal hygiene. Although not expert in the diagnosis of cognitive problems, a gynecologist can perform initial screening that either reassures or prompts more formal evaluation by a geriatrician or neurologist. During Medicare Annual Wellness Visits (AWV), cognitive evaluation is a mandatory component.

For screening purposes, the test choice ideally matches the level of concern. For patients in whom cognitive impairment is thought unlikely, the clock-drawing test can provide reassurance. For this test, a person is asked to draw a clock with "the hands set to 10 past 11." A correct clock has numbers 1 through 12 labeled correctly in a clockwise fashion, with two arms (of any length) pointing at the correct numbers for the time requested. Any error or refusal to complete the clock is considered abnormal.

The Mini-Cog Test can also screen for mild cognitive impairment in the primary care setting (Janssen, 2017). The Mini-Cog test requires approximately 3 minutes to administer and begins by giving the patient three items to remember early in the interview. Later in discussion, she is asked to recall those three items. For a Mini-Cog Test result suggestive of dementia, referral to an internist, geriatrician, or neurologist is indicated.

Last, in those for whom impairment is a possibility, the Montreal cognitive assessment (MOCA) can be used to screen (Nasreddine, 2005). This tool assesses different cognitive domains and may characterize a cognitive impairment more precisely than the clock or Mini-Cog tests.

Mental Health

Depression

For women of all ages, mood disorders are pervasive and account for significant morbidity and mortality. These are discussed in detail in Chapter 14 (p. 302) and should be screened for

TABLE 1-16. Insomnia Medications Approved by the U.S. Food and Drug Administration

Medication: Brand	Dose
Benzodiazepines	
Temazepam: Restoril	7.5–30 mg
Estazolam: ProSom	0.5–2 mg
Triazolam: Halcion	0.125–0.25 mg
Flurazepam: Dalmane	15–30 mg
Quazepam: Doral	7.5–15 mg
Benzodiazepine-receptor Agonists	
Eszopiclone: Lunesta	1–3 mg
Zolpidem: Ambien,	5–10 mg
Ambien CR[a]	6.25–12.5 mg
Intermezzo[b]	1.75 mg
Zaleplon: Sonata	5–20 mg
Melatonin-receptor Agonist	
Ramelteon: Rozerem	8 mg
Melatonin-receptor Agonist	
Doxepin: Silenor	3–6 mg
Dual Orexin-receptor Antagonist	
Suvorexant: Belsomra	5–20 mg

[a]Extended release form.
[b]Indicated for middle-of-night awakening.

during routine health visits. For depression, the Personal Health Questionnaire-2 (PHQ2) is a simple, two-question screening tool (Kroenke, 2003). Questions are: "During the past 2 weeks, have you felt down, depressed, or hopeless?" and "Have you felt little interest or pleasure in doing things?" A positive screening result should prompt evaluation for depression (Chap. 14, p. 303).

Insomnia

Insomnia is common. It is defined as trouble initiating or maintaining sleep, despite adequate opportunity and circumstances for sleep, and is associated with daytime consequences (Sateia, 2017). Insomnia may be primary or may be secondary to other conditions such as depression, restless leg syndrome, stimulant use, menopause symptoms, and sleep apnea (Baker, 2018).

Insomnia is typically treated first with cognitive-behavioral therapy (CBT) (Sateia, 2017). Cognitive therapy is aimed at changing patients' beliefs and attitudes regarding sleep. Components include control of sleep timing and duration, attempts to improve the bedroom environment, or relaxation or biofeedback techniques. Medications may be added to aid sleep, and many work via benzodiazepine receptors. Table 1-16 lists medications FDA-approved for insomnia. Although lacking an FDA indication for insomnia, commonly prescribed agents are benzodiazepines, sedating antidepressants, sedating antipsychotics, and anticonvulsants (Buysse, 2013). Shared decision-making is ideally used for insomnia pharmacotherapy as evidence is insufficient to support use of medications, both FDA-approved and off label, for chronic insomnia.

Preconceptional Counseling

Value lies in counseling women before conception so that each pregnancy is planned with the goal to achieve the best maternal and fetal outcomes. With this in mind, topics found in Table 1-17 are ideally addressed.

TABLE 1-17. Preconceptional Counseling Topics

Topic	Recommendations
Abnormal weight	Calculate BMI yearly. *BMI ≥25 kg/m²:* Counsel on diet. Test for DM and metabolic syndrome if indicated *BMI ≤18.5 kg/m²:* Assess for eating disorder
Exercise	Uncomplicated pregnancy, engage in exercise before, during, and after
Substance abuse	Discuss perinatal effects of opioids, cocaine, methamphetamine, alcohol, smoking. Offer cessation options
Heart disease	Optimize function. Discuss warfarin, ACE inhibitor, and ARB teratogenicity, and if possible, switch agents prior to conception. Offer genetic counseling to women with congenital cardiac anomalies.
Hypertension	*Long-standing HTN*: assess ventricular hypertrophy, retinopathy, and renal disease. Discuss ACE inhibitor and ARB teratogenicity, and switch agents prior to conception
Asthma	Optimize function. Provide appropriate influenza and pneumococcal vaccines
Thrombophilia	Question for personal or family history of thrombotic events or recurrent poor pregnancy outcomes. If found, screen those contemplating pregnancy. Offer genetic counseling to those with known thrombophilia. Discuss warfarin teratogenicity, and switch agent, if possible, prior to conception
Renal disease	Optimize HTN. Discuss ACE inhibitor and ARB teratogenicity, and switch agents prior to conception
GI disease	*Inflammatory bowel disease:* Counsel on subfertility and risks of adverse pregnancy outcomes. Discuss MTX and mycophenolate mofetil, and switch agents, if possible, prior to conception

(Continued)

TABLE 1-17. Preconceptional Counseling Topics *(Continued)*

Topic	Recommendations
Liver disease	*Hepatitis B:* Vaccinate all high-risk women prior to conception (Table 1-1, p. 4). Counsel chronic carriers on transmission prevention to partners and fetus *Hepatitis C*: Screen as indicated in Table 1-1, p. 4. Counsel affected women on risks of perinatal transmission. Refer for antiviral treatment, discuss risks of treatment during pregnancy
Blood disorders	*Iron-deficiency anemia:* Offer iron supplementation *Sickle-cell disease:* Screen all black women. Test partner as indicated *Thalassemias:* Screen all women *von Willebrand disease:* Counsel regarding postpartum hemorrhage risk
Diabetes	Optimize glucose control, especially periconceptionally due to known teratogenicity. Evaluate for retinopathy, nephropathy, HTN
Thyroid disease	Screen those with thyroid disease symptoms. Ensure iodine-sufficient diet. Treat overt hyper- or hypothyroidism prior to conception
CT disease	*RA and other inflammatory arthritides*: Counsel on flare risk after pregnancy. Discuss MTX and leflunomide teratogenicity, and switch agents prior to conception *SLE*: Optimize disease. Discuss mycophenolate mofetil and cyclophosphamide teratogenicity, and switch agents, if possible, prior to conception
Neurologic disorder	*Seizure disorder:* Optimize control using monotherapy, if possible
Psychiatric disorder	*Depression:* Screen for symptoms. If affected, counsel on risks of treatment and of untreated illness and high risk of peripartum exacerbation
Skin disease	Discuss isotretinoin and etretinate teratogenicity, and switch agents prior to conception
Cancer	*Current:* Counsel on fertility preservation options prior to cancer therapy and on decreased fertility following certain agents. Offer genetic counseling to those with mutation-linked cancers. Evaluate cardiac function in those given cardiotoxic agents. Discuss SERM teratogenicity, and switch agents prior to conception. Discuss possible teratogenic effects of chemotherapy if continued during pregnancy *Prior:* Update mammography for those given childhood chest radiotherapy. Discuss pregnancy risks of childhood abdominopelvic radiation (Chap. 28, p. 616)
Infectious diseases	*Influenza:* Vaccinate all women prior to flu season *Malaria:* Avoid travel to endemic areas; chemoprophylaxis during conception *Rubella* or *Varicella:* Assess immunity, vaccinate as needed, and offer effective BCM during next 3 mos. *Tuberculosis:* Screen high-risk women and treat *Tetanus:* Update vaccination, as needed *Zika:* Abstain or use condoms after possible exposure for males (3 mos.) or females (2 mos.)
STDs	*Gonorrhea, syphilis, chlamydial infection:* Screen per Table 1-1 (p. 4) and treat as indicated *HIV:* For infection, treat prior to conception to decrease perinatal transmission. For discordant couple prevention, discuss PrEP if male partner viral load is not suppressed or is unknown (Chap. 3, p. 87). *HPV:* Screen per guidelines (Chap. 29, p. 630). Vaccinate as indicated *HSV:* Provide serological screening to asymptomatic women with affected partners. Counsel affected women on perinatal transmission risks and prophylaxis during the third trimester and labor

ACE = angiotensin-converting enzyme; ARB = angiotensin-receptor blocker; BMI = body mass index; CT = connective tissue; DM = diabetes mellitus; GI = gastrointestinal; HIV = human immunodeficiency virus; HPV = human papillomavirus; HSV = herpes simplex virus; HTN = hypertension; MTX = methotrexate; PrEP = preexposure prophylaxis; RA = rheumatoid arthritis; SERM = selective estrogen-receptor modulator; SLE = systemic lupus erythematosus; STD = sexually transmitted disease.

Compiled from American College of Obstetricians and Gynecologist, 2017c,e, 2019; Centers for Disease Control and Prevention, 2017b, 2018b; Jack, 2008; Kim, 2018.

VIOLENCE AGAINST WOMEN

Sexual Violence

Sexual violence is a broad term that includes rape, unwanted genital touching, intimidation to acquiesce to sex, and forced viewing of or involvement in pornography (Basile, 2014). *Rape* is a legal term and in the United States refers to penetration or attempted penetration of a body orifice without consent and with force or the threat of force or incapacity (Federal Bureau of Investigation, 2013). A few states mandate clinicians to report rape of a competent adult to a law enforcement agency, and one list is provided by the National District Attorney Association (2016). In other states, law enforcement is involved at the patient's request. For the elderly and children, reporting is mandatory.

Large population-based surveys indicate a lifetime prevalence for sexual violence of 19 percent among women (Smith, 2017). Certain populations are at greater risk and include the disabled; lesbian, bisexual, or transgender individuals; college students; and persons younger than 24 years (Basile, 2016; Fedina, 2018; Taylor, 2016; Walters, 2013).

Examination and Documentation

Initial evaluation of a sexual violence victim concentrates on identifying serious injuries that may be genital or often nongenital (Riggs, 2000; Zilkens, 2017a). Once life-threatening injuries are excluded, a systematic, thorough, and compassionate approach to obtaining a history and collecting evidence is essential for appropriate treatment of the victim and for future prosecution of her assailant (American College of Obstetricians and Gynecologists, 2016a).

Valid evidence may be collected from 3 to 7 days after sexual assault, and timing varies by jurisdiction. Immediate examination enhances the opportunity to obtain valuable physical evidence. Consent is obtained prior to examination and evidence collection and is essential for entry of evidence in a court. Most states have standardized kits for collection, and completed kits are stored in a locked site to ensure that legal evidence procedures are maintained. Evidence collection does not commit a victim to pressing criminal charges. A patient is also counseled that she may terminate an examination if it is too emotionally or physically painful.

Evidence gathering follows the steps outlined in Table 1-18 (Department of Justice, 2013). In approximately 25 percent of female rape victims, evidence of anogenital injury is detected (Larsen, 2015; Zilkens, 2017b). Frequent injury types include tears, ecchymosis, abrasions, redness, and swelling (TEARS) (Slaughter, 1997). Common sites include the posterior fourchette, inner labial minora, and hymen. Colposcopy is used if available, and this technique raises detection rates of more subtle injuries (Astrup, 2012; Lenahan, 1998).

Treatment

Pregnancy Prevention. Medication prophylaxis to prevent pregnancy following sexual assault can be provided to at-risk women with reproductive organs. Among reproductive-aged victims, the risk of rape-related pregnancy approximates 5 percent per rape (Holmes, 1996). Emergency contraception can be administered for up to 120 hours after rape but is most effective in the first 24 hours (Table 5-10, p. 131).

A negative pregnancy test to exclude a preexisting pregnancy is confirmed before administering emergency contraception. This is especially true for ulipristal (Ella), a progesterone antagonist,

TABLE 1-18. Important Elements of Examination and Evidence Collection Following Sexual Assault

Physical Examination
Perform full body examination; record injuries on body diagram
Inspect vulva, inner thighs, anus, and buttock; add colposcopic inspection if available; record injuries on anogenital diagram
Inspect vagina and cervix; add colposcopic inspection if available
Evidence Collection
Collect clothing and associated debris as a patient disrobes onto cloth sheet
Comb head hair; trim any matted hair that contains secretions. Cut head hairs from patient for comparison[a]
Comb pubic hair; trim any matted hair that contains secretions. Cut pubic hair from patient for comparison[a]
Scrape debris from beneath fingernails if the victim scratched assailant's skin or clothing
Collect swabs from vagina, mouth, and anus if penetrated during assault
Wipe sites of possible secretion exposure with saline moistened swab; save and label swab. Common examples include inner labia minora, perineum, breasts, or neck
Smear each swab onto individual microscope slide; save and label slide[a]
Laboratory Testing
Obtain toxicology testing if examination suggests or if patient states drugging
Collect patient's blood or saliva to serve as DNA reference
Obtain swabs and blood for STD testing and prophylaxis as detailed in Table 1-19.

[a]Collection practices varies by jurisdiction.
STD = sexually transmitted disease.
From Department of Justice, 2013.

TABLE 1-19. Pregnancy and Sexually Transmitted Disease Prophylaxis Following Sexual Assault

Testing

Pregnancy test (urine or serum); repeat at 4–6 wks
Serum testing for hepatitis B surface antigen, surface antibody, and core antibody
Serum testing for HIV and syphilis; repeat at 4–6 wks and 3 mos.
NAAT for *Neisseria gonorrhoeae* and *Chlamydia trachomatis* from each penetrated site
NAAT for *Trichomonas vaginalis* from vagina
Microscopic evaluation of saline wet mount of vaginal discharge
If HIV PEP[a] is planned, add HCV antibody. Draw serum LFTs and serum creatinine level[b] and repeat both at 4–6 wks

Treatment

Levonorgestrel, ulipristal, or Yuzpe method for candidates: all dosages in Table 5-10 (p. 131)
Ceftriaxone 250 mg intramuscularly, single dose[c]
Azithromycin 1 g orally, single dose[c]
Metronidazole 2 g orally, single dose[c]
Hepatitis B vaccination if not previously vaccinated (Table 1-1, p. 4)
HPV vaccination if not previously vaccinated (Table 1-1, p. 4)
If exposure ≤72 hrs ago, HIV PEP offered to suitable candidates (see text). Regimen given daily for 28 days:
Tenofovir disoproxil fumarate/emtricitabine (Truvada[d]) once daily ***plus*** raltegravir 400 mg (Isentress) twice daily

[a]Questions regarding PEP can be directed to the Clinician Consultation Center at 1-888-448-4911.
[b]With renal dysfunction and creatinine clearance <60 mL/min, tenofovir disoproxil fumarate/emtricitabine is not recommended, and consultation for other regimens is suggested.
[c]Antibiotic alternatives for exposure to *N gonorrhoeae*, *C trachomatis*, and *T vaginalis* are found in Chapter 3 (p. 56).
[d]Caution in those with chronic hepatitis B.
CBC = complete blood count; HCV = hepatitis C virus; HIV = human immunodeficiency virus; HPV = human papillomavirus; LFTs = liver function tests; NAAT = nucleic acid amplification test; PEP = postexposure prophylaxis.
Compiled from Centers for Disease Control and Prevention, 2015, 2016, 2018a; Seña, 2015.

because of fetal loss risks if used in the first trimester. With estrogen/progestin combinations, nausea and vomiting is a potential side effect, and an antiemetic can be prescribed 30 minutes prior to hormone administration (Table 42-9, p. 916).

Patients are informed that their next menses may be delayed following this prophylaxis. Although current regimens are 74 to 89 percent effective, pregnancy testing is repeated at the follow-up visit at 4 to 6 weeks (Task Force on Postovulatory Methods of Fertility Regulation, 1998; Trussell, 1996; Yuzpe, 1982).

Sexually Transmitted Disease Prevention. The risk of acquiring an STD after rape has been estimated but varies by circumstances. The risk for trichomoniasis approximates 12 percent; gonorrhea, 4 percent to 12 percent; chlamydial infection, 2 to 14 percent; and syphilis, 5 percent (Jenny, 1990; Schwarcz, 1990). General recommendations for STD screening and for prophylaxis are listed in Table 1-19.

Of these, postexposure prophylaxis (PEP) for human immunodeficiency virus (HIV) is recommended in selected cases following sexual assault. These include rape by an assailant known to be HIV infected or by a person of unknown HIV status if exposure represents a substantial risk for acquisition (Seña, 2015). With known HIV infection, the estimated acquisition risk is 1 per 10,000 receptive penile-vaginal exposures and 138 per 10,000 receptive penile-anal exposures (Patel, 2014). HIV transmission associated with receptive oral intercourse is rare.

For potential HIV PEP candidates, the risks and side effects of the medications and need for close monitoring are discussed. Nausea is a common side effect. Thus, a prescription for an antiemetic such as promethazine, to be used as needed, is commonly provided. Importantly, if an initial HIV test result in the victim is positive, PEP is stopped and replaced with appropriate long-term antiretroviral therapy.

Because of the emotional intensity of the experience, a woman may not recall all the information provided, and thus written instructions are helpful. Survivors are referred to local rape crisis centers and encouraged to visit within 1 to 2 days. Sexual assault victims receive subsequent medical reevaluation 1 to 2 weeks later. After 4 to 6 weeks, if initial test results were negative for pregnancy, HIV, or syphilis, these are repeated (see Table 1-19). These later tests capture conditions that may have been undetectable during initial screening. HIV is again screened for at 3 months (Centers for Disease Control and Prevention, 2016). Additional hepatitis B and HPV vaccines are provided as dictated by vaccination schedule (p. 9).

Psychological Response to Sexual Assault. Survivors of sexual assault may display an array of reactions that frequently include anxiety, agitation, crying, or a quiet, removed affect. Burgess and Holmstrom (1974) first characterized the "rape trauma syndrome" and its two response phases. The first acute disorganization phase lasts several weeks and is followed by a reorganization phase, lasting several weeks to years. Acutely,

shock and disbelief, fear, shame, self-blame, humiliation, anger, isolation, grief, somatic manifestations, and loss of control are common. During the reorganization phase, feelings of vulnerability, despair, guilt, and shame may continue. Longitudinal data indicate that sexual assault survivors are at increased lifetime risk for posttraumatic stress disorder (PTSD), mood disorders, somatic symptoms, and suicide contemplation or attempt (Linden, 2011; Smith, 2017). Health care providers ideally enlist the input of social workers or rape crisis counselors to help evaluate the patient's immediate and future emotional and safety needs.

Child Sexual Abuse

Definitions of sexual abuse in the child mirror those in the adult (Basile, 2014; Federal Bureau of Investigation, 2013). From one large U.S. survey, the estimated overall prevalence of youth sexual violence for females is 8 percent (Merrick, 2018). Thus, indicators that should prompt evaluation include: (1) statements by the minor or family of abuse, (2) genital or anal injury without concordant history of unintentional trauma, (3) identification of semen or pregnancy, or (4) STD diagnosis beyond the incubation period of vertical (natal mother-to-child) transmission. Health care providers in the United States are mandated to report suspected child maltreatment to an appropriate agency, such as child protective services or a law enforcement agency (Child Welfare Information Gateway, 2016).

Determining whether anogenital findings in children are normal variants or indicative of assault can be difficult, and these have been categorized according to the likelihood of associated sexual abuse. An exhaustive list of normal and indeterminate signs has been compiled by Adams and associates (2018), and those considered diagnostic are listed in Table 1-20. A provider completing the examination should have formal training in the evaluation of suspected child sexual abuse. Importantly, acute injuries associated with child sexual abuse heal and resolve rapidly. Thus, examination is completed as soon as assault is suspected (Smith, 2018b). As signs may be subtle, a careful history and full examination are carried out with the aid of photodocumentation, preferably using a colposcope.

The prevalence of STDs in child victims of sexual abuse is low (Girardet, 2009a). Thus, the decision to obtain specimens from a child is individualized. Situations that typically prompt child testing include: (1) signs or complaints of genital penetration or of an STD, (2) one STD already diagnosed, (3) suspected assailant with a high risk for STDs, (4) another household member with an STD, (5) abuse by a stranger, or (6) community with a high STD rate (Centers for Disease Control and Prevention, 2015).

Recommended testing includes a nucleic acid amplification test (NAAT) for *Neisseria gonorrhoeae* and *C trachomatis* from urine or vagina. Culture and wet mount evaluation of a vaginal swab specimen are preferred for *Trichomonas vaginalis* infection (Adams, 2018). Decisions regarding serologic testing for *Treponema pallidum*, HIV, and hepatitis B virus are individualized.

Although STDs found beyond the neonatal period raise suspicious for sexual abuse, this has exceptions. Perinatal transmission of *N gonorrhoeae*, *C trachomatis,* HIV, *T pallidum*, and *T vaginalis* is possible. Outside this circumstance, these infections suggest sexual contact. In contrast, herpes simplex virus, human papillomavirus, and *Molluscum contagiosum* infections can be transmitted nonsexually (Adams, 2018). Most hepatitis B virus infections in children result from household exposure to those chronically infected with the virus.

Routine STD prophylaxis for children who have been sexually abused is generally not recommended due to lower rates of infection and a greater guarantee of scheduled follow-up for test results. However, if the clinical setting dictates or if test results are found to be positive for infection, antibiotics are provided. Rates of HIV transmission following sexual abuse are also very low in children (Girardet, 2009b). However, HIV PEP is well tolerated by children and can be offered based on

TABLE 1-20. Findings of Sexual Contact in Suspected Child Sexual Abuse

Acute genital laceration or extensive bruising[a]
Acute perianal laceration
Hymeneal petechiae or abrasions
Perianal or fourchette scarring[a]
Healed hymeneal cleft(s) below 3 or 9 o'clock locations that extends to hymeneal base.
Signs of female genital mutilation (see Table 1-21)
Bite marks
Torn oral frenulum
Positive testing for *Neisseria gonorrhoeae, Chlamydia trachomatis, HIV, Treponema pallidum*[b]
Pregnancy
Sperm identified in specimens taken directly from a child's body

[a]If other medical conditions such as Crohn disease, coagulopathy, accident, or labial adhesion not explanatory for findings.
[b]If perinatal transmission, transmission from blood products, and needle contamination have been excluded.
HIV = human immunodeficiency virus.
Compiled from Adams, 2007, 2018; Chiesa, 2017.

the clinical setting and within the first 72 hours. The CDC (2015) recommends consulting professionals who specialize in care of HIV-infected children.

Elder Abuse

This is an intentional act or failure to act by a trusted individual that causes or creates a risk of harm to an older adult. Elder abuse may include neglect or physical, psychologic, sexual, or financial abuse (Hall, 2016). Approximately 10 percent of the elderly are mistreated each year (Acierno, 2010). Identified risk factors are caregiver stress, patient cognitive impairment, need for assistance with daily life activities, conflicted family relationships, and poor social support (Hoover, 2014). Similar to other forms of violence, elderly victims can suffer subsequent depression, anxiety, PTSD, and poor self-reported health (Acierno, 2017; Wong, 2017).

Signs that can be associated with abuse are decubitus ulcers, poor hygiene, poor adherence to medication regimens, or signs of trauma, sexual assault, dehydration, or malnutrition. Psychologic clues include depression, anxiety, cowering, vague somatic complaints, and social withdrawal (Lachs, 2015). Physicians are mandated in most states to report suspicion of elder abuse, and each state's "mandatory reporting" requirements are posted by the Department of Justice (2016). Sexual and physical assault will involve local law enforcement. Reports of other abuse forms are typically filed with the Adult Protective Services agency of the given state (National Adult Protective Services, 2018).

Intimate Partner Violence

Intimate-partner violence (IPV) refers to harm inflicted by one intimate partner on the other, with the intent of causing pain or controlling the other's behavior. *Domestic violence, violence against women,* and *gender-based violence* are older synonyms. *Honor-based violence (HBV)* is a subcategory in which male family members act against female members to maintain family honor in the community.

IPV takes various forms and includes sexual violence, physical violence, stalking, and psychological aggression or coercion (Breiding, 2015). Most victims have been assaulted more than once and often over the course of years. In the United States, nearly one third of women experienced physical violence by an intimate partner in their lifetime, one quarter suffered severe violence, and 16 percent have described contact sexual violence (Smith, 2017). Rates of IPV are higher in adolescents and those who witnessed violence as a child (Jung, 2019; Kann, 2018; Smith, 2017). Pregnant women may also be victims, and homicide is the leading cause of death during pregnancy (Palladino, 2011; Shadigian, 2005).

Diagnosis

Numerous health complications follow IPV. Short-term sequelae include acute injuries, pregnancy, and STD acquisition (Smith, 2017). Gravely, in the United States in 2015, 45 percent of female homicides were IPV-related (Jack, 2018). Long term, mental health consequences such as PTSD, anxiety, depression, suicide attempt, and substance abuse are prominent (Iverson, 2013). Chronic somatic complaints often focus on gastrointestinal dysfunction, genitourinary pain, and other chronic pain (Campbell, 2002; Centers for Disease Control and Prevention, 2008). Effects on sexual function are discussed in Chapter 14 (p. 313).

Women who have been assaulted are far more likely to seek help from their medical provider. Although some clinicians may feel awkward asking patients, researchers agree that the single most important thing a physician can do for a battered woman is to ask about violence (American College of Obstetricians and Gynecologists, 2012). Additionally, symptoms or behaviors that may be associated with victimization are investigated. Numerous formal assessment tools are available from the CDC (Basile, 2007).

Management

If a patient discloses IPV, a clinician should validate and normalize a patient's perspective. Patients are counseled that many women have assault experiences, that most are afraid to confide these, that memories of the experience can be painful, and that a fear of future assaults is a reasonable fear. Following a patient's disclosure, a provider expresses concern for the woman's health and safety and conveys a willingness to discuss relationship issues at any time. Moreover, information describing community resources is offered. The National Domestic Violence Hotline (1-800-799-SAFE (7233)) is a nonprofit telephone referral service with access to more than 5000 shelters nationally.

Battery is a crime, yet few states specifically require mandatory reporting of IPV. Accordingly, each clinician should know their state laws, and one list has been compiled by Durborow and associates (2013). In addition, providers ideally thoroughly document physical findings of violence. Such data may be required if criminal charges are pursued.

Female Genital Mutilation

This practice refers to medically unnecessary vulvar modification. In the United States, it is a federal crime to perform unnecessary genital surgery on a girl younger than 18 years or to send or attempt to send her outside the country so it can be performed. That said, female genital mutilation (FGM) is practiced in countries within Africa, the Middle East, and Asia. As many as 200 million women worldwide have undergone one of these procedures, and approximately 513,000 girls in the United States were at risk for this practice in 2012 (Goldberg, 2016; UNICEF, 2016). Cultural sensitivity is imperative, because many women may be offended by the suggestion that they have been assaulted or mutilated (American College of Obstetricians and Gynecologists, 2014). The World Health Organization (2008) classifies genital mutilations into four types (Table 1-21).

Long-term complications from surgery and its associated scarring include infertility, chronic vulvar pain, diminished sexual quality of life, propensity for urogenital infection, difficulty passing menstrual blood, and formation of a vulvar neuroma, epidermoid cyst, or keloid (Almroth, 2005; Andersson, 2012; World Health Organization, 2018). Moreover, cervical cancer screening may not be possible.

In general, women with significant symptoms following type III procedures are candidates for *defibulation*. This procedure sharply divides scar tissue at the midline to reopen the

TABLE 1-21. World Health Organization Classification of Female Genital Mutilation

Type Ia	Prepuce (clitoral hood) removal
Ib	Prepuce, clitoris removal
Type IIa	Labia minora removal
IIb	Labia minora, clitoris removal
IIc	Labia majora and minora, clitoris removal
Type IIIa	Removal and surgical apposition of labia minora ± clitoris removal
IIIb	Removal and surgical apposition of labia majora ± clitoris removal
Type IV	Pricking, piercing, incising, scraping, cautery, or other genital injury

vulva (Chap. 43, p. 992). Following surgery, sexual functioning is typically improved (Krause, 2011; Nour, 2006). Also, gravidas with type III FGM may benefit from lower rates of both cesarean delivery and higher-order perineal laceration following defibulation (Berg, 2018).

In contrast, results of clitoral reconstruction are mixed, and outcome data are limited. Surgery provides a visible clitoris in approximately 75 percent of cases. Average improvement scores for desire, dyspareunia, pleasure, and sexual frequency range from 40 to 60 percent. However, worsening of these last four parameters is seen in 2 to 20 percent of women (Berg, 2018). During presurgical evaluation for clitoral reconstruction, patients may be best served by a team that includes gynecologic, psychological, and sexual counseling to discuss treatment options (De Schrijver, 2016).

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CHAPTER 2

Techniques Used for Imaging in Gynecology

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Several technical advances in recent decades currently allow superb imaging of female pelvic structures. As a result, use of sonography in gynecology now equals that in obstetrics. Enhancements to traditional sonography continue to fill important clinical gaps. For example, technical refinements now allow three-dimensional (3-D) imaging to rival the roles of computed tomography (CT) and magnetic resonance (MR) imaging for many conditions. In addition, application of MR imaging now includes MR-guided high-intensity focused-ultrasound therapy, used for uterine leiomyomas.

SONOGRAPHY

Physics

In sonography, the picture displayed on a screen is produced by sound waves reflected back from an imaged structure. To begin, alternating current is applied to a transducer containing piezoelectric crystals, which convert electric energy to high-frequency sound waves. A water-soluble gel applied to the skin acts as a coupling agent. Sound waves then pass through tissue layers, encounter an interface between tissues of different densities, and are reflected back to the transducer. Converted back into electric energy, they are displayed on a screen.

Dense material, such as bone, or a synthetic material, such as an intrauterine device (IUD), produces high-velocity reflected waves, also termed *echoes*, which are displayed on a screen as white. These are described as *echogenic*. Conversely, fluid is *anechoic,* generates few reflected waves, and appears black on a screen. Middle-density tissues variably reflect waves to create various shades of gray, and images are described as *hypoechoic* or *hyperechoic* relative to tissues immediately adjacent to them. Images are generated so quickly—50 to 100 frames per second—that the picture on the screen appears to move in real time.

Sound reflection is greatest when the difference between the acoustic impedance of two structures is large. This explains why cysts are so well demonstrated with sonography. Strong echoes are produced from the cyst walls, but no echoes arise from the cyst fluid. As more sound traverses the cyst, more echoes are received from the area behind the cyst, a feature known as *through transmission* or *acoustic enhancement* (Fig. 2-1). In contrast, with a dense structure, the sound passing through it is diminished, which creates a band of reduced echoes beyond it, known as *acoustic shadowing* (Fig. 2-2).

The frequency of emitted ultrasound waves is expressed in megahertz (MHz), which means million vibrations per second. The frequency is inversely related to its wavelength. Thus, transducers emitting pulses of high frequency generate waves of shorter length, which result in higher spatial resolution or sharpness between interfaces but achieve less penetration. Curved transducers provide a wider field of view but often generate lower-frequency waves than linear transducers. Higher-frequency probes (10 to 15 MHz) are used to image superficial structures, such as breast masses or lost etonogestrel implants in the upper arm. Lower frequencies are required to image deeper structures. As such, transabdominal transducers are typically in the

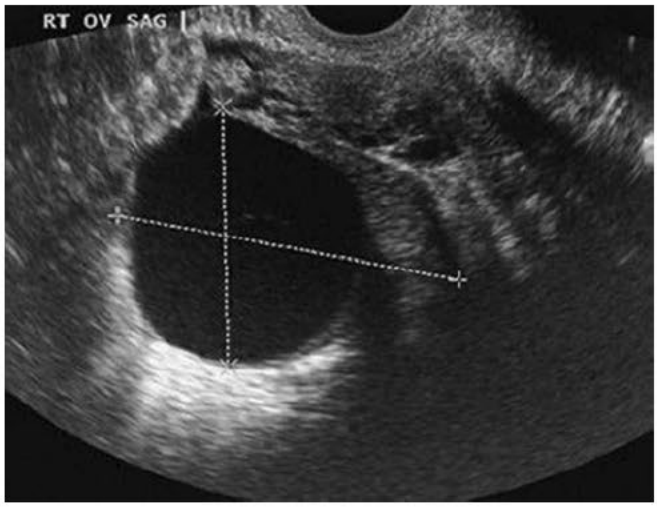


FIGURE 2-1 Transvaginal sonogram of a premenopausal ovary containing a follicular cyst. The cyst fluid appears black or anechoic. Note the white or hyperechoic area under the cyst, a sonographic feature called *posterior acoustic enhancement* or *through transmission*.

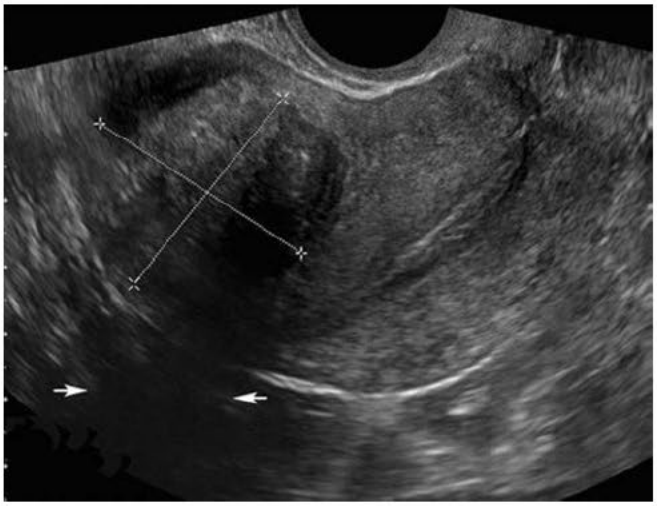


FIGURE 2-2 Transvaginal sonogram shows a leiomyoma marked by calipers and demonstrates *posterior acoustic shadowing* (*arrows*).

3 to 5 MHz range, whereas transvaginal transducers are generally 5 to 10 MHz.

Examination Techniques

Guidelines for sonographic examination of the female pelvis have been established by The American Institute of Ultrasound in Medicine (2014). These serve as quality assurance standards for patient care and provide assistance to practitioners performing sonography. Guidelines describe equipment and documentation and may be accessed at: http://www.aium.org/resources/guidelines/femalePelvis.pdf.

All probes are cleaned after each examination, and vaginal probes are covered by a protective sheath prior to insertion. A female staff member should always chaperone transvaginal sonography. Guidelines describe the examination steps for each organ and anatomic region in the female pelvis. For the uterus, uterine size, shape, orientation, and description of the endometrium, myometrium, and cervix are documented. The examination and its interpretation are permanently recorded, appropriately labeled, and placed in the medical record. A copy is also kept by the facility performing the study.

Grayscale Imaging

Various examination techniques can be used for sonographic study of the female pelvis. Of these, transabdominal evaluation, using a curved-array 3- to 5-MHz transducer, is the first component of general gynecologic examinations. It provides global identification of all pelvic organs and their spatial relationships. In a nonpregnant patient, a full bladder is preferred for adequate viewing, as it pushes the uterus upward from behind the pubic symphysis and displaces small bowel from the field of view. Moreover, the bladder acts as an *acoustic window*, to improve ultrasound wave transmission. In patients with large lesions or masses located superior to the bladder dome, transabdominal sonography provides a panoramic view for greater disease evaluation. Still, endometrial cavity assessment is limited with a transabdominal approach and often requires the transvaginal technique.

Transvaginal sonography (TVS) uses higher-frequency (5- to 10-MHz) transducers and is the second component of general gynecologic examinations. Because of its greater sensitivity and spatial image resolution, TVS is ideal for interrogating pelvic anatomy within the confines of the true pelvis. With larger masses, imaging may be incomplete and is complemented by transabdominal sonography.

For TVS, the probe is positioned in the vaginal fornices to place the transducer close to the region of interest and thereby lessen beam attenuation by superficial soft tissues. In contrast to transabdominal imaging, the bladder is emptied prior to a transvaginal study. TVS has few limitations. The only two absolute contraindications are imperforate hymen and patient refusal. A relative contraindication is a patient with a virginal or strictured introitus. These women, however, can usually undergo comfortable examination with proper counseling.

Transrectal and *transperineal techniques* employ transrectal probes and conventional transducers placed over the perineal region, respectively, for image acquisition. Much less commonly used, they are selected for indications such as pelvic floor imaging (p. 38).

Harmonic Imaging

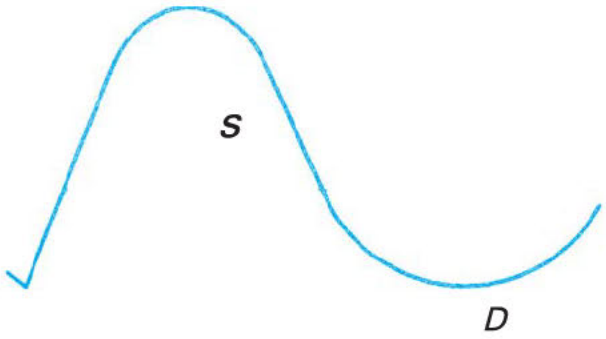
This recent modification of sonography improves image quality by using several frequencies at once from the transmitted ultrasound beam instead of just a single frequency. Newer probes and postprocessing features enhance image resolution, particularly at surface interfaces. Visual artifacts that arise from superficial structures such as adipose are reduced. As such, tissue harmonic imaging is routinely used in our institution's ultrasound examinations.

Doppler Technology

This ultrasound technique can be performed with either transabdominal or transvaginal sonography to determine blood flow through pelvic organs, based on the red blood cell (RBC) velocity within vessels, especially arteries. *Color Doppler* captures and characterizes the spectral waveform of flow through certain vessels seen during real-time imaging. Ratios are often used to compare these different waveform components. The simplest is the systolic-diastolic ratio (S/D ratio), which compares the maximal (or peak) systolic flow and end-diastolic flow to evaluate downstream impedance to flow (Fig. 2-3). Of arterial Doppler spectral waveform parameters, the *resistance index* and *pulsatility index* also are commonly calculated. These quantitative indices estimate the impedance to RBC velocity within the artery by expressing the differences between the peak systolic and end-diastolic velocities.

A second application is *color Doppler mapping*, in which the color-coded pulsed-Doppler velocity information is superimposed on the real-time grayscale image. The color is scaled such that the color brightness is proportional to the flow velocity. Additionally, color Doppler also provides information regarding blood flow direction, and color is assigned to this. Flow approaching the transducer is customarily displayed in red, and flow away from it is shown in blue.

Color Doppler is not applied during every general gynecologic examination. One frequent indication is adnexal mass



$$\frac{S}{D} = S/D \text{ Ratio}$$

$$\frac{S-D}{S} = \text{Resistance index}$$

$$\frac{S-D}{\text{Mean}} = \text{Pulsatility index}$$

FIGURE 2-3 Doppler systolic–diastolic waveform indices of blood flow velocity. *S* represents the peak systolic flow or velocity, and *D* indicates the end-diastolic flow or velocity. The mean, which is the time-average mean velocity, is calculated from computer-digitized waveforms. (Reproduced with permission from Dashe, 2018.)

interrogation. Neovascularity within cancer is composed of abnormal vessels that lack smooth muscle and contain multiple arteriovenous shunts. Consequently, low-impedance flow is expected with such masses (Fig. 2-4) (Timmerman, 2016; Weiner, 1992). Other indications include evaluation of ovarian masses for torsion, detection of extrauterine vascularity associated with ectopic pregnancy, and assessment of uterine perfusion in patients with leiomyomas and endometrial disorders (Navve, 2013; Wang, 2016a). Because of safety concerns regarding the higher intensities generated by color and spectral Doppler, use of Doppler imaging in the first trimester is discouraged, unless clear indications are present.

Power Doppler imaging also maps RBC motion. It detects the energy of Doppler signals generated from moving RBCs using

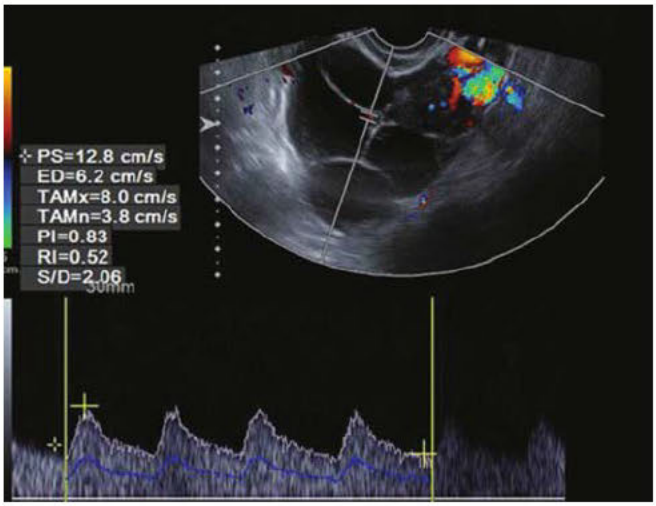


FIGURE 2-4 Complex ovarian mass with irregular cystic areas demonstrating low-impedance (pulsatility index = 0.83) flow in a septation.

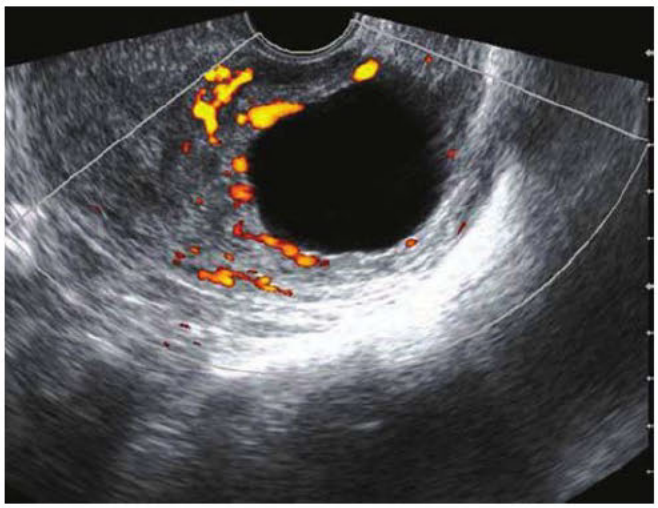


FIGURE 2-5 Power Doppler evaluation of a gestational sac in the lower uterine segment. Circular flow is depicted, consistent with the peritrophoblastic flow of an implanted pregnancy.

signal-to-noise characteristics of the vessels compared with surrounding tissues. This modality gives no information regarding blood flow direction, and thus data are displayed as a single color, usually yellow or orange. However, power Doppler is more sensitive to low-flow velocities, such as in veins and small arteries. Although employed less often than color Doppler mapping, power Doppler can gather additional information regarding endometrial and ovarian abnormalities (Fig. 2-5).

Saline-Infusion Sonography

Also called *sonohysterography*, saline-infusion sonography (SIS) displays detailed endometrial cavity anatomy by distending the cavity with sterile saline (American College of Obstetricians and Gynecologists, 2016). It is commonly selected after an endometrial mass is identified or suspected during general TVS. SIS can also assist in some infertility investigations and aid viewing of the central endometrial echo if it is poorly imaged because of uterine position or pathology.

After voiding, a woman first undergoes a comprehensive TVS evaluation. A vaginal speculum is then inserted, and the vagina and cervix are swabbed with an antiseptic solution. A catheter primed with sterile saline is advanced into the cervical canal and past the internal os. We do not routinely use a tenaculum for this. Contact with the uterine fundus is ideally avoided when advancing the catheter to avert pain or vasovagal response. It can also shear away endometrium, causing false-positive results. Once in the lower uterine segment, the catheter balloon is inflated. The speculum is carefully removed, the transvaginal probe is reinserted, and sterile saline is injected through the catheter at a rate based on the patient's tolerance. Usually not more than 5 to 40 mL is required to distend the endometrial cavity, depending on the patient's hormonal status and intracavitary pathology (Fig. 2-6). During this time, the cavity is observed with TVS. The sonographer scans in the longitudinal plane, imaging from one cornu to the other, and in the transverse plane, from the top of the fundus to the cervix. Endometrial surface irregularities are well delineated by the anechoic contrast of saline. At the procedure's conclusion,

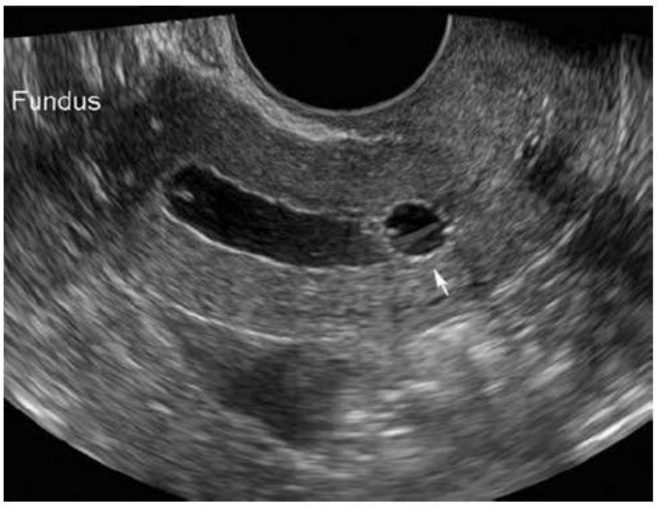


FIGURE 2-6 Saline-infusion sonography of a normal endometrial cavity. The infusion catheter balloon (*arrow*) is seen in the uterine isthmus.

the catheter is withdrawn under sonographic visualization. The uterine isthmus, endocervical canal, and upper vagina and vaginal fornices also may be evaluated, and this technique is referred to as *sonovaginography*. On average, the entire procedure lasts 5 to 10 minutes.

Many different catheter systems are available, including rigid systems and flexible catheters with and without attached balloons. We use a 7F SIS balloon catheter set, which tamponades the internal cervical os. This blockade prevents backflow of the distending medium and provides stable filling and adequate distention. We have found it easy to place and well tolerated (Fig. 2-7). Several distending solutions have been described, including saline, lactated Ringer solution, and 1.5-percent glycine. Sterile saline is inexpensive and provides optimal imaging. Alternatively, gel and foam substances have been developed to avoid backflow problems. However, these alternative products have not been extensively investigated and are not used widely in clinical practice.

In the premenopausal woman, SIS is best performed within the first 10 days of the menstrual cycle, and optimally on cycle days 4, 5, or 6 when the lining is thinnest. This timing is recommended to avoid misinterpreting menstrual blood clots as intrauterine pathology or missing pathology obscured by thick endometrial growth. In addition, such timing usually precludes disturbing a potential pregnancy. For the postmenopausal woman, timing of the procedure is not cycle-dependent.

Complications of SIS are minimal, and the risk of infection is <1 percent (Bonnamy, 2002). The American College of Obstetricians and Gynecologists (2018) recommends prophylactic antibiotics for women with prior pelvic inflammatory disease (PID) or identified hydrosalpinges, in which cases doxycycline 100 mg orally twice daily is prescribed for 5 days. Although not evidence based, we also routinely give a single dose of doxycycline, 200 mg orally, following SIS in women with diabetes and to infertile patients because of the risk for significant tubal damage associated with pelvic infection. Pain is usually minimal. In our experience, women with prior tubal ligation have greater discomfort, likely because fluid is unable to efflux through the fallopian tubes. A nonsteroidal antiinflammatory drug (NSAID) given 30 minutes prior to the procedure will typically minimize discomfort.

Contraindications to SIS include hematometra, pregnancy, active pelvic infection, or obstruction such as with an atrophic or stenotic cervix or vagina. In postmenopausal women with cervical stenosis, we have found the following steps to be helpful. First, a 200-μg misoprostol tablet is taken orally the evening before and the morning of the procedure. During SIS, a paracervical block with 1-percent lidocaine without epinephrine is provided; a tenaculum is placed on the cervix for traction; and the cervix undergoes sonographically guided sequential cervical dilation with lacrimal duct dilators. To overcome severe cervical stenosis, Pisal and colleagues (2005) inserted a 20-gauge spinal needle directly into the uterine cavity under sonographic guidance to deliver the saline.

Hysterosalpingo-Contrast Sonography

In the past, a fallopian tube could be detected with sonography only when distended by fluid, such as with obstruction. Injection of echogenic contrast during real-time sonography,

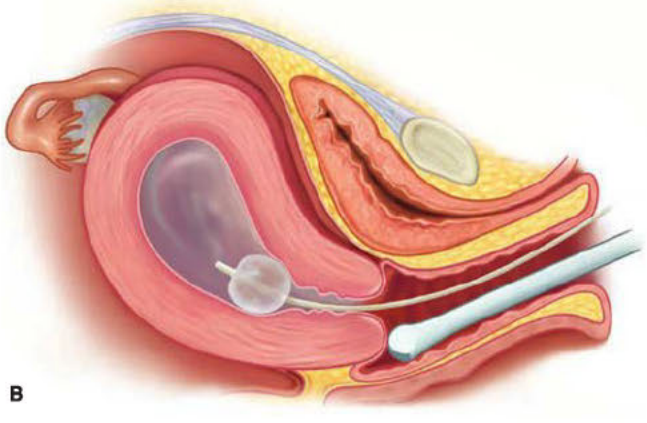


FIGURE 2-7 **A.** Saline-infusion sonography catheter. **B.** Saline-infusion sonography technique.

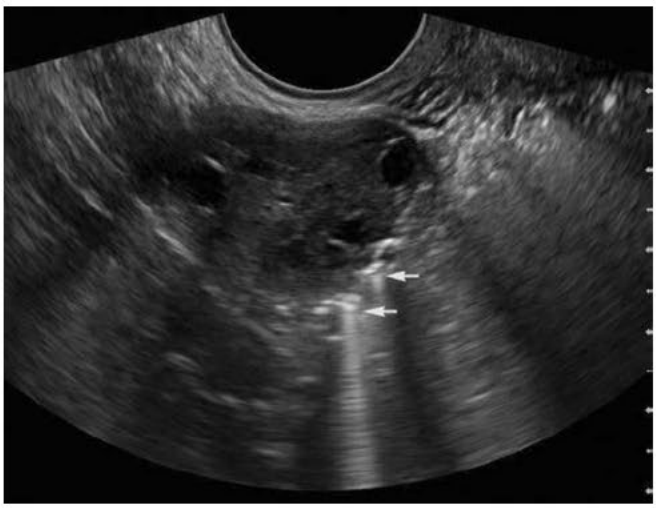


FIGURE 2-8 Transvaginal image of an ovary with echogenic bubbles adjacent to it (*arrows*) as seen during hysterosalpingo-contrast sonography (HyCoSy). The air in the saline contrast produces the bright echo and ring-down artifacts. Visualization of these echoes adjacent to the ovary represents contrast exiting the tube, consistent with tubal patency.

called *sonosalpingography*, *sonohysterosalpingography*, or *hysterosalpingo-contrast sonography (HyCoSy)*, is now an accurate first-line procedure to assess tubal patency (Lo Monte, 2015).

HyCoSy is done in a manner similar to SIS. Fluid egress from the uterine cavity is blocked by a balloon catheter within the cervical canal. Using transvaginal sonography, the fallopian tubes are identified at the point where they join the uterine cornua. A hyperechoic sonographic contrast medium (Echovist, Albunex, or Infoson) is injected through the catheter to fill the cavity and then the fallopian tubes (Fig. 2-8). Air coupled with sterile saline solution is another contrast option. With either medium choice, patent tubes appear hyperechoic as they fill with contrast. Color or pulsed Doppler techniques raise the diagnostic accuracy of HyCoSy by showing flow velocity within the tubes (Kupesic, 2007). We use the FemVue Sono Tubal Evaluation System, which simultaneously introduces air and sterile saline in a controlled fashion. The positive pressure flow of the echogenic mixture creates "scintillations" that are visually followed using real-time ultrasound. In patent tubes, flow proceeds from the uterotubal junction, through the length of the tube, and out the fimbriated end. Bubbles then surround the ovary or fill the posterior cul-de-sac. At present no large studies quantitate a risk for post-HyCoSy pelvic infection, and our periprocedural antibiotic prophylaxis mirrors that for SIS.

HyCoSy performed in conjunction with SIS provides a comprehensive "one-stop" outpatient assessment of tubal patency, adnexal architecture, and uterine cavity and myometrial anatomy. Comparable to hysterosalpingography (HSG) in detecting tubal pathology and anatomy, HyCoSy is well tolerated and avoids x-ray exposure or iodine-related allergic reaction (Lo Monte, 2015; Luciano, 2014).

However, HyCoSy does have limitations. First, similar to HSG, tubal spasm can provide false-positive occlusion results with HyCoSy. In addition, a patent tube does not always correlate with normal tubal function. Second, the entire fallopian tube often cannot be visualized due to normal tubal tortuosity. To that end, recent studies have evaluated the combination of 3-D sonography with HyCoSy for more accurate delineation of tubal anatomy (Alcázar, 2016; Exacoustos, 2017; Wang, 2016b).

Three-Dimensional Sonography

Technical Aspects. The ability to obtain certain views of pelvic organs in two dimensions is inherently limited. Transabdominally, the bony pelvis prevents scanning from the pelvic sidewall. Transvaginally, the views obtainable are restricted by the range of vaginal probe mobility. Sonography scanners now can collect 3-D data and represent it on a two-dimensional (2-D) screen. With 3-D imaging, any desired plane through a pelvic organ can be obtained, regardless of the sound beam orientation during acquisition. For example, the "face-on" or coronal plane through the uterus is routinely seen in 3-D imaging but is rarely viewed during 2-D scanning. This view of the uterus is essential for assessing the external contour, particularly of the fundus, for congenital uterine anomaly diagnosis.

With 3-D sonography, a volume, rather than a slice, of sonographic data is acquired and stored. The stored data can be reformatted and analyzed in numerous ways, and navigation through the saved volume can show countless planes. At any time, the volume can be retrieved, studied, reconstructed, and reinterpreted as needed. In addition, the level of energy with 3-D sonography is no higher than with 2-D, and manipulations of the obtained volumes are performed "off-line" to avoid additional ultrasound scanning time.

The three main components of 3-D sonography are volume acquisition, processing, and display. First, the preferred method to acquire volumes is automated and uses a dedicated 3-D probe that contains a mechanized drive. When these probes are activated, the transducer elements automatically sweep through the operator-selected region of interest, called a *volume box*, while the probe is held stationary.

After the appropriate volume is acquired, the user can begin to process the volume using the modes available in the ultrasound machine. The acquired volume can be displayed multiple ways. The most common is multiplanar reconstruction, in which three perpendicular planes, sagittal (the longitudinal plane that divides the body into right and left sections), axial (the transverse plane that divides the body into top and bottom sections), and coronal (the frontal plane that divides the body into front and back sections), are displayed simultaneously. Correlation between the three planes in the multiplanar display is accomplished by placing the planar center dot at the point of interest in one plane and observing the location of the corresponding center dots in the other two planes (Fig. 2-9A–C).

Abuhamad and associates (2006) have described a straightforward postprocessing technique that aids in the manipulation of 3-D volumes of the uterus, called the *Z technique*. The anatomic basis of the Z technique is such that, in aligning the midsagittal and midtransverse planes of the uterus parallel to the horizontal axis, the midcoronal plane of the uterus will easily and consistently be displayed. In addition, all or part of the saved volume can be processed into a rendered image that can

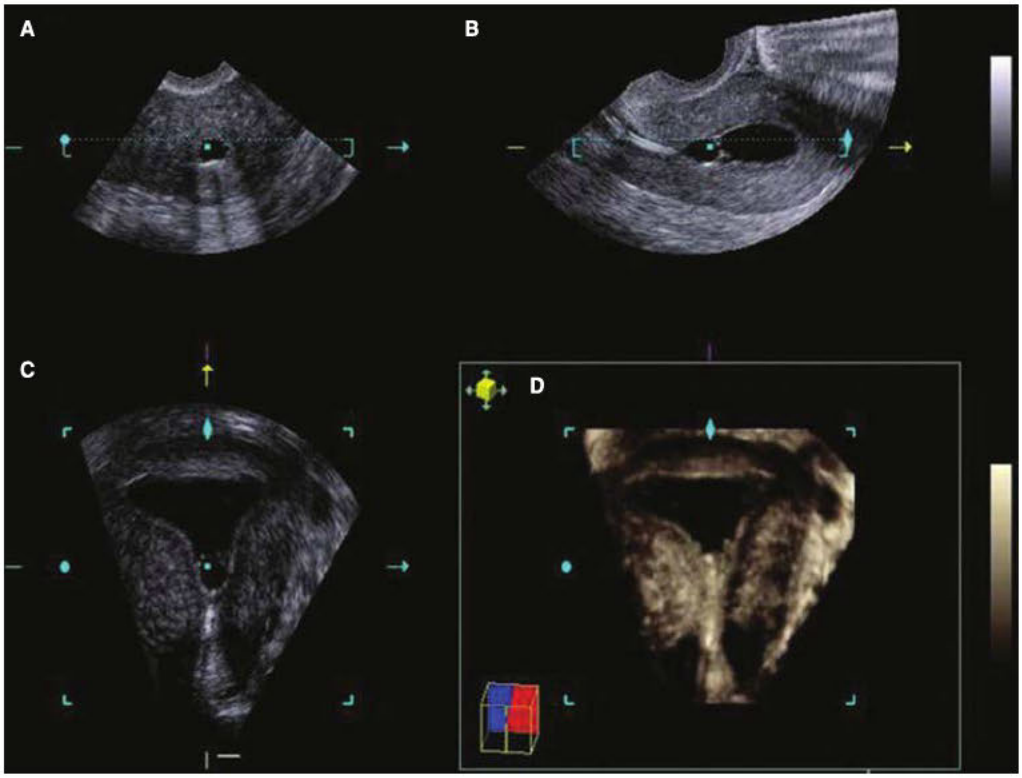


FIGURE 2-9 Multiplanar display of a 3-dimensional volume of a uterus and normal endometrial cavity during saline-infusion sonography. The views were obtained from a midsagittal reference plane using the Z technique. The planes are as follows: **A.** transverse, **B.** sagittal, **C.** coronal, **D.** rendered image.

be shown alone or in correlation with the multiplanar display. A rendered image is a "sum" of all the coronal planar images (see Fig. 2-9D). This is the display method that has been publicized in obstetrics, when showing the image of a fetal face in utero.

The inverse mode is a rendering technique of the entire volume in which all cystic areas within the volume become digitally opaque and all solid areas become transparent. This technique is useful when trying to see cystic areas that might be hidden in a volume, such as within an ovarian mass. Last, the volume can be displayed in parallel tomographic slices, similar to the displays used by CT and MR imaging.

3-D imaging is not without shortcomings. With 3-D sonography, the same type of acoustic artifacts that occur with 2-D imaging are encountered, such as acoustic shadowing and enhancement, refraction and reverberation, and motion artifacts from bowel peristalsis and vascular pulsation. Another potential pitfall in 3-D imaging of the pelvis involves spatial orientation within the saved volume data. Uterine flexion or version or left versus right may not be readily apparent on review of saved volumes. As such, during the preliminary real-time scanning, the operator must determine the orientation of the area of interest and notate it accordingly.

Another problem is related to the limited size of the volume box. Because of this, the entire uterus is often not acquired in a single volume. In some cases, it may be necessary to acquire two volumes, one for the cervix and a second for the uterine body. Likewise, a very large adnexal mass may not be imaged completely in any single volume of data obtained transvaginally. The size of the volume box provided by the abdominal probe is greater. Thus with 3-D sonography, a large mass may need to be imaged transabdominally instead of transvaginally.

Clinical Use. Because it can study organs in numerous scanning planes, 3-D imaging has become invaluable in gynecology to assess the uterine cavity, complex ovarian masses, ovarian fertility reserve, uterine anomalies, and interstitial pregnancies. It simultaneously provides anatomic and dynamic information from pelvic floor structures and also from mesh implants.

Of these, mapping leiomyoma location relative to the endometrial cavity and surrounding structures is an essential step in triaging patients for treatment (Chap, 9, p. 206). For such mapping, 3-D sonography, in particular 3-D SIS, has been used in place of convention SIS or MR imaging (Keizer, 2018; Mavrelos, 2011). In patients receiving gonadotropin-releasing hormone (GnRH) agonists or following uterine artery embolization (UAE), 3-D sonography can also monitor leiomyoma volume reductions. However, following UAE, MR imaging is more often used.

Abnormalities of the endometrium and adjacent myometrium, especially focal endometrial thickenings such as polyps and cancer, may be better defined with 3-D technology (Fig. 2-10) (Benacerraf, 2008). In a recent Cochrane database review, 3-D SIS offered uterine cavity and endometrial thickness visualization rates comparable to hysteroscopy (Nieuwenhuis, 2017). We now routinely implement 3-D imaging for evaluation of abnormal endometrium during our TVS studies and with all SIS procedures.

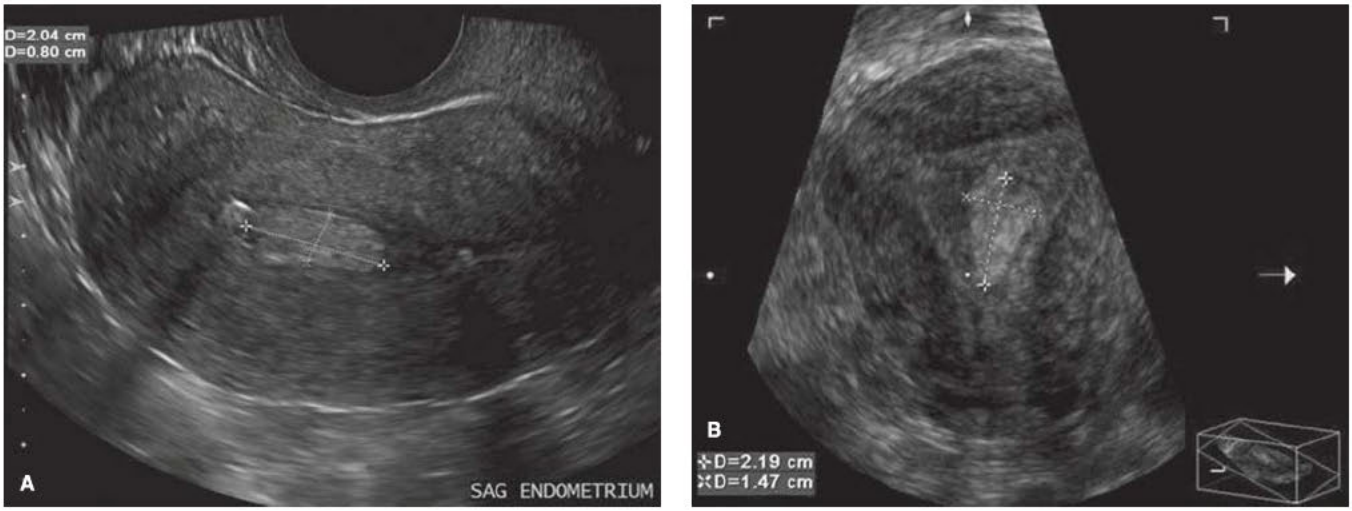


FIGURE 2-10 A. Transvaginal sonogram displays endometrial polyp measured by calipers. **B.** Three-dimensional image in the coronal plane of a polyp (*calipers*).

Although investigational, 3-D sonography with power Doppler angiography (3D-PDA) can help discriminate benign from malignant endometrial disease in women with postmenopausal bleeding and a thickened endometrium (Makled, 2013). Endometrial lesions in infertile women are another potential indication (Ni, 2019). 3D-PDA can assess endometrial volume, which may more accurately reflect true tissue volume than a 2-D endometrial thickness measurement. Another tool, 3-D power Doppler imaging enhanced by intravenous (IV) contrast, also is being studied to distinguish benign endometrial polyps from endometrial cancer (Lieng, 2008; Song, 2009).

IUD positioning within the endometrial cavity can be documented adequately in most cases with traditional 2-D TVS. That said, 3-D sonography offers improved visualization, especially with the levonorgestrel-containing IUDs (Moschos, 2011). The coronal plane images, which are not possible with 2-D imaging, provide views of the arms and shaft of the device and their relation to the endometrial cavity (Benacerraf, 2009). At our institution, patients undergoing gynecologic sonography with an IUD in situ, regardless of the study indication, have both a standard 2-D evaluation and a 3-D volume acquisition of the uterus. The coronal view of the endometrial cavity is reconstructed to establish IUD type, location, and positioning (Fig. 2-11). TVS also is an acceptable method to confirm proper Essure coil positioning (Fig. 2-12) (Carretti, 2019; Legendre, 2010).

For adnexal mass interrogation, most agree that 3-D sonography provides detailed internal anatomy (Alcázar, 2003). Moreover, 3D-PDA displays the internal architecture and also the neovascularization characteristic of malignant neoplasms. However, 3D-PDA does not significantly improved diagnostic accuracy compared with that of grayscale and 2-D power Doppler imaging (Jokubkiene, 2007; Ohel, 2010).

In reproductive medicine, 3-D imaging acquires more precise ovarian volumes and follicle counts than measurements

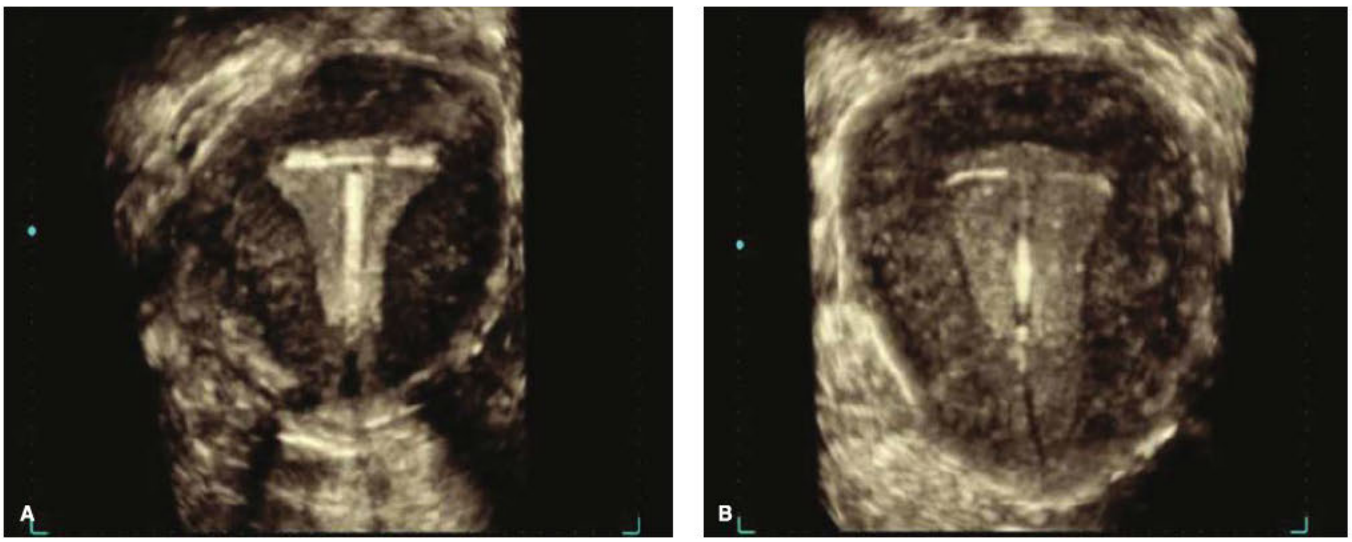


FIGURE 2-11 Intrauterine devices (IUDs). The coronal planes of 3-dimensional sonography best depict the type and positioning of the Copper T 380A IUD (ParaGard) **(A)** and levonorgestrel-containing IUD (Mirena) **(B)** within the endometrial cavity.

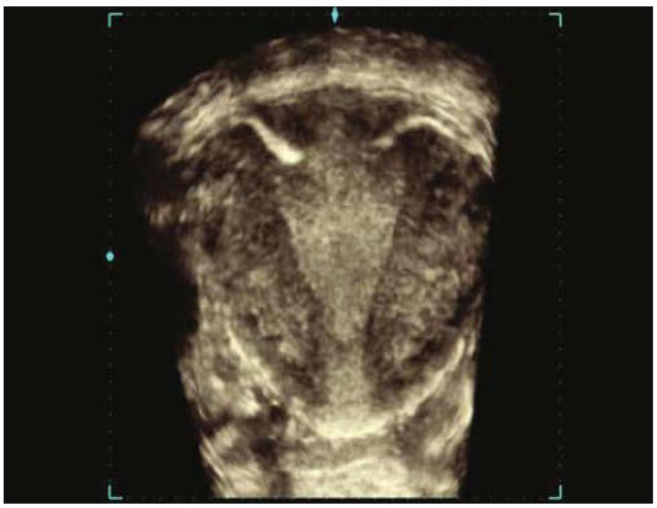


FIGURE 2-12 Essure contraception. Three-dimensional image in the coronal plane demonstrates the microinsert coils in the bilateral cornua of the uterus, corresponding to proper placement of the devices.

estimated from 2-D imaging. It is becoming the preferred ultrasound technique for infertility ovarian evaluation (Nylander, 2017; Peres Fagundes, 2017). Moreover, 3-D sonography can also examine endometrial vascularity and volume to help predict endometrial receptivity prior to ovarian stimulation (Wu, 2003; Zollner, 2012).

For congenital müllerian uterine anomalies, 3-D ultrasound is as sensitive as hysteroscopy and as accurate as MR imaging. It provides detailed images of both endometrial cavity shape and external fundal contour (Bermejo, 2010; Ghi, 2009). Because the uterine horns and fundal contour are displayed clearly in the same plane, müllerian anomalies can be differentiated (p. 41) (Troiano, 2004). This can help preoperative planning.

For pelvic reconstructive surgery indications, 3-D ultrasound can evaluate pelvic floor anatomy and pelvic support. In addition, polypropylene mesh implants appear as echogenic interwoven interfaces with ultrasound. In contrast, these are poorly depicted with radiography or MR imaging. As a result, 3-D vaginal and perineal sonography is now selected for this evaluation (Dietz, 2012, 2017; Fleischer, 2012). However, cranial aspects of mesh or retropubic mesh may be poorly imaged with 3-D ultrasound. For these patients, MR imaging may be helpful.

As a second indication, postprocessing reconstruction in a coronal plane improves views of the urethra and the periurethral tissue, which are inaccessible with 2-D ultrasound techniques. 3-D images are obtained with abdominal transducers using a translabial-transperineal approach or with transvaginal probes using specialized rotational transducers (Dietz, 2007, 2012; Santoro, 2011).

In women with pelvic floor dysfunction, the reconstructed ultrasound images afforded by 3-D ultrasound are particularly useful to quantify the degree of levator ani muscle defects (Dietz, 2017; Hedge, 2017). Perhaps most importantly, 3-D imaging can provide not only anatomic but also dynamic information about the pelvic floor structures, as imaging can be executed with the patient performing the Valsalva maneuver or actively contracting the pelvic floor musculature (Fleischer, 2012).

Contrast-Enhanced Sonography

This newer technique couples IV contrast with traditional sonography. With contrast-enhanced sonography, the density (or signal intensity) of a focal lesion and its density compared with the surrounding normal organ tissue can be enhanced.

Ultrasound contrast agents used intravenously are small, stabilized microbubbles, usually 1 to 10 μm in diameter, and composed of perfluorocarbon or nitrogen gas encapsulated in albumin, phospholipid, or polymer shells. The gas-liquid interface contributes to the echogenicity of the microbubbles. Also, a high impedance mismatch between the microbubbles and adjacent RBCs in the blood vessels causes greater scatter and reflection of the ultrasound sound beam. This heightens the ultrasound signal and thereby increases brightness or echogenicity (Hwang, 2010). The degree of echo enhancement depends on many factors, including microbubble size, contrast agent density, bubble compressibility, and the interrogating ultrasound frequency. The greater the size, density, and compressibility of the agent, the more reflection and echogenicity are elicited (Eckersley, 2002).

For ovarian cancer, contrast-enhanced sonography may highlight tumor neovascularization in developing microscopic tumors (Wu, 2015). In addition, because vascular channels associated with malignancy are often incompetent, the resultant extravasation of RBCs and contrast agent may be detected (Fleischer, 2008). Accordingly, its preoperative interrogation of cervical and endometrial carcinomas can help determine the extent of invasion (Song, 2009; Zheng, 2018).

Other promising clinical applications of contrast-enhanced sonography include monitoring tumor and therapeutic angiogenesis, inflammation assessment, evaluation of ischemia and reperfusion injury, early detection of transplant rejection, and targeted drug delivery (Hwang, 2010; Peng 2016).

Sonoelastography

Elastography is an ultrasound imaging technique that measures tissue stiffness in both physiologic and pathologic states. With this modality, a source of "stress" promotes tissue deformation to assess stiffness (Stoelinga, 2014). For gynecologic imaging, vibration sonoelastography employs low-amplitude, low-frequency shear waves that propagate through the organ of interest. Simultaneously, real-time color Doppler techniques generate an image of tissue movement in response to the external vibrations (Taylor, 2000). For example, if a hard inhomogeneous mass, such as a tumor, lies within a region of soft tissue, the vibration amplitude is decreased at the tumor site.

Potential areas of investigation include distinguishing endometrial polyps from submucous pedunculated myomas, endometrial cancer from benign endometrial thickening, cervical cancer from normal cervical stroma, and leiomyomas from adenomyosis (Stoelinga, 2014, 2018). Moreover, uterine and cervical stiffness during pregnancy may help predict or manage preterm or postterm complications (Xie, 2018).

Focused-Ultrasound Therapy

Ultrasound energy during conventional imaging propagates harmlessly through tissue with little energy being absorbed. This energy is deposited as heat but dissipates by the cooling effects of perfusion and conduction. No harmful effects have been recorded at the intensities used for diagnostic purposes (American Institute of Ultrasound in Medicine, 2009).

If, however, the ultrasound beam carries high energy and is brought into tight focus, this energy is rapidly converted into heat. When target spot temperatures rise above 55°C, proteins are denatured, cells die, and coagulative necrosis follows. In contrast, surrounding tissues are warmed but not to lethal temperatures. In gynecology, this tool offers an option for leiomyoma ablation (Chap. 9, p. 210).

Normal Sonographic Findings

Reproductive Tract Organs

In the reproductive years, a normal uterus measures approximately 7.5 × 5.0 × 2.5 cm but is smaller in prepubertal, postmenopausal, or hypoestrogenized women. Normal uterine stroma returns low-level, uniform echoes, and the endometrial and endocervical canals are indicated by linear echogenic stripes that represent the interfaces between mucus and mucosa (Fig. 2-13). The cervix is best visualized transvaginally with the tip of the probe placed 2 to 3 cm from it. The endocervical canal is a continuation of the endometrial cavity and appears as a thin echogenic line (Fig. 2-14). The vagina is seen as a hypoechoic tubular structure with an echogenic lumen that curves inferiorly over the muscular perineal body at the introitus.

The ovaries are ellipsoid and normally lie in the ovarian fossa with their long axes parallel to the internal iliac vessels (Fig. 2-15). Ovarian volume ranges from 4 to 10 cubic centimeters depending on hormonal status (Cohen, 1990). Ovarian volume is calculated using the formula for an ellipse: $\pi/6 \times (A \times B \times C)$. In this formula, A, B, and C are the ovarian diameters in centimeters, measured in the three different planes.

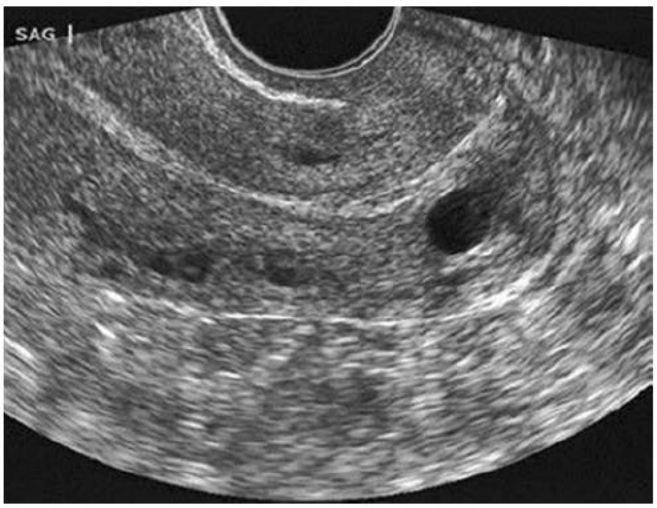


FIGURE 2-14 Transvaginal sonogram in the sagittal plane of a uterine cervix. An endocervical cyst is seen posterior to the thin, echogenic endocervical canal.

Ovarian follicles appear as spherical anechoic structures within the ovary and may reach a normal size of 3 cm. Normal fallopian tubes are not visible.

Endometrium

Functionally, the endometrium has two main layers: the *stratum basale*, which comprises the densely cellular supporting stroma and varies little with menstrual cycle phase, and the *stratum functionale*, which proliferates during each cycle and partially desquamates at menses. These layers cover the entire cavity.

Sonographically, the endometrium's appearance during the menstrual cycle correlates with the phasic changes in its histologic anatomy. During the follicular phase, when the endometrium is provided estrogen from ovarian folliculogenesis, the stratum basale appears echogenic due to spectral reflections from the mucus-laden glands. In contrast, the stratum functionale is relatively hypoechoic because of its orderly arrangement

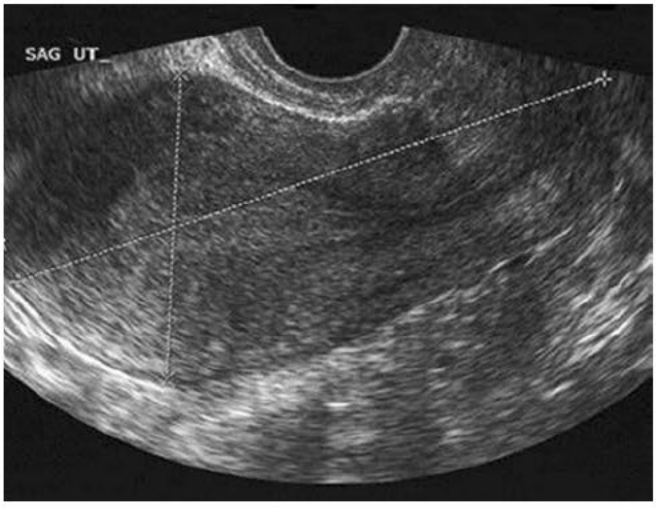


FIGURE 2-13 Transvaginal sonogram in the sagittal plane of an anteverted anteflexed uterus. Calipers demonstrate measurements of the uterine length (+) and the anterior-posterior dimension (×).

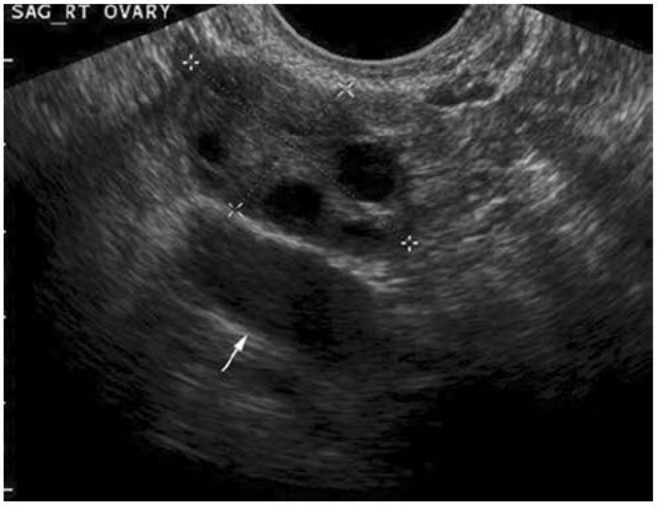


FIGURE 2-15 Transvaginal sonogram in the sagittal plane of an ovary (*calipers*) in a premenopausal woman. The ovary normally lies in the ovarian fossa, anterior to the internal iliac vessel (*arrow*).

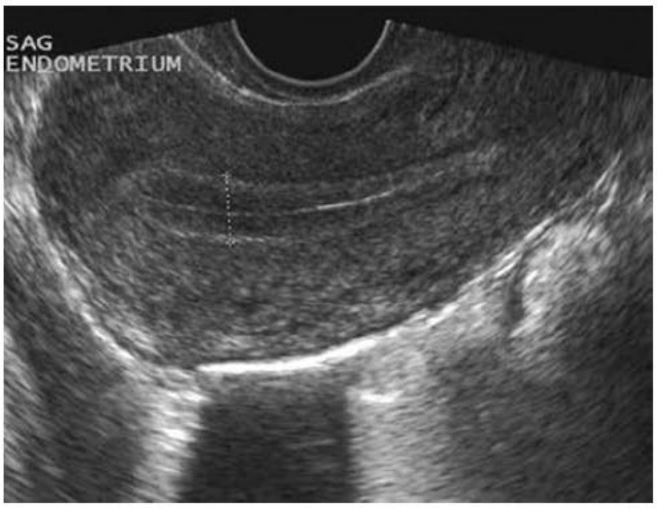


FIGURE 2-16 Transvaginal sonogram in the sagittal plane of a characteristic trilaminar proliferative endometrium. Calipers demonstrate proper measurement of the "double-layer" thickness made of the alternating hyper-hypo-hyperechogenic lines.

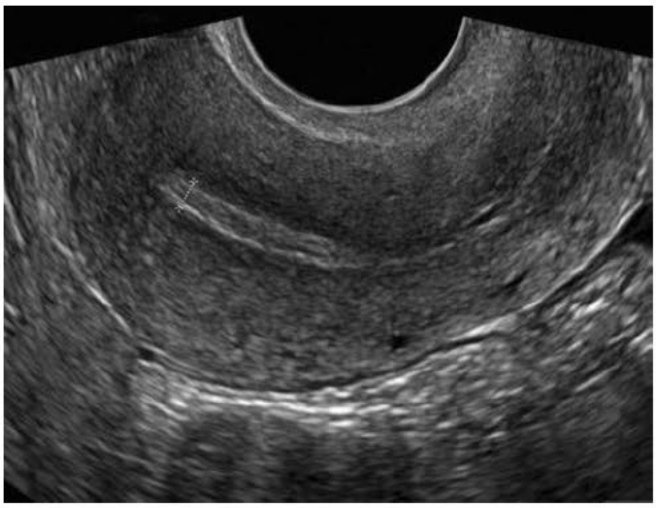


FIGURE 2-18 Transvaginal sonogram in the sagittal plane of a menstrual-phase endometrium, which is marked by calipers.

of glands that lack secretions. The central opposing surfaces of these two endometrial layers manifest as a highly reflective, thin midline strip. Together, the three echogenic lines create the characteristic trilaminar appearance of the proliferative endometrium (Fig. 2-16).

To measure the *endometrial thickness*, one caliper is placed at the echogenic interface of the anterior basale layer and myometrium. The other is positioned at the similar echogenic interface of the posterior basale layer. It thus represents a "double thickness." The hypoechoic halo outside of and adjacent to the endometrium is not included in the measurement, as this is actually the inner compact layer of myometrium. Sonographically, the endometrium is measured from a sagittal or long-axis image of the uterus in the plane where the central endometrial echo is contiguous with the endocervical canal and is distinct from the myometrium. Endometrial thickness correlates approximately with the day of the menstrual cycle up to day 7 or 8.

With ovulation and progesterone production from the corpus luteum, glandular enlargement and secretory vacuoles are seen histologically. During this secretory phase, the endometrium achieves its maximum thickness as the stroma becomes more vascular and edematous. Sonographically, these changes cause the endometrium to appear echogenic (Fig. 2-17).

With menstruation, the endometrium displays as a slightly irregular echogenic interface, which derives from sloughed tissue and blood. The thinnest endometrial measurements are found at the conclusion of menses (Fig. 2-18).

With cessation of estrogen stimulation, the endometrium atrophies, and cyclic sloughing ceases. The postmenopausal endometrium appears thin and uniform (Fig. 2-19).

Pelvic Floor

Sonography is widely used to evaluate pelvic floor anatomy and function (Dietz, 2017). First, various 2-D techniques,

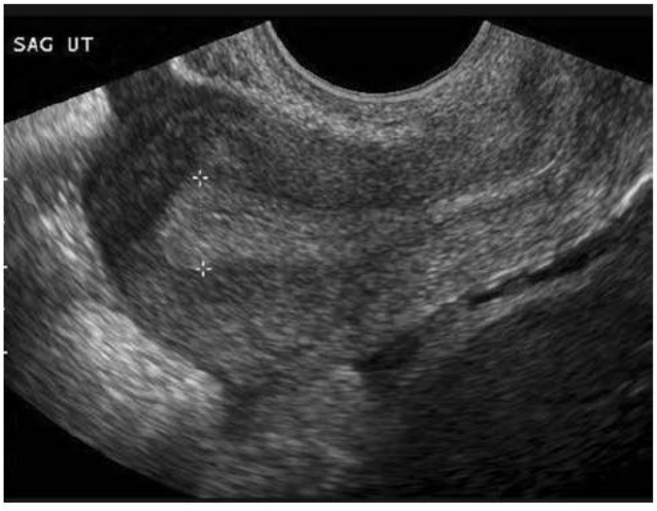


FIGURE 2-17 Transvaginal sonogram in the sagittal plane of a secretory endometrium. The endometrium, which is marked by calipers, has become uniformly echogenic.

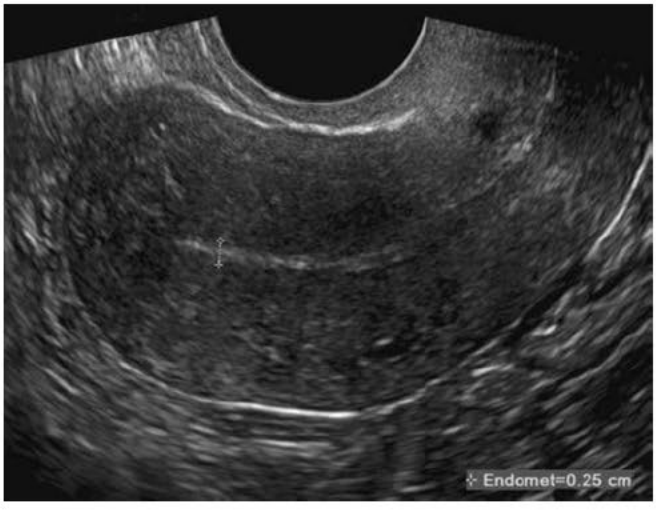


FIGURE 2-19 Transvaginal sonogram in the sagittal plane of an atrophic postmenopausal endometrium, which is marked by calipers.

including transvaginal, transrectal, transperineal, and intraurethral sonography, can display urethral anatomy. In addition, anorectal morphology and the pelvic floor both can be assessed with vaginal sonography using a rotating endorectal probe or standard transvaginal probe (Chap. 25, p. 564). Less commonly, transrectal sonography can assess anal sphincter morphology after childbirth. This method requires special equipment and distention of the anal canal. The technique has limited value in the immediate puerperium and only provides information regarding the anal sphincter. Thus, without levator ani muscle assessment, the posterior compartment is incompletely evaluated.

Perineal sonography requires filling the bladder with approximately 300 mL of saline. With the woman either supine or erect, a 3.5- to 6-MHz curved-array transducer is placed in sagittal orientation to the perineum. This allows real-time imaging of the pubic symphysis, levator ani muscles, urethra, bladder neck, bladder, vagina, rectal ampulla, and anal canal simultaneously and with little transducer manipulation (Dietz, 2017; Schaer, 1995; Vellucci, 2018). Last, 3-D ultrasound is increasingly selected, and evaluation of pelvic anatomy, support, and mesh implants are some indications.

CLINICAL APPLICATIONS OF SONOGRAPHY

Transvaginal sonography is often preferred for early evaluation of pelvic pain, abnormal uterine bleeding, pelvic mass, early pregnancy complications, and infertility practices. Many of these topics and their radiologic characteristics are covered in other chapters. Some remaining important subjects are presented in the following sections.

Intraabdominal Fluid

During general sonographic evaluation of the pelvis, a small amount of free fluid, as little as 10 mL, is commonly present in the posterior cul-de-sac (Khalife, 1998). If free fluid is seen extending to the fundus of the uterus, it is considered moderate in amount. Once identified, moderate free fluid should prompt further evaluation of the paracolic gutters and Morison pouch in the right upper quadrant to assess the fluid's extent (Fig. 2-20). If it fills these areas, then the minimum volume of intraperitoneal fluid approximates 500 mL (Abrams, 1999; Branney, 1995). Large amounts of anechoic free peritoneal fluid generically described as *ascites* suggest a volume status abnormality or an infectious or inflammatory etiology. Free fluid that contains low-level echoes or echogenic debris is consistent with hemoperitoneum with clot, such as with a ruptured hemorrhagic ovarian cyst or ectopic pregnancy.

Focused assessment with sonography for trauma (FAST) is a limited sonographic examination directed solely to help diagnosis intraperitoneal bleeding. With FAST, four specific areas are imaged: perihepatic (right upper quadrant), perisplenic (left upper quadrant), pelvis, and pericardium. For intraperitoneal free fluid identification, FAST is a rapid, noninvasive, bedside test and has significant advantages compared with diagnostic peritoneal lavage or with CT. However, FAST has a significant false-negative rate (Scalea, 1999). This stems in part from examination being carried out early when only a small amount of free fluid may have collected in dependent portions of the peritoneal cavity.

Malignant Ovarian Characteristics

Sonography is commonly the initial and often the only imaging procedure performed during pelvic and ovarian mass evaluation, as most can be correctly categorized based on grayscale and Doppler ultrasound characteristics. Found in Table 10-2 (p. 221), recommendations from a Society of Radiologists in Ultrasound consensus conference summarize a reasonable management approach to asymptomatic ovarian and other adnexal cysts imaged sonographically (Levine, 2010).

Sonography is the best preoperative diagnostic technique to determine the malignant potential of an ovarian mass

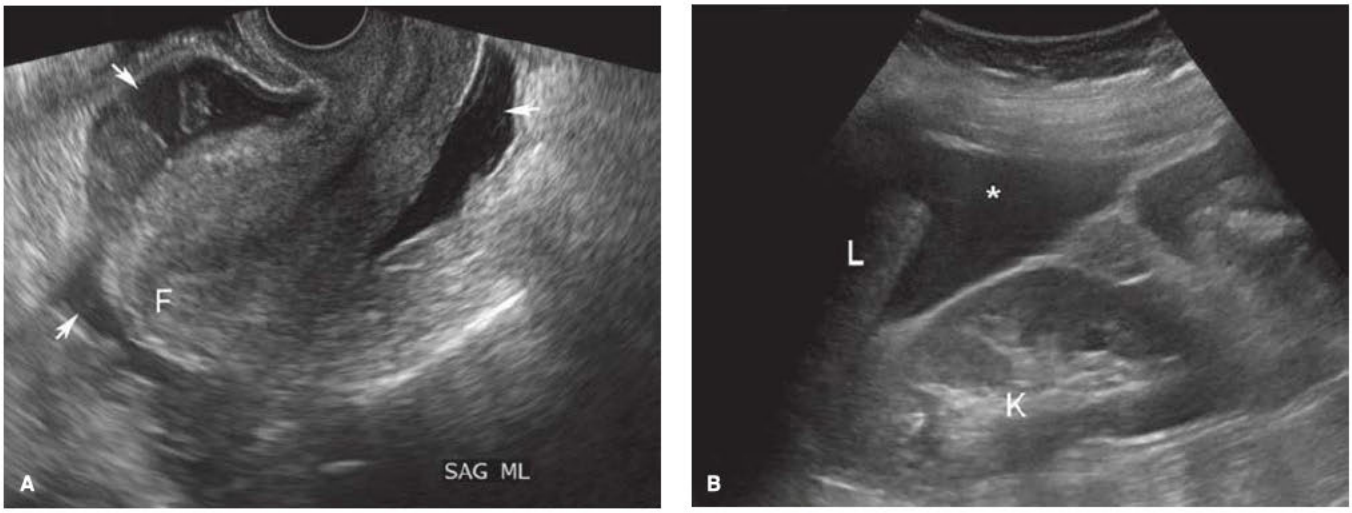


FIGURE 2-20 Hemoperitoneum. **A.** In this transvaginal image, a large amount of free fluid (*arrows*) is seen in the posterior cul-de-sac, above the fundus of the uterus, and in the anterior cul-de-sac. Floating clot is also seen in the anterior cul-de-sac. **B.** Transabdominal image of Morison pouch in the right upper quadrant. Free fluid, corresponding to the dark anechoic area (*asterisk*), is visualized between the liver edge (*L*) and the kidney (*K*), which suggests a large-volume hemoperitoneum.

(Twickler, 2010). To this end, morphologic scoring systems based on number and thickness of septa, presence and number of papillations, and proportion of solid tissue within the mass have been proposed to standardize findings (DePriest, 1993; Sassone, 1991). When size, morphology, and structure of adnexal masses are combined with color Doppler and spectral analysis of flow signals, the specificity and positive predictive value of sonographic diagnosis are increased (Buy, 1996; Fleischer, 1993; Jain, 1994; Kinkel, 2000). The International Ovarian Tumor Analysis (IOTA) Group has developed the most accurate mathematic model to date to calculate the malignancy risk of an adnexal mass based on sonographic features (Timmerman, 2005, 2016). We use the Ovarian Tumor Index developed by Twickler and colleagues (1999) at our institution.

Neovascularity secondary to angiogenesis within a malignant neoplasm increases color Doppler flow signals. These new vessels are abnormal, lack smooth muscle, and contain multiple arteriovenous shunts. Consequently, low-impedance flow is expected with such masses (see Fig. 2-4) (Kurjak, 1992; Weiner, 1992). Moreover, most malignant lesions appear well-vascularized and display flow signals in both peripheral and central regions—including within septations and solid tumor areas. In contrast, most benign tumors appear poorly vascularized. Of Doppler parameters, the color content of a tumor probably reflects tumor vascularity better than any other. The overall impression of this vascularity reflects both the number and size of vessels and their functional capacity. The IOTA group scoring system uses this subjective semiquantitative assessment of flow to describe the vascular features of ovarian masses (Ameye, 2009; Timmerman, 2005). A four-point color score is used to describe tumor blood flow only within septa and solid portions of the mass (Timmerman, 2000). However, because of overlap of vascular parameters between malignant and benign neoplasms, a firm differential diagnosis based on spectral Doppler evaluation alone is not possible (Valentin, 1997).

Pelvic Inflammatory Disease

With acute salpingitis, pelvic sonography is commonly performed as part of an acute pain assessment. However, large studies evaluating its sensitivity, specificity, or overall usefulness for PID diagnosis are lacking (Romosan, 2014). Sonographic findings vary according to disease severity, and in early infection, anatomy may appear normal. With progression, early nonspecific findings include free pelvic fluid, endometrial thickening, endometrial cavity distention by fluid or gas, and indistinct borders of the uterus and ovaries. Enlarged ovaries with increased numbers of small cysts—a "polycystic ovary appearance"—can correlate with PID. With treatment, this ovarian enlargement resolves (Cacciatore, 1992).

Sonographic findings of the fallopian tubes are the most striking and specific landmarks of PID (Fig. 2-21). Although normal tubes are rarely seen unless surrounded by ascites, tubal wall inflammation allows visualization with sonography. As the lumen occludes distally, the tube distends and fills with pus. Various appearances result. The tube may become ovoid or pear shaped, filling with fluid that may be anechoic or echogenic. The tubal wall becomes thickened, measuring ≥5 mm, and

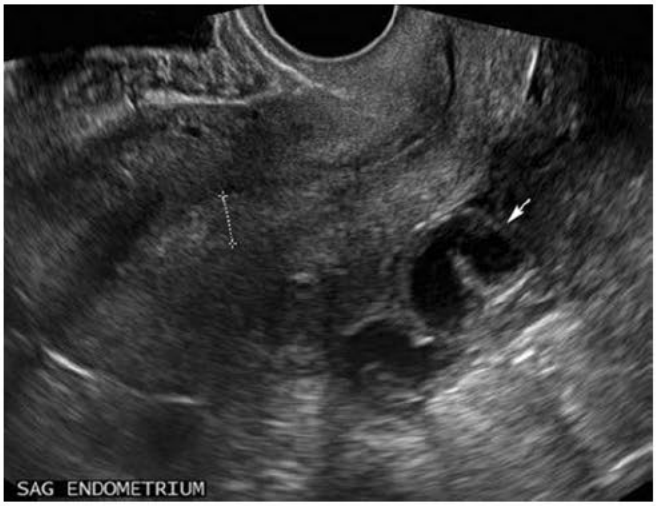


FIGURE 2-21 Transvaginal sonogram of an inflamed, dilated fallopian tube (*arrow*) demonstrating thickened tubal walls, incomplete septa, and intratubal fluid.

incomplete septa are common as the tube folds back on itself. If the distended tube is viewed in cross section it may demonstrate the cogwheel sign, due to thickened endosalpingeal folds (Timor-Tritsch, 1998). Typically, the swollen fallopian tubes extend posteriorly into the cul-de-sac, rather than extending cephalad and anterior to the uterus as large ovarian tumors tend to do. Fluid-debris levels are often visualized in the dilated tubes, and rarely, gas-fluid levels or echogenic bubbles of gas are seen. Color and power Doppler show increased flow from hyperemia in the walls and in incomplete septa of the inflamed tubes (Tinkanen, 1993).

As the disease progresses, the ovary can become involved. When an ovary adheres to the fallopian tube, but is still visualized, it is called a *tuboovarian complex*. In contrast, a *tuboovarian abscess (TOA)* results from a complete breakdown of ovarian and tubal architecture such that the separate structures are no longer identified (Fig. 2-22). If the contralateral side was

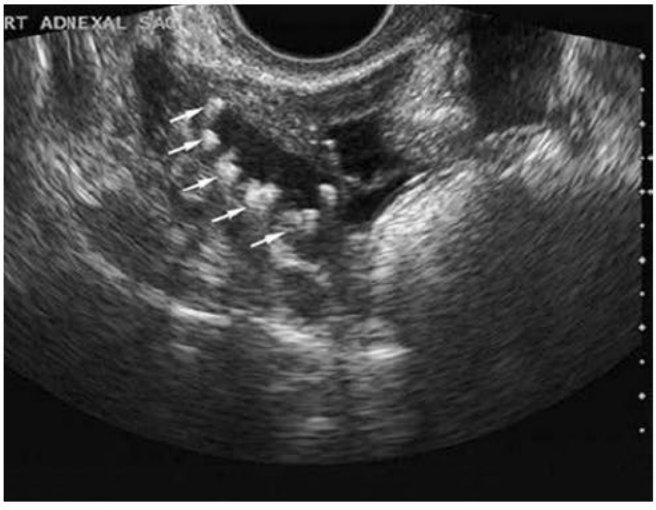


FIGURE 2-22 "Beads on a string" sign. The echogenic mural nodules shown here (*arrows*) within this tuboovarian abscess are thought to represent flattened and fibrotic endosalpingeal folds of the inflamed fallopian tube.

not affected initially, it may become so. When both tubes are inflamed and occluded, the entire complex typically acquires a U-shape as it fills the cul-de-sac, extending from one adnexal region to the other. The lateral and posterior uterine borders become obscure, and individual tubes and ovaries cannot be distinguished. In women not responding to medical therapy, sonography or CT can be used to guide percutaneous or transvaginal drainage of TOAs.

Findings of chronic PID include hydrosalpinx. As discussed in Chapter 10 (p. 229), several sonographic findings such as its tubular shape, incomplete septa, and hyperechoic mural nodules can help to distinguish a hydrosalpinx from other cystic adnexal lesions. If color flow is detected in a hydrosalpinx, it tends to be less exuberant than flow seen in acute PID. Molander and colleagues (2002) found a higher pulsatility index in patients with a chronic hydrosalpinx (1.5 ± 0.1) than with acute PID (0.84 ± 0.04).

A small number of women with prior PID may have a peritoneal inclusion cyst. These form when ruptured ovarian cyst fluid is trapped around the ovary by adhesions. This diagnosis is suspected if the ovary is surrounded by fluid loculations created by thin septations.

Infertility

For female infertility evaluation, sonography can help identify abnormal pelvic anatomy, detect contributory pathology, and evaluate cyclic physiologic uterine and ovarian changes. During treatment, sonography aids ovarian surveillance to guide management.

Sonography easily demonstrates many uterine defects that may affect both gamete passage and ovum implantation. TVS can display submucous leiomyomas and polyps, but their relationships with the endometrial surface are better seen with SIS. As a screening tool for cavity evaluation in this setting, SIS appears to be twice as accurate as HSG or TVS (Seshadri, 2015). Many infertility specialists now incorporate SIS as a first-line screening tool for uterine evaluation before embryo transfer in women undergoing IVF, ovum donation, or IVF-surrogacy. Intrauterine adhesions, also termed *synechiae*, are displayed as hypoechoic lines disrupting the echogenic endometrium. These are more definitively seen during SIS as echogenic bands extending from one endometrial surface to the other (Fig. 2-23).

TVS also can help detect congenital uterine anomalies related to infertility or early spontaneous abortion. The addition of 3-D techniques raises sonographic test performance to a level similar to that of HSG, laparoscopy, and MR imaging. Thereafter, MR imaging is used to characterize and evaluate complicated or equivocal cases, especially preoperatively (p. 49).

Of abnormalities, a fusion anomaly, such as uterus didelphys, can be accurately diagnosed by sonography. In this setting, two divergent uterine horns are separated by a deep fundal cleft, and a wide angle separates the two endometrial cavities (Fig. 2-24). In contrast, bicornuate and septate uterine anomalies are less confidently differentiated by traditional 2-D TVS techniques. Ideally, the angle between the two endometrial cavities is $\geq 105°$ for bicornuate uterus, but $\leq 75°$ for septate uterus. The fundal shape shows a >1-cm notch for bicornuate uterus, but a <1-cm notch for septate uterus (Reuter, 1989).

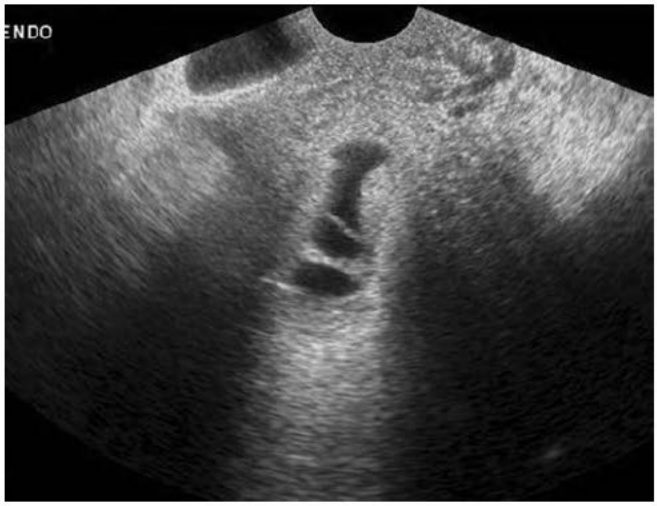


FIGURE 2-23 Asherman syndrome. Transvaginal saline-infusion sonography demonstrates echogenic intrauterine synechiae.

However, in many cases, the distinctions between bicornuate and septate uteri are subtle. In a 3-D coronal plane, relationship between the uterine fundus and the *intercornual line*—the line joining both horns of the uterine cavity—can be measured to aid diagnosis (Fig. 2-25). Similarly, arcuate versus partial septate uteri can be correctly differentiated using quantitative measurements of the endometrial cavity fundal indentation depth in the coronal plane. Combining 3-D TVS findings with SIS provides accuracy up to 90 percent to distinguish the two anomalies. Although MR imaging is frequently employed, 3-D sonography is considered by many to be the best noninvasive method for distinguishing between these uterine anomalies (Bermejo, 2010).

A unicornuate uterus without a rudimentary horn is seen as a small, well-formed elliptical uterus that deviates to one side. The fundus is concave. With 3-D imaging, the unicornuate uterus has a classic "banana" configuration (Fig. 2-26). In 65 percent of cases, however, the unicornuate uterus is associated with a

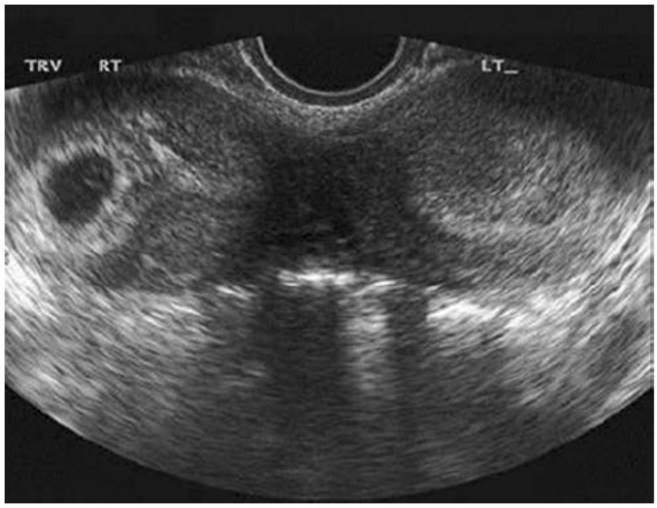


FIGURE 2-24 Uterus didelphys. Transvaginal sonogram in the transverse plane best depicts the two completely separate uterine horns. A gestational sac is evident in the right uterus.

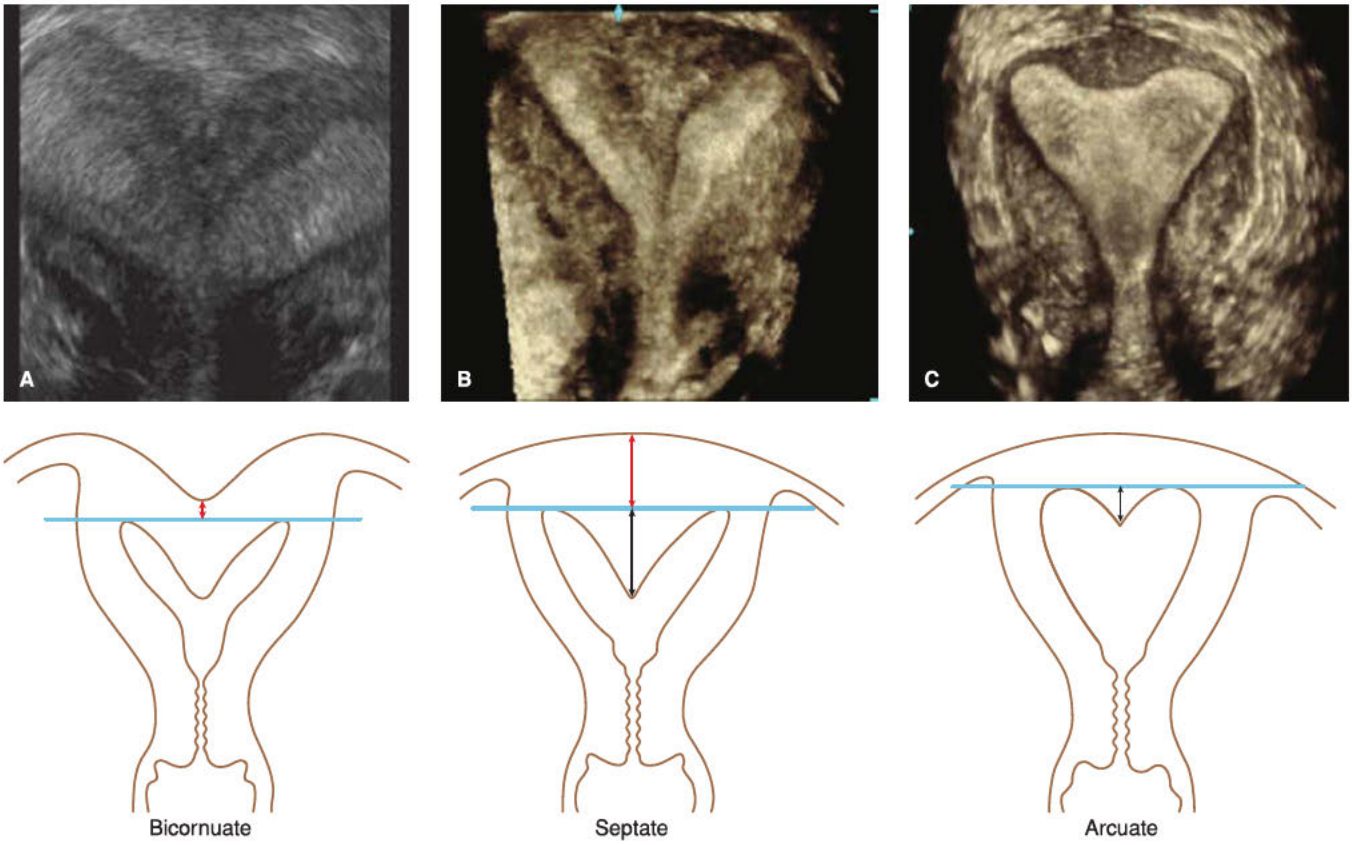


FIGURE 2-25 Three-dimensional (3-D) images of müllerian uterine anomalies in the coronal plane and corresponding diagrammatic uteri. **A.** Bicornuate uterus. This 3-D rendered image demonstrates a concave external fundal contour that dips to a point near the intercornual line. This point lies no further than 5 mm from the intercornual line (*red line*), which characterizes a bicornuate uterus. The 5-mm defining distance, either above or below the intercornual line, is used to differentiate bicornuate and septate uteri. **B.** Septate uterus. This image depicts the narrow angle between the two small endometrial cavities, which is characteristic of a septate uterus, and shows a normal uterine serosal contour. This contour extends >5 mm (*red line*) above the intercornual line, which is characteristic of a septate uterus. The septum ends at the uterine isthmus and does not extend into the cervix. Thus, this anomaly is properly termed *subseptate*. **C.** Arcuate uterus. This image illustrates the normal uterine contour and obtuse angle of the endometrial cleft that is characteristic of an arcuate uterus. The cleft extends <15 mm (*black line*) below the intercornual line, which is characteristic of arcuate uterus. In diagram B, the distance (*black line*) between the cleft and intercornual line is >15 mm, which reflects a septate uterus. This 15-mm defining distance is used to differentiate arcuate and septate uteri.

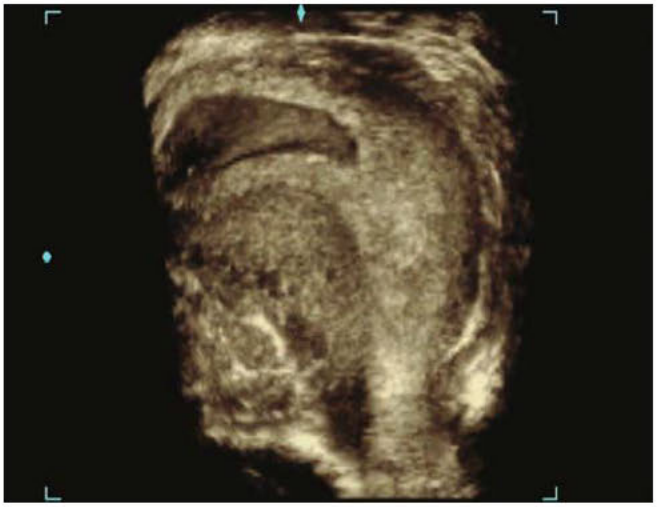


FIGURE 2-26 Unicornuate uterus. The coronal plane of 3-dimensional sonography illustrates the classic "banana" configuration. A gestational sac is seen within the endometrial cavity.

rudimentary horn, which is difficult to recognize sonographically (Fig. 19-11, p. 420) (Jayasinghe, 2005). A rudimentary horn is often misdiagnosed as a uterine or adnexal mass. Complete evaluation of these cases often requires MR imaging. With most uterine anomalies, especially if unilateral, proper positioning of the kidneys should be documented with transabdominal imaging. This is because of the close link between reproductive and urinary anomalies. Last, in women with complex anomalies associated with vaginal agenesis or imperforate hymen, hematocolpos is often seen and frequently is associated with hematometra or hematosalpinx.

Pelvic endometriosis is a prominent cause of infertility, and sonography is the most common imaging procedure in suspected cases. It is most effective to evaluate endometriotic ovarian cysts, and its capability to detect small implants and adhesions is limited. Endometriomas exhibit various sonographic appearances, the most frequent being a pelvic mass with a thick wall and diffuse low-level echoes within the cyst (Fig. 11-4, p. 239). Magnetic resonance imaging is more specific than sonography for identifying endometriomas, and thus,

it is indicated in cases with unclear anatomy sonographically (Fig. 11-5, p. 240).

Sonography is invaluable for infertility treatment surveillance. First, folliculogenesis both in normal and stimulated cycles can be monitored. Observation of a developing follicle and ovulation prediction allow optimal timing for postcoital testing, human chorionic gonadotropin (hCG) administration, intercourse, insemination, and ovum collection. At ovulation, the dominant follicle usually disappears, and fluid is observed in the cul-de-sac. At the follicular site, the corpus luteum appears as an irregular oval containing a small quantity of fluid, internal echoes, and a thick wall. In general, blood flow in the ovulating ovary diminishes throughout the menstrual cycle. At ovulation, blood flow velocities dramatically rise in vessels surrounding the corpus luteum because of neovascularization and are seen as low-impedance waveforms. In women undergoing in vitro fertilization (IVF), low ovarian vessel impedance may correlate directly with pregnancy rates (Majeed, 2018).

Sonography can be used to guide interventional maneuvers such as oocyte retrieval and transfer of embryos into the endometrial cavity (Figs. 21-10 and 21-12, p. 465). In stimulated cycles, sonographic detection of too many follicles allows withholding of hCG induction to prevent ovarian hyperstimulation syndrome (Fig. 21-4, p. 457). If this develops, sonography is used to grade disease severity through measurements of ovarian size, detection of ascites, and analysis of renal flow resistances.

Ultrasound Beyond the Pelvis

Ultrasound is used throughout the body. It is often the initial tool in radiologic evaluation, given its lack of ionizing radiation, low cost, and availability. In the abdomen, common indications for solid organ evaluation include abdominal and flank pain, jaundice, hematuria, organomegaly, or palpable mass. Abnormal blood tests, including elevated liver function tests and creatinine, also may be indications for an abdominal ultrasound. Typically, a limited or right upper quadrant ultrasound includes the liver, gallbladder, common bile duct, pancreas, and right kidney. A complete abdominal ultrasound adds the spleen, left kidney, and images of the aorta and inferior vena cava in the upper abdomen. Ideally, a patient has fasted prior to sonographic evaluation of the abdomen. This minimizes bowel gas and permits adequate gallbladder distention. A renal ultrasound focuses on the kidneys, proximal collecting systems, and urinary bladder. Outside of the abdomen and pelvis, a gynecologist may select ultrasound to evaluate superficial structures, like the thyroid gland and breasts. Breast imaging is discussed fully in Chapter 13 (p. 279).

Compression Sonography

Compression sonography, often combined with color Doppler sonography, is the initial test currently used to detect deep-vein thrombosis (DVT) (Hanley, 2018; Needleman, 2018). Leg vein interrogation is divided into two components. First, the groin and thigh are examined with the patient supine. Then, the popliteal region is evaluated with the patient sitting or lying on her side with the thigh abducted and externally rotated. Some institutions also evaluate the calf veins. Impaired visibility, noncompressibility, and the typical echo pattern of a thrombosed vein confirm the diagnosis (Fig. 2-27).

Examination of the femoral, popliteal, and calf trifurcation veins in symptomatic patients is more than 90-percent sensitive and greater than 99-percent specific for proximal DVT (Davis, 2001). Moreover, in 220 patients with suspected DVT, Lensing and coworkers (1989) compared compression sonography with contrast venography, which is the gold standard for DVT detection. Both the common femoral and popliteal veins were fully compressible—no thrombosis—in 142 of 143 patients who had a normal venogram (99-percent specific). All 66 patients with proximal vein thrombosis had noncompressible femoral or popliteal veins or both (100-percent sensitive).

For detecting calf vein thrombosis, compression sonography is significantly less reliable. Eventually, isolated calf thromboses extend into the proximal veins in up to a fourth of cases. They do so within 1 to 2 weeks of presentation and thus are usually detected by serial sonographic compression examinations (Bates, 2004). The safety of withholding anticoagulation for those symptomatic patients who have a normal compression examination has been established (Birdwell, 1998; Friera, 2002). Importantly, normal venous sonographic findings do not necessarily exclude pulmonary embolism (PE) because the thrombosis may have already embolized or because it arose from deep pelvic veins, which are inaccessible to sonographic evaluation (Goldhaber, 2004).

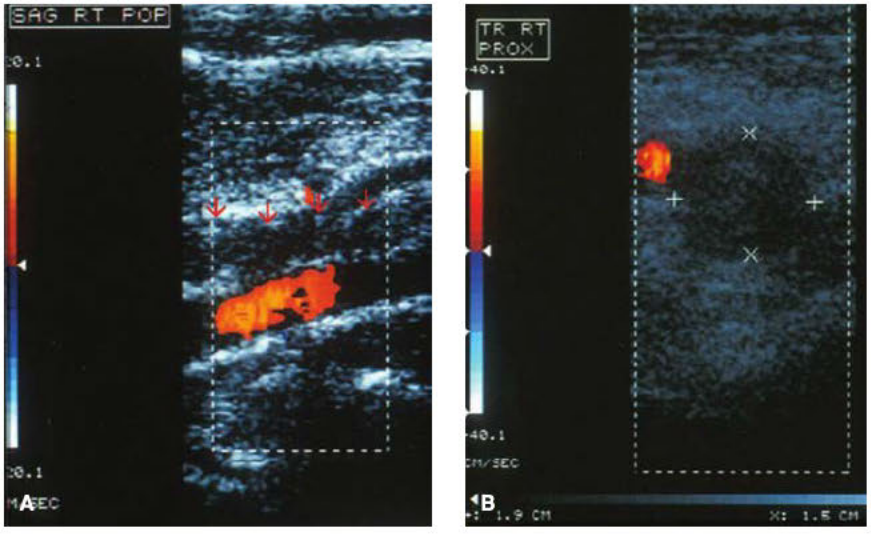


FIGURE 2-27 Sagittal **(A)** and transverse **(B)** images from a lower extremity. Color Doppler ultrasound study in a woman with popliteal vein thrombosis. **A.** Red arrows demarcate the popliteal vein with no flow suggesting clot in the lumen, which sits above the artery demonstrating normal flow as evidenced by the red color map. **B.** The transverse image shows the large size of the vein due to the thrombus (*cursors*), as well as normal flow in the artery, evidenced by the red color map.

RADIOGRAPHY

Radiographs are used in gynecologic practice in a manner similar to other medical specialties. Of frequently used studies, the *acute abdominal series* includes an upright radiograph of the chest to exclude free air under the diaphragm, an upright film of the abdomen to exclude air-fluid levels within bowel loops, and a supine image to measure bowel loop widths. It is commonly selected as an initial modality if bowel obstruction or perforation is a concern. Importantly, images from those with recent laparotomy or laparoscopy often show expected subdiaphragmatic air. In contrast, a single supine radiograph of the abdomen is called a KUB (kidneys, ureters, and bladder). It may help identify an extrauterine location of a missing IUD or a collecting-system stone.

In women with gynecologic malignancies, radiographs also may be informative. Examples are chest radiographs to screen for pulmonary metastases during cancer staging and during surveillance after initial treatment. As discussed in the next sections, several specialized radiographic procedures are especially useful or specific for gynecology.

Intravenous Pyelography

Excretory urography, also called *intravenous pyelography (IVP)*, provides serial images of the urinary tract. The initial radiograph, termed a *scout film*, helps identify radiopaque urinary calculi. IV contrast is then administered, and the concentrating function of the proximal tubules renders renal parenchyma radiodense within 1 to 3 minutes. This *nephrogram phase* displays renal size, contour, and axis. Next, a radiograph obtained 5 minutes after agent injection depicts contrast excreted into the collecting system. During this *pyelogram phase,* the calyces and proximal ureters are evaluated for symmetry and excretion promptness. Serial imaging is obtained as the more distal collecting system and bladder are opacified by contrast, and a final postvoid radiograph completes the series.

Up to 5 to 10 percent of women have an allergic reaction to iodide during IVP, and 1 to 2 percent of reactions are life threatening. In addition, hyperosmolar ionic contrast can be nephrotoxic because of direct tubular insult and ischemic injury. Notably, women with diabetes, renal impairment, and congestive heart failure are at high risk for this contrast nephrotoxicity. As alternatives, nonionic low and isoosmolar iodinated contrast media carry a five- to 30-fold lower incidence of allergic reactions and are less nephrotoxic (Mishell, 1997). Because of this improved safety profile, most centers no longer use intravascular hyperosmolar ionic contrast.

Preoperatively, IVP may be selected to identify urinary anomalies coexistent with congenital reproductive tract defects or confirm lower urinary tract compression by an adjacent pelvic mass. However, many preoperative IVPs have been replaced with multiphasic CT urography protocols performed on multislice CT scanners (Beyersdorff, 2008). For example, as it now is a suitable element of cervical cancer staging, many clinicians substitute CT imaging for IVP in initial cervical cancer evaluation. Of value, CT allows the cervix, parametria, uterus, adnexa, retroperitoneal lymph nodes, liver, and ureters to be imaged concurrently.

For suspected nephrolithiasis, the American College of Radiology recommends primary evaluation using noncontrast CT given its superior sensitivity for these stones (Moreno, 2015). To evaluate hematuria, noncontrast combined with contrast-enhanced CT images (CT urography) is most appropriate because of its improved sensitivity for renal and urothelial masses. Although IVP has higher in-plane spatial resolution, the current recommendations are to move immediately to initial one-step CT evaluation as CT is frequently needed regardless of IVP results to delineate abnormalities (Cowan, 2007, 2012). That said, IVP may still play a role, especially in resource-poor areas, in postoperative patients, and in those for whom radiation exposure is ideally minimized. Specifically, IVP delivers an average adult effective dose of 1 to 10 mSv, whereas CT urography carries an average adult effective dose of 10 to 30 mSv (Moreno, 2015).

Voiding Cystourethrography and Positive Pressure Urethrography

These radiographic procedures are used to evaluate the female urethra. Voiding cystourethrography (VCUG) is performed by placing a small catheter into the urinary bladder to instill contrast media. If present, diverticula that open into the urethra will fill with contrast. In cases of suspected vesicovaginal or urethrovaginal fistula, the contrast trail connecting the two involved structures is seen.

In comparison, MR imaging permits superior visualization of urethral abnormalities and is more sensitive than VCUG or positive pressure urethrography (PPUG) for delineating diverticula with complex structure (Chou, 2008; Neitlich, 1998). For this reason, VCUG is currently more often used to evaluate lower urinary tract injury, such as fistulas, and patients with prolonged urinary retention, incontinence, or suspected vesicoureteral reflux.

Described in more detail in Chapter 26 (p. 583), PPUG use has declined. This stems mainly from fewer technicians trained to complete the study, difficulty finding appropriate equipment, and the higher sensitivity of MR imaging.

Hysterosalpingography

This radiographic imaging technique is typically used during infertility evaluations to assess the endocervical canal, the endometrial cavity, and the fallopian tube lumina by injecting radiopaque contrast material through the cervical canal (Chap. 20, p. 438). An average HSG study is performed in 10 minutes, involves approximately 90 seconds of fluoroscopic time, and has an average radiation exposure to the ovaries of 0.01 to 0.02 Gy. As discussed previously (p. 32), hysterosalpingo-contrast sonography is used by some initially in place of HSG to assess tubal patency.

Hysterosalpingography is performed between cycle days 5 and 10. During this time, cessation of menstrual flow minimizes infection and the risk of flushing an ovum from the fallopian tube following ovulation. The test causes cramping, and an NSAID taken 30 minutes prior to the procedure may limit discomfort. To begin, a designated balloon-tipped injection catheter or acorn cannula is introduced just beyond the internal os in

the lower endometrial cavity, as this location is more comfortable for the patient. However, the catheter may also be positioned just beyond the external os within the endocervical canal if necessary. A paracervical block may be indicated in selected patients, such as those with cervical stenosis. Because rapid injection may cause tubal spasm, slow contrast injection of usually no more than 3 to 4 mL of contrast medium allows a clear outline of the uterine cavity. Generally, few radiographic views are needed: a preliminary view before injecting contrast, a view showing uterine cavity filling, and the third demonstrating spill of contrast from the tubes into the peritoneal cavity. An additional image with the catheter deflated and pulled back into the endocervical canal will typically be obtained at the conclusion of the examination to evaluate the lower uterine cavity and internal os.

A normal endometrial cavity is usually triangular or sometimes T-shaped in the anteroposterior (AP) projection (Fig. 20-6, p. 439). In a lateral view, it is oblong. The contour of the endometrium is usually smooth. It occasionally has polypoid filling defects that can be isolated or diffuse and can be difficult to distinguish from endometrial polyps or hyperplasia. Inadvertent injection of air bubbles introduces artifact. In these instances, SIS is often later obtained to further interrogate the endometrial cavity.

Contraindications to HSG include acute pelvic infection, active uterine bleeding, pregnancy, and iodine allergy. HSG complications are rare but can be serious. Of these, the overall risk of acute pelvic infection serious enough to require hospitalization is <1 percent but can reach 3 percent in women with prior pelvic infection (Stumpf, 1980). In patients with no history of pelvic infection, HSG is performed without prophylactic antibiotics. If HSG demonstrates dilated fallopian tubes, doxycycline, 100 mg orally twice daily for 5 days, is given to reduce the incidence of post-HSG PID. In patients with a history of pelvic infection, doxycycline can be administered before the procedure and continued if dilated fallopian tubes are found (American College of Obstetricians and Gynecologists, 2018). Pelvic pain, uterine perforation, and vasovagal reactions also may occur. From the contrast, allergic reaction and entry into the vascular system from high injection pressure are potential risks.

Selective Salpingography

In some cases, it is not possible to distinguish whether tubal blockage seen by HSG is caused by anatomic occlusion or tubal spasm. Described in Chapter 44 (p. 1067), hysteroscopic tubal cannulation can further clarify and treat many cases of proximal tubal occlusion. Alternatively, transcervical selective salpingography and tubal catheterization (SS-TC) under fluoroscopic guidance is another suitable procedure. Similar to HSG, it is performed during the follicular phase. The tubal catheter is forwarded through the cervix and advanced by tactile sensation to the tubal ostium. The position of the catheter is checked fluoroscopically, and water- or oil-soluble contrast is injected. If the obstruction is overcome, the tubal contour is outlined with contrast agent. If the proximal tubal obstruction persists, a guide wire is threaded through the inner cannula of the catheter, advanced toward the obstruction, and gently manipulated to overcome the blockage. The guide wire is then withdrawn, and contrast medium is injected through the catheter to confirm patency. This fluoroscopic tool is effective at diagnosing and treating proximal tubal blockage, as discussed in Chapter 21 (p. 459) (Capitanio, 1991; Thurmond, 1991).

Bone Densitometry

Depending on its mineral density, bone absorbs x-rays to different degrees. Because of this, bone density can be determined, and most measurements provide site-specific information. However, these studies do not assess current or past bone remodeling rates. Thus, sequential density measurements are necessary to monitor rates of bone loss over time (Kaplan, 1995).

Dual-energy x-ray absorptiometry (DEXA) measures integral bone (cortical and trabecular bone) mineral density and is the preferred method to diagnose osteoporosis and monitor treatment (Fig. 22-9, p. 488). DEXA employs two x-ray beams of differing energy levels and accurately measures bone density in the hip and spine. The spine is commonly scanned between the first and fourth lumbar vertebrae. DEXA measurements are accurate; radiation dose is low (<5 mrem); and patient acceptability is high because the procedure time is usually only 5 to 15 minutes (Jergas, 1993). Of disadvantages, DEXA is a 2-D technique that cannot distinguish between cortical and trabecular bone. In addition, bone spurs, aortic calcifications, and arthritis may falsely elevate reported bone density.

Quantitative computed tomography (QCT) evaluates bone mineral in high-turnover trabecular bone. QCT uses multiple x-rays to provide a cross-sectional view of the vertebral body. As the rate of turnover in trabecular bone is nearly eight times that in cortical bone, this technique can detect early metabolic changes in this highly vulnerable tissue. It provides a volumetric density, which is an advantage in situations in which DEXA may underestimate bone mineral density (Damilakis, 2007). Although its precision is excellent, it has never been validated for World Health Organization (WHO) criteria and is not routinely used as a screening modality.

COMPUTED TOMOGRAPHY

This procedure involves multiple exposures of thin x-ray beams that are translated to 2-D axial images, termed a *slice*, of the particular area of interest. Multiple slices of the targeted body part are obtained along its length. Multiple-channel helical CT, also called *spiral CT*, allows for continuous acquisition of images in a spiral and the potential for image reformatting in multiple planes. This technique is much faster and permits images to be manipulated for analysis after they have been acquired. Many variables affect radiation dose, especially slice thickness and number of cuts obtained. If a study is performed with multiple phases of contrast, each added phase or acquisition multiplies the total patient dose of radiation.

IV contrast enables superior evaluation of solid organ parenchyma and vasculature. By adding IV contrast, masses become more obvious due to density differences. Dedicated thin-slice evaluation of vasculature, termed CT angiography (CTA) can be done throughout the body. Traditional (fluoroscopic) angiography is still performed, but cross-sectional CT imaging provides

accurate information and is technically easier. As discussed earlier, IV nonionic low and isoosmolar iodinated contrast media can induce nephrotoxicity and are used with caution in patients with or with risks for renal insufficiency. IV hydration before and after an examination can help reduce contrast-induced nephrotoxicity. One option is 0.9-percent saline at 100 mL/hr beginning 6 to 12 hours before imaging and continuing 4 to 12 hours after the examination (American College of Radiology, 2018).

Oral contrast may enhance CT images if gastrointestinal disease is sought or if bowel must be differentiated from adjacent structures. Positive oral contrast is most frequently used and is dense (white) on scan images. Patients with documented allergies to IV contrast are rarely allergic to oral contrast. Intraluminal contrast in the rectum or urinary bladder also is dense (white) and can be used to address a specific concern, such as rectovaginal fistula or bladder injury, respectively.

Normal Pelvic Anatomy

The uterus appears as a homogenous, soft tissue oval or triangle situated posterior to the bladder (Fig. 2-28). The uterine walls enhance after IV contrast. However, unlike sonography and MR imaging, the endometrium is poorly delineated by CT imaging. The cervix also may not enhance like the remainder of the uterus, and the inner stromal layer typically enhances less than the outer stromal layer (Yitta, 2011). The endocervical canal, which can be identified by MR imaging, is indistinct using CT imaging. The lateral margins of the cervix can typically be differentiated from parametrial fat because of differences in density. However, CT is not sensitive for parametrial involvement in the setting of cervical cancer (Hricak, 2005). Imaging of the vagina and vulva is very limited with CT. Typically, the ovaries are relatively hypodense, vary in appearance and position, and are usually situated lateral to the uterus.

Imaging Following Gynecologic Surgery

CT is well suited to diagnose potential complications of gynecologic procedures. For ureteral injuries, CT with IV contrast or CT urography is useful. To detect obstruction or injury, CT images are obtained after the kidneys have excreted the contrast and have opacified the collecting systems. High-density (white) contrast that abruptly stops within the ureter suggests obstruction. With ureteral disruption, contrast may flow freely from the injury site or may form an encapsulated collection, a *urinoma* (Titton, 2003).

For bladder injury, CT cystography may be informative. For this, the bladder is retrograde filled with 300 to 400 mL of dilute iodinated contrast by gravity drip. This is followed by helical CT of the bladder with multiplanar reformations (Chan, 2006). The technique is sensitive and specific for diagnosis of extraperitoneal and intraperitoneal bladder rupture and can also demonstrate fistulas connecting to the bladder (Jankowski, 2006; Yu, 2004).

CT also outperforms conventional radiography and barium studies for diagnosing bowel complications, such as small bowel obstruction (Maglinte, 1993). For characterizing an abdominal-pelvic fluid collection such as abscess or hematoma, CT with intravenous and oral contrast may be more helpful than other imaging tools (Fig. 3-8, p. 71) (Gjelsteen, 2008).

Gynecologic Malignancy

In most instances, sonography is the preferred initial method of evaluating the female pelvis. For additional information, MR imaging is now often preferable to CT imaging because it avoids radiation exposure and iodinated IV contrast, provides excellent soft-tissue contrast, and displays pelvic structures in multiple planes. However, in many settings, the greater availability of CT is another advantage compared with MR imaging. In addition, to evaluate and monitor gynecologic malignancies, CT imaging is probably the most frequently used imaging technique. Although its sensitivity for intraperitoneal metastases is limited, CT can estimate bulky metastases, such as in women with advanced ovarian cancer.

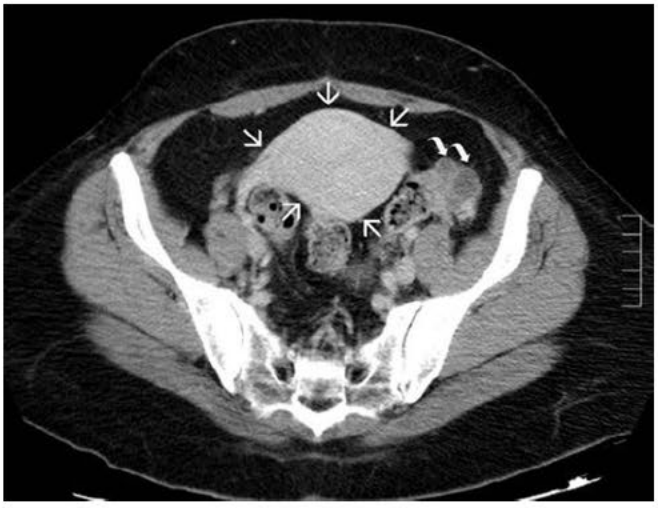


FIGURE 2-28 Computed tomography (CT) of the female pelvis in the axial plane demonstrates the normal uterus (*arrows*) as well as cysts in the left ovary (*curved arrows*).

MAGNETIC RESONANCE IMAGING

With this technology, images are constructed based on the radiofrequency signal emitted by hydrogen nuclei after they have been "excited" by radiofrequency pulses in the presence of a strong magnetic field. The radiofrequency signal emitted has characteristics called *relaxation times*. These include the T1 relaxation time and the T2 relaxation time. The signal intensity of one tissue compared with another, that is, the contrast, can be manipulated by adjusting parameters of the acquisition. Examples are varying the elapsed time between applications of radiofrequency pulses, which is called *repetition time,* and the time between a radiofrequency pulse and sampling the emitted signal, called the *echo delay time*.

Sequences with a short repetition time and short echo delay time are called *T1-weighted*. Sequences with a long repetition time and long echo delay time are regarded as *T2-weighted*. As examples, the hydrogen molecules in a water-containing area have longer relaxation times than those in a solid tissue. Thus, on T1-weighted images, urine in the bladder will appear dark or have low signal intensity. On T2-weighted images, the same urine

will appear bright or have high signal intensity. By manipulating multiple parameters and imaging planes, MR imaging can achieve superior soft-tissue contrast. The strength of the magnetic field within the bore of the magnet is measured in tesla (T) (1 tesla = 10,000 gauss). For reference, the earth's magnetic field is approximately 0.5 gauss. Most clinical magnets used for MR imaging are 1.5 to 3 T or 15,000 to 30,000 gauss.

Technique

The standard imaging technique for the pelvis includes both T1- and T2-weighted sequences that are acquired in at least two planes, usually axial and sagittal. The T2-weighted sequence provides detailed definition of internal organ architecture, such as the uterus, vagina, and ovaries. The T1-weighted sequence clearly delineates organ boundaries and surrounding fat, allows optimal visualization of lymph nodes, and is necessary for tissue and fluid content characterization.

To aid accurate diagnosis, highly paramagnetic gadolinium-based contrast agents (GBCA) are often administered prior to imaging. The most frequently used GBCA types are extracellular agents administered intravenously. Gadolinium shortens the T1 relaxation time of adjacent protons. This increases signal intensity on T1-weighted images to enhance information regarding tissue vascularity (Gandhi, 2006). Side effects are rare, and MR contrast can be used even in those with prior reactions to other contrast agents (American College of Radiology, 2018). MR contrast is given in concentrations and doses significantly lower than that used in CT imaging, undergoes renal excretion within 24 hours, and is safe for patients with mildly compromised renal function. Of note, the Food and Drug Administration recommends caution in administering IV GBCA to patients with moderate to end-stage renal disease due to the rare but serious risk of developing nephrogenic systemic fibrosis (NSF). The risks and benefits of using GBCA are discussed by the requesting physician and radiologist. Written informed consent from the patient is obtained if GBCA use is required for those with a severely diminished glomerular filtration rate. Providing hemodialysis immediately after administration of GBCA for patients in this renal category for NSF prevention has not been proven.

In addition to intravascular GBCA, water-soluble ultrasound gel can be placed endoluminally in the vagina or the rectum to better delineate anatomy. This technique can also aid detection of fistulas or congenital vaginal septa (Gupta, 2016).

Additional imaging parameters include fat saturation to detect bulk fat and opposed-phase imaging to highlight microscopic fat. Diffusion-weighted imaging (DWI) with quantitative measurement of apparent diffusion coefficient (ADC) characterizes proton movement in tissues. Highly cellular tissues restrict random Brownian motion and yield a high DWI signal and low ADC value. This cellularity information can help identify tumor, abscess, and lymph nodes (Moore, 2014).

Safety

To date, harmful or mutagenic effects have not been reported from MR imaging at field strengths used clinically, that is, 3 T or lower. Additionally, the American College of Radiology considers MR imaging in pregnancy to be risk free, regardless of trimester. Using the ALARA (as low as reasonably achievable) principle, imaging during pregnancy is typically limited to 1.5 T. Moreover, GBCA is not used routinely in pregnancy due to the theoretic risk of toxic gadolinium ion dissociation into the amnionic fluid (American College of Radiology, 2017).

TABLE 2-1. Safety of MR Imaging with Some Implanted Devices

Device	Safe (S), Conditional (C), or Unsafe (U)	
	1.5 T	3 T
Intrauterine Devices		
Paragard	S	C
Mirena	S	S
Skyla	—	C
Tubal Occlusion Devices		
Essure	S	C
Adiana (Silicone)	S	S
Adiana (Radiopaque)	S	C
Filshie Clips	S	C
Hulka (Clemens) Clip	S	C
Implants		
Implanon/Nexplanon	S	S
Saline or silicone breast	S	S
Tissue expander with non-magnetic injection site	S	—
Tissue expander with magnetically localizable injection site	U	U
Biopsy Needles/Markers		
Localization wires	U	U
Biopsy needles	U	U
Coaxial needles	U	U
Breast biopsy markers (e.g., HydroMARK)	S	C

Some, but not all, devices preclude MR imaging. For example, many implanted devices unique to women can be safely imaged (Table 2-1). Contraindications to entering the MR environment include mechanically, electrically, or magnetically activated implanted devices such as internal cardiac pacemakers, neurostimulators, cardiac defibrillators, electronic infusion pumps, and cochlear implants. Certain intracranial aneurysm clips and any metallic foreign body in the globe of the eye contraindicate scanning. Before the patient enters the MR environment, radiology personnel should obtain documentation of the type of patient implant (manufacturer, model and type) and verify its MR safety rating.

Use in Gynecology

Although sonography is widely used for suspected gynecologic disease, MR imaging may add information when sonographic

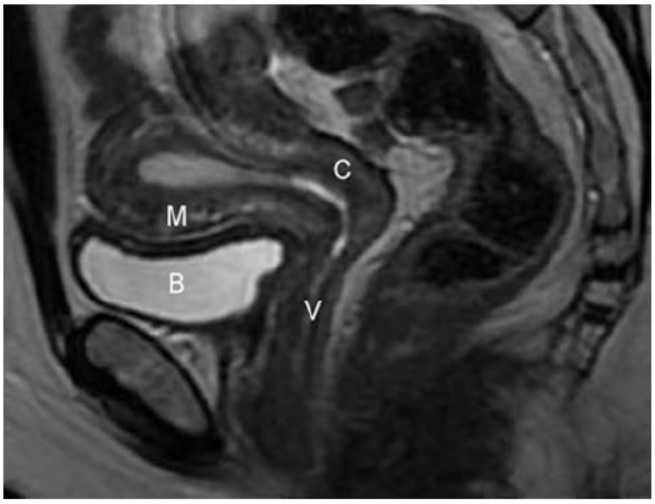


FIGURE 2-29 Sagittal T2-weighted magnetic resonance (MR) image of a normal uterus and cervix (C). B = bladder; M = myometrium; V = vagina.

findings are equivocal. Specifically, its multiplanar imaging, superior soft-tissue contrast, and large field of view are distinct MR imaging advantages. Accordingly, common indications for MR imaging include distorted pelvic anatomy, large masses that are poorly delineated with sonography, indeterminate cases of adenomyosis, and endometrial disorders in poor surgical candidates. In some instances, pelvic MR imaging may help tailor management. Also, MR imaging can be selected for primary evaluation and subsequent surveillance of pelvic malignancies.

Normal Findings

The pelvic organs show generally moderate to low signal intensity on T1-weighted images. T2-weighted images of the menstrual uterus depict a high-signal-intensity endometrium; contiguous low-signal-intensity inner myometrium, which is the junctional zone; and a moderate-signal-intensity outer myometrium (Fig. 2-29) (McCarthy, 1986).

The cervix can be distinguished from the uterine body by its prominent fibrous stroma, which has an overall lower signal intensity. The internal architecture of the cervix is seen on T2-weighted images as central high signal intensity (endocervical glands and mucus) surrounded by low signal intensity (fibrous stroma) and peripheral moderate signal intensity (smooth muscle intermixed with fibrous stroma) (Lee, 1985). Similarly, T2-weighted images of the vagina display central high-signal-intensity mucosa and mucus, which is surrounded by a low-signal-intensity muscular wall (Hricak, 1988). Ovaries are normally seen on the T2-weighted sequence as stroma with moderately high signal intensity that contains very high-signal-intensity follicles (Dooms, 1986). The fallopian tubes are not typically visualized. Hormonal status influences the MR appearance of all structures and reflects associated physiologic changes.

Benign Disease

Leiomyomas

For suspected leiomyomas, the initial imaging technique is sonography. However, its limited field of view, image resolution that declines with increasing patient body fat, and distorted anatomy from large or multiple myomas are potential hindrances (Wolfman, 2006). False-negative rates may reach 20 percent with TVS, and tumors measuring <2 cm are routinely missed (Gross, 1983). Thus, MR imaging is used when TVS findings are equivocal or nondiagnostic (Ascher, 2003). For conservative myoma treatment, the effects of GnRH agonist therapy to shrink tumor volume can be quantified with MR imaging (Lubich, 1991). Moreover, MR imaging is warranted before UAE or focused-ultrasound myoma treatments and often selected prior to hysteroscopic myoma resection. In these cases, imaging verifies leiomyoma location, seeks tumor qualities that portend outcome success or failure, and excludes other causes of patient symptoms such as unsuspected malignancy or indeterminate intracavitary masses (Cura, 2006; Rajan, 2011).

Shown in Figure 2-30, leiomyomas have a variable but characteristic MR appearance and thus can be differentiated from

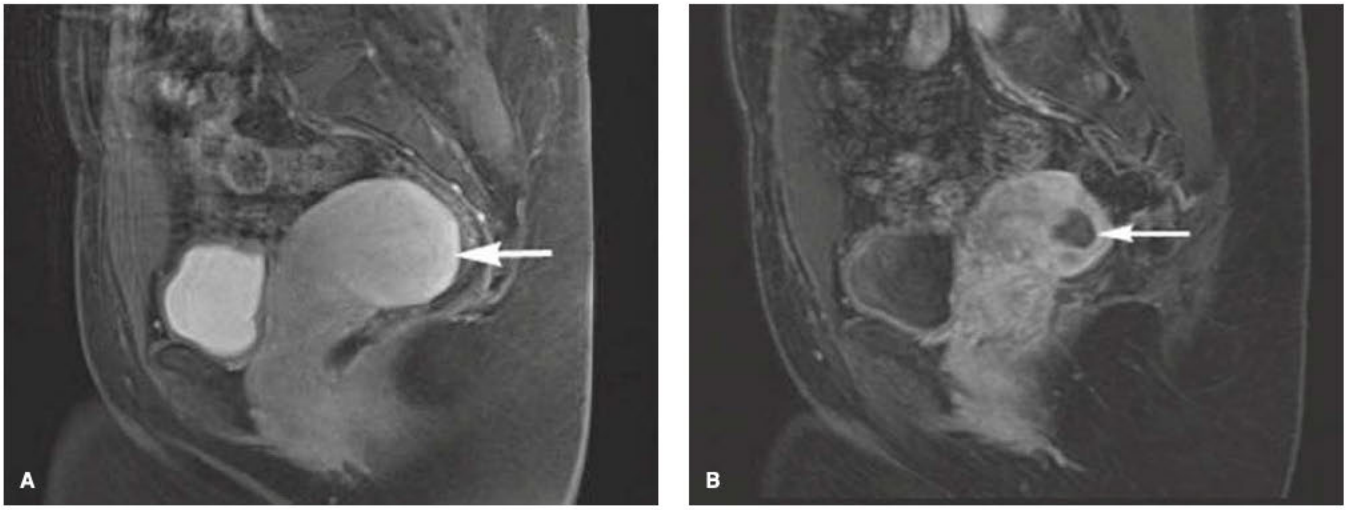


FIGURE 2-30 **A.** Sagittal T1-weighted post-contrast image demonstrates a 5.6-cm enhancing leiomyoma at the uterine fundus (*arrow*). **B.** Sagittal T1-weighted post-contrast image of the same patient 2 months after uterine artery embolization demonstrates lack of enhancement in the fibroid and significant interval decrease in size (now measuring 2 cm).

adenomyosis or adenomyoma with 90-percent accuracy (Mark, 1987; Togashi, 1989). This is important when myomectomy is considered. Leiomyomas, even those as small as 0.5 cm, are best seen on T2-weighted images and appear as round, sharply marginated masses with low signal intensity relative to the myometrium. Tumors >3 cm often are heterogeneous because of varying degrees and types of degeneration (Hricak, 1986; Yamashita, 1993). With MR imaging, multiplanar views allow for accurate tumor localization as subserosal, intramural, or submucosal. Moreover, pedunculated myomas and their bridging stalk can be defined. Of myoma types, intramural or subserosal leiomyomas are frequently circumscribed by a high-signal-intensity rim that represents edema from dilated lymphatics and veins.

Of treatment options, magnetic resonance–guided focused ultrasound (MRgFUS), also called *magnetic resonance high-intensity focused ultrasound (MR-HIFU)*, directs high-power ultrasound pulses—*sonications*—into the myoma. Without MR guidance, focused-ultrasound therapy is hampered by imprecise beam targeting. Fortunately, excellent soft-tissue resolution with MR imaging enables precise tissue targeting. Moreover, MR imaging can measure accurate, near real-time thermometry. This permits power adjustments to reach adequate treatment temperatures yet minimize thermal injury. Pulse duration lasts generally 15 seconds, and a cooling interval is inserted between pulses. The average procedure duration approximates 3.5 hours (Hindley, 2004). This has improved with updated devices. Outcomes, candidate selection, and comparisons with UAE are described in Chapter 9 (p. 209).

Congenital Anomalies

Discussed in Chapter 19 (p. 419), müllerian duct anomalies comprise a spectrum of developmental malformations. In the past, full evaluation required laparoscopy, laparotomy, HSG, and hysteroscopy. These invasive techniques were largely replaced by MR imaging, which has an accuracy of up to 100 percent (Carrington, 1990; Fielding, 1996).

MR imaging is particularly adept at differentiating septate and bicornuate uteri, which is imperative as these two have differing clinical implications and surgical management. IV contrast is not routinely needed. If a vaginal septum is suspected clinically, ultrasound gel placed within the vagina prior to imaging may be helpful (Gupta, 2016). T2-weighted images and coronal planes are typically the most informative. With these, the septate uterus generally displays a convex fundal contour. The bicornuate uterus typically has a significant fundal notch >1 cm. However, any notch depth within 5 mm of the intercornual line qualifies for bicornuate (Behr, 2012). The endometrial cavities of a bicornuate uterus have a normal width and communicate. Although a less-reliable marker, an intercornual distance typically measures >4 cm with a bicornuate uterus (Carrington, 1990; Fedele, 1989).

With a septate uterus, a fibrous septum divides the two uterine horns. Collagen has low signal intensity on both T1- and T2-weighted images, whereas the intervening myometrium of a bicornuate uterus has high signal intensity on T2-weighted images. The fundal contour of the septate uterus can be convex, flattened, or mildly concave, but if present, the fundal notch lies >5 mm above the intercornual line (Behr, 2012). Also in contrast to the bicornuate uterus, the intercornual distance of a septate uterus is not increased, and thus each uterine cavity is smaller than usual (Carrington, 1990; Forstner, 1994).

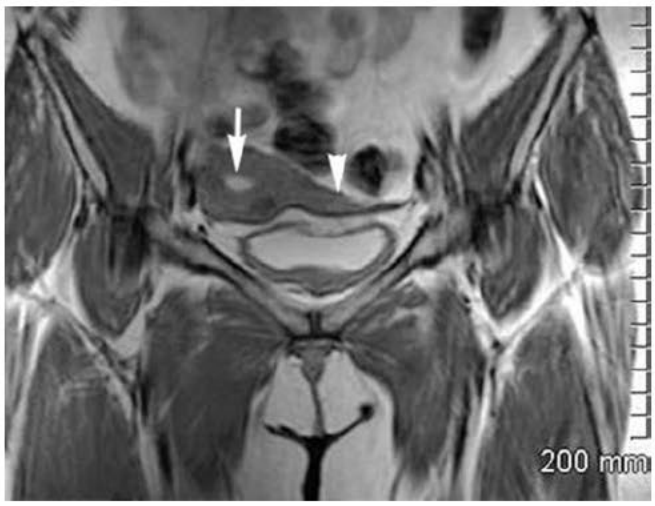


FIGURE 2-31 Unicornuate uterus. This coronal T2-weighted image demonstrates a protrusion of myometrial tissue from the left lateral uterine body (*arrowhead*). It is isointense to myometrium but does not demonstrate normal uterine zonal anatomy. Specifically, endometrium (*arrow*) is noted in the developed right uterine horn but not in the left rudimentary horn.

MR imaging also offers detailed evaluation of a unicornuate uterus, especially in evaluation for a rudimentary horn (Fig. 2-31). On MR imaging, if endometrial tissue is present within a rudimentary horn, zonal anatomy will be preserved. Moreover, communication of an endometrium-containing rudimentary horn is of considerable clinical importance (Chap. 19, p. 422). In a menstruating woman, a noncommunicating horn containing endometrium will often be evident as a hematometra when the cavity becomes distended with blood. MR imaging can also identify uterine didelphys, agenesis, or hypoplasia.

Other Gynecologic Indications

MR imaging is equivalent or superior to sonography to diagnose adenomyosis and has a sensitivity of 88 to 93 percent and a specificity of 66 to 99 percent (Ascher, 1994; Dueholm, 2001; Reinhold, 1996). Compared with sonography, MR imaging reliably diagnoses adenomyosis, particularly focal adenomyomas, in the setting of concomitant pathology such as leiomyomas. In addition, MR imaging reproducibility allows accurate treatment monitoring (Reinhold, 1995).

With adenomyosis, the low-signal-intensity junctional zone (inner myometrium) on T2-weighted images measures >12 mm (Fig. 2-32). A normal junctional zone can be up to 8 mm, and measurements from 8 to 12 mm are considered indeterminate (Novellas, 2011). Low-signal-intensity areas of adenomyosis often contain internal ovoid or punctate foci of increased signal on both T1- and T2-weighted images. These foci are nests of ectopic endometrium with dilated endometrial glands, with or without hemorrhage (Reinhold, 1995, 1996). Contrast

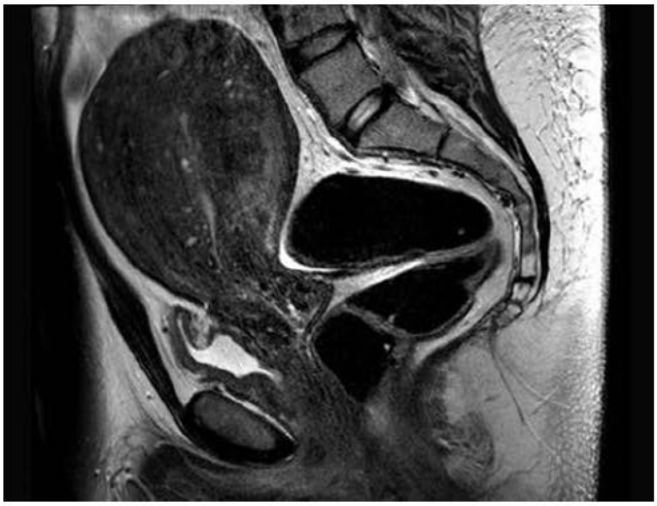


FIGURE 2-32 Sagittal T2-weighted magnetic resonance image of a uterus with diffuse adenomyosis. Adenomyosis is shown as circumferential thickening of the junctional zone.

administration does not increase the diagnostic accuracy for adenomyosis (Outwater, 1998).

For polyps and endometrial hyperplasia, TVS and SIS are common diagnostic tools. MR imaging may be helpful if these modalities are nondiagnostic in a patient who is a poor surgical candidate for direct endometrial sampling. However, distinguishing intracavitary myomas and endometrial polyps can be problematic with MR imaging if necrosis and inflammation are present.

For diagnosing ovarian endometriomas, MR imaging offers 98-percent specificity, which is similar to TVS. These cysts show imaging characteristics of old blood products that include "shading" signal loss on T2-weighted images and a hyperintense signal on T1-weighted images (Chamie, 2011). However, MR imaging differs from TVS in that it can provide evaluation for endometriosis in locations that are not easy to access sonographically or laparoscopically, especially in the setting of advanced disease. For diagnosing pelvic deep infiltrating endometriosis, MR imaging has a sensitivity of 90 percent, specificity of 91 percent, and accuracy of 91 percent (Bazot, 2004). Additional endometriosis features include the stellate margins of fibrotic plaques, tethering, and obliteration of normal pelvic spaces. On T1-weighted images, foci with hyperintense signals aids diagnosis of multifocal lesions involving the bladder, rectum, or ureters.

For other adnexal masses, MR imaging can further characterize anatomy if sonography is nondiagnostic or inconclusive. MR imaging frequently provides added information regarding soft-tissue composition and the origin and extent of pelvic pathology that may be nongynecologic. Although both sonography and MR imaging are highly sensitive for the detection of adnexal malignancy, MR imaging is slightly more specific (Adusumilli, 2006; Jeong, 2000; Yamashita, 1995).

Gynecologic Malignancies

For cervical cancer, imaging can be a component of strict clinical staging (Chap. 30, p. 661). Also, MR imaging is an excellent adjunct for preoperative assessment of gynecologic neoplasms. Its superior soft-tissue contrast and ability to image directly in multiple planes allow evaluation for local tumor extension and lymphadenopathy.

Although CT imaging is typically used for assessment of nodal disease and distant metastases, MR imaging consistently outperforms clinical and CT evaluation of cervical cancer in the assessment of local tumor extension (Choi, 2004; Hricak, 1996, 2007). Current recommendations for MR imaging of cervical cancer include tumors with a transverse diameter >2 cm based on physical examination, endocervical or predominately infiltrative tumors that cannot be accurately assessed clinically, and women who are pregnant or have concomitant uterine lesions that make evaluation difficult (Ascher, 2001; Hricak, 2007). When the extent of parametrial and sidewall invasion is unclear clinically, MR imaging can play an important role as it has a 95- to 98-percent negative predictive value for parametrial invasion (Hricak, 2007; Subak, 1995).

For endometrial carcinoma, surgery is currently the most accurate preoperative staging method. MR imaging may assess the degree of myometrial and cervical extension, which can affect the planned hysterectomy type, extent of lymph node dissection, and decision to provide neoadjuvant intracavitary radiation (Boronow, 1984; Frei, 2000). MR imaging has 92-percent accuracy in staging endometrial cancer, and 82-percent accuracy in assessing myometrial invasion depth (Hricak, 1987). Thus, MR imaging is often considered if lymph node metastases are likely, such as from a high-grade tumor; with papillary or clear cell histology; with cervical invasion; or if multifactorial assessment of myometrial, cervical, and lymph node involvement is required (Ascher, 2001).

For ovarian neoplasms, MR imaging is reserved for evaluation when TVS or CT scanning is indeterminate or nondiagnostic, or in cases with a desire to minimize ionizing radiation (Kang, 2018). However, in a Society of Radiologists in Ultrasound consensus statement, MR imaging was recommended to assess simple ovarian cysts >7 cm. This factored sonography's limitations in detecting mural nodules in larger ovarian masses (Ekerhovd, 2001; Levine, 2010). MR imaging also can better determine adnexal mass origin as uterine, ovarian, or nongynecologic. For those of the ovary, MR imaging helps clarify whether the mass is neoplastic or functional and is malignant or benign. MR imaging of an adnexal mass ideally includes gadolinium-enhanced images to assess tumor vascularity and incorporates fat-saturation techniques to differentiate blood from fat (Ascher, 2001). Although histology cannot be diagnosed, imaging findings that are suspicious for malignancy include enhancing solid components, thick septations, nodules, or papillary projections.

Sensitivity of MR imaging for detecting adnexal pathology ranges from 87 to 100 percent, which is comparable to sonography and CT scanning (Siegelman, 1999). The advantages of MR imaging compared with CT scanning in the evaluation of suspected ovarian cancer include its superior contrast resolution and greater sensitivity for detecting uterine invasion, extrapelvic peritoneal and lymph node metastases, and tumor extension to omentum, bowel, bone, and vessels (Low, 1995; Tempany, 2000). However, MR imaging has a lower sensitivity for implants <1 cm compared with CT (Sala, 2013).

Urogynecology

Pelvic floor evaluations previously performed fluoroscopically are now more often performed with MR imaging. MR imaging provides detailed soft-tissue evaluation of the female urethra, levator ani muscles, and adjacent pelvic structures (Pannu, 2002). Contrast agents placed in the vagina, rectum, and/or bladder can enhance imaging.

Functional data also can be obtained. For example, dynamic MR imaging is completed as the patient performs the Valsalva maneuver. With MR defecography, the patient both performs Valsalva maneuver and defecates rectal contrast (ultrasound gel) during rapid cine acquisitions. Protocols vary significantly from center to center, and upright open MR units are not universally available. We employ supine MR defecography at our institution (Khatri, 2015; Kumar, 2014). MR defecography can evaluate patients with pelvic organ descent, incontinence, constipation, and defecatory dysfunction. It may add information prior to complex pelvic floor reconstruction or after failed previous repairs (Macura, 2006).

NUCLEAR MEDICINE

Nuclear medicine examinations are used similarly in the gynecologic patient as in other medical specialties. Small amounts of radioactive material are ingested or injected to diagnose, and at times treat, various diseases. Thyroid studies use radioactive iodine to assess or ablate function. Bone scans may be elected to seek metastatic disease. Various renal scans can offer information regarding renal function, perfusion, and possible obstruction. Ventilation-perfusion (V/Q) scans can help identify pulmonary emboli. Controversy remains regarding whether pulmonary artery CTA or V/Q scan is most appropriate in pulmonary emboli evaluation. The V/Q scan does not use nephrotoxic agents and is often preferred in those with renal insufficiency. However, radiopharmaceuticals are not always readily available, and thus pulmonary artery CTA is frequently employed.

Positron emission tomography (PET) uses short-lived radiochemical compounds to serve as tracers for measuring specific metabolic processes suggestive of malignancy or infection (Juweid, 2006). This enables detection of early cancer biochemical anomalies that precede structural changes. With FDG-PET, a radiolabeled analogue of glucose, 2-[^{18}F]fluoro-2-deoxy-D-glucose (FDG), is injected intravenously and is taken up by metabolically active cells such as tumor cells. PET provides a poor depiction of detailed anatomy, thus scans are frequently read side-by-side or fused with CT scans. The combination allows correlation of metabolic and anatomic data. As a result, current PET scanners are now commonly integrated with CT scanners, and the two scans can be performed during the same session.

PET/CT has become a vital clinical tool, particularly for cancer diagnosis and management. The most common PET radiochemical tracer used clinically is FDG. This tracer highlights areas of accelerated glycolysis, which is common in neoplastic cells (Goh, 2003).

Several studies have demonstrated high sensitivity and specificity of FDG-PET for the initial staging of cervical cancer. This may be most valuable in patients with no evidence of extrapelvic metastatic disease by MR or CT imaging (Gjelsteen, 2008; Park, 2005). The ability of FDG-PET imaging to assess nodal status in cervical cancer has both prognostic and therapeutic implications (Fig. 2-33). Prior to lymph node radiation treatment planning, the added anatomic data obtained with PET/CT can be used to guide intensity-modulated radiotherapy

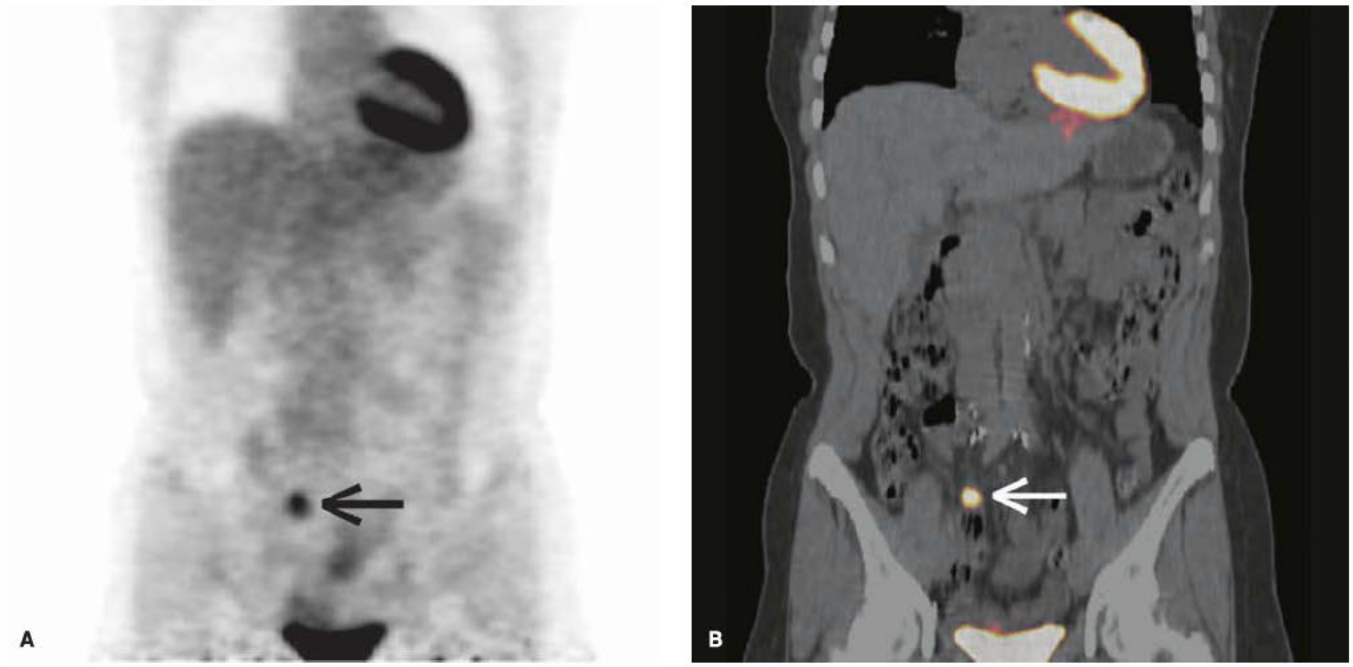


FIGURE 2-33 Positron emission tomography (PET) **(A)** and PET-computed tomography (PET-CT) fusion **(B)** images of a woman with recurrence of ovarian cancer. Arrows demarcate abnormal uptake of tracer in the pelvis that represented a 1-cm lymph node. The biopsy of this lymph node revealed recurrent ovarian cancer. (Reproduced with permission from Dr. Dana Mathews.)

(Chap. 28, p. 612). This significantly reduces the amount of radiation delivered to surrounding normal structures (Havrilesky, 2003; Wong, 2004).

INTERVENTIONAL RADIOLOGY

In gynecology, procedures often provided by interventional radiologists include image-guided biopsy or drainage. In those with advanced cervical cancer, percutaneous nephrostomy may be needed to preserve renal function or to decompress an infected collecting system. UAE is a vascular intervention that employs angiography to delineate the uterine arteries. Once catheterized, each artery is injected with embolic particles to occlude uterine vasculature. Discussed in Chapter 9 (p. 209), UAE can provide definitive independent treatment of uterine leiomyomas. Although adenomyosis was initially thought to be a contraindication for UAE success, studies are now showing durable treatment efficacy (Kim, 2007). Given the frequent concomitant presence of adenomyosis and uterine leiomyomata, treatment success and improvement in symptoms also have been reported in populations with both diseases after UAE (Froeling, 2012). Rarely, UAE may be selected to control severe uterine bleeding in women who are not considered surgical candidates.

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CHAPTER 3

Gynecologic Infection

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NORMAL VAGINAL FLORA

The vaginal flora of a normal, asymptomatic, reproductive-aged woman includes multiple aerobic, facultative anaerobic, and obligate anaerobic species. Of these, anaerobes predominate and outnumber aerobic species approximately 10 to 1 (Bartlett, 1977). These bacteria exist with the host in a symbiotic relationship, which is alterable depending on the microenvironment.

Certain bacterial species normally found in vaginal flora have access to the upper reproductive tract. The female upper reproductive tract is not sterile, and the presence of these bacteria does not indicate active infection (Hemsell, 1989; Spence, 1982). Together, these findings illustrate the potential for infection following gynecologic surgery and the need for antimicrobial prophylaxis.

Vaginal pH

Typically, the vaginal pH ranges between 4 and 4.5. This is due in part to gram-positive aerobic *Lactobacillus* species producing lactic acid, fatty acids, and other organic acids. Other bacteria also can add organic acids from protein catabolism, and anaerobic bacteria donate by amino acid fermentation.

Glycogen, which is present in healthy vaginal mucosa, provides nutrients for many vaginal ecosystem species and is metabolized to lactic acid (Boskey, 2001). Glycogen content within vaginal epithelial cells normally diminishes after menopause and is low in childhood. As a result, postmenopausal women not receiving estrogen replacement and young girls have a lower prevalence of *Lactobacillus* species and less acid production compared with that of reproductive-aged women. This leads to a rise in vaginal pH. For menopausal women, hormone replacement therapy restores vaginal lactobacilli populations, which protect against vaginal pathogens (Dahn, 2008).

Altered Flora

Changing other elements of the vaginal ecology may alter the prevalence of various species and may lead to infection. With the menstrual cycle, transient changes in flora are observed. These are predominantly during the first days of the cycle and are presumed to be associated with hormonal changes (Keane, 1997). Menstrual fluid can serve as a nutrient source for several bacterial species, resulting in their overgrowth. The role of this in the development of upper reproductive tract infection following menstruation is unclear, but an association may be present. For example, women symptomatic with acute gonococcal upper reproductive tract infection classically are menstruating or have just completed their menses. Last, treatment with broad-spectrum antibiotics may result in symptoms attributed to inflammation from *Candida albicans* or other *Candida* species by eradicating other balancing species in the flora.

Bacterial Vaginosis (BV)

This common, complex, and poorly understood clinical syndrome reflects vaginal flora in which anaerobic species are overrepresented. These include *Gardnerella*, *Prevotella*, *Mobiluncus*, and *Bacteroides* species; *Atopobium vaginae*; and BV-associated bacteria, provisionally named BVAB1, BVAB2, and BVAB3. These latter three are newly recognized bacteria found in women with BV (Fredricks, 2005). BV is also associated with a significant reduction of normal *Lactobacillus* species.

Molecular ribosomal RNA gene sequencing techniques have greatly aided classification of specific bacteria within vaginal flora ecosystems, which are also called *vaginal microbiota* or *vaginal biomes*. There are five types of vaginal microbiota, referred to as *community state types (CSTs)*. CSTs are defined by their specific clustering of specific species. And, a woman can be categorized to one of these five CSTs based on her vaginal microbiota composition (Ravel, 2011). Researchers have begun to quantify the

risk of BV by these CST groups. Specifically, CSTs I, II, III, and V are lactobacilli rich. In contrast, CST IV is a heterogeneous microbiota of strict anaerobes and is associated with BV. CSTs vary racially, and CST IV is also the most common in asymptomatic, healthy black women (Fettweis, 2014).

In evaluating risks for BV, this condition is not considered by the Centers for Disease Control and Prevention (CDC) (2015) to be a sexually transmitted disease (STD). However, a greater risk of BV is associated with multiple or new sexual partners, female partners, and oral sex, whereas condom use lowers the risk (Fethers, 2008). Moreover, rates of STD acquisition are increased in affected women, and a possible role of sexual transmission in the pathogenesis of recurrent BV has been proposed (Atashili, 2008; Bradshaw, 2006; Wiesenfeld, 2003). Other potential risks are douching, black race, smoking, and intrauterine device (IUD) use.

BV is the most common cause of vaginal discharge among reproductive-aged women. Of symptoms, a nonirritating, malodorous vaginal discharge is characteristic but may not always be present. The vagina is usually not erythematous, and cervical examination reveals no abnormalities.

For diagnosis, clinical criteria first proposed by Amsel and associates (1983) include: (1) microscopic evaluation of a vaginal-secretion saline preparation, (2) release of volatile amines produced by anaerobic metabolism, and (3) determination of the vaginal pH. A saline preparation, also known as a "wet prep," contains a swab-collected sample of discharge mixed with drops of saline on a microscope slide. Clue cells are the most reliable indicators of BV and were originally described by Gardner and Dukes (1955) (Fig. 3-1). These vaginal epithelial cells contain many attached bacteria, which create a poorly defined stippled cellular border. At least 20 percent of the epithelial cells should be clue cells. The positive predictive value of this test for BV is 95 percent.

Adding 10-percent potassium hydroxide (KOH) to a fresh sample of vaginal secretions releases volatile amines that have a fishy odor. This is often colloquially referred to as a "whiff test." The odor is frequently evident even without KOH. Similarly, alkalinity of seminal fluid and blood are responsible for foul-odor complaints after intercourse and with menses. The finding of both clue cells and a positive whiff test result is pathognomonic, even in asymptomatic patients.

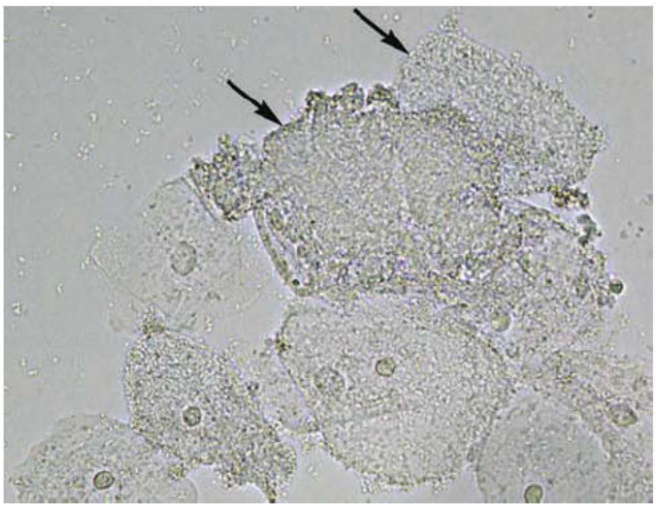

FIGURE 3-1 Photomicrograph of saline wet preparation reveals clue cells. Several of these squamous cells are heavily studded with bacteria. Clue cells are covered to the extent that cell borders are blurred and nuclei are not visible (*arrows*). (Reproduced with permission from Dr. Lauri Campagna and Mercedes Pineda, WHNP.)

Characteristically with BV, the vaginal pH is >4.5, and this stems from diminished acid production by bacteria. Similarly, *Trichomonas vaginalis* infection also is associated with anaerobic overgrowth and elaboration of amines. Thus, women diagnosed with BV should have no microscopic evidence of trichomoniasis.

Used primarily in research studies rather than clinical practice, the Nugent Score is a system employed for diagnosing BV. During microscopic examination of a gram-stained vaginal discharge smear, scores are calculated by assessing bacteria staining and morphology.

Last, molecular DNA assays against the more frequent organisms found in women with BV have suitable accuracy (Coleman, 2018). However, these tests assess for bacteria that may also be part of normal flora in asymptomatic women. Moreover, compared with traditional methods, molecular tests have yet to show superior health outcomes but do add substantial cost.

Several gynecologic adverse health outcomes have been observed in women with BV. These include vaginitis, endometritis, postabortal endometritis, pelvic inflammatory disease (PID) unassociated with *Neisseria gonorrhoeae* or *Chlamydia trachomatis*, susceptibility to human immunodeficiency virus (HIV) acquisition, and acute pelvic infections following pelvic surgery, especially hysterectomy (Atashili, 2008; Larsson, 1989, 1991, 1992; Soper, 1990). Pregnant patients with BV have an elevated risk of preterm delivery and postpartum endometritis (Hillier, 1995; Watts, 1990).

Several regimens are available for nonpregnant women (Table 3-1). The newest of these is secnidazole, a 5-nitroimidazole in granule form taken once orally (Schwebke, 2017). Cure rates with regimens in Table 3-1 range from 80 to 90 percent at 1 week, but within 3 months, 30 percent of women have experienced a recurrence. Many of these are correlated with heterosexual contact (Amsel, 1983; Gardner, 1955; Wilson, 2004). However, treatment of male sexual partners does not benefit women with this recurring condition and is not recommended. Moreover, other forms of therapy such as introduction of lactobacilli, acidifying vaginal gels, and use of probiotics have shown inconsistent efficacy (Senok, 2009).

Limited evidence supports specific ways to prevent BV. Alteration of previously mentioned risk factor behaviors can be considered. Of these, some data suggest elimination or diminished use of vaginal douches may have benefits (Brotman, 2008; Klebanoff, 2010).

GENITAL ULCER INFECTIONS

Ulceration defines complete loss of the epidermal covering with invasion into the underlying dermis. In contrast, *erosion* describes partial loss of the epidermis without dermal penetration. These are distinguished by clinical examination. Biopsies are generally not helpful. But if taken, samples obtained from the edge of new lesions are the most likely to be informative.

TABLE 3-1. Single-Agent Bacterial Vaginosis Treatment

Recommended regimens	
Metronidazole (Flagyl)	500 mg orally twice daily for 7 days
Metronidazole gel 0.75% (Metrogel vaginal)	5 g (1 full applicator) intravaginally once daily for 5 days
Clindamycin cream[a] 2% (Cleocin, Clindesse)	5 g (1 full applicator) intravaginally at bedtime for 7 days
Alternative regimens	
Secnidazole (Solosec)	2 g orally once[b]
Tinidazole (Tindamax)	2 g orally once daily for 2 days
	1 g orally once daily for 5 days
Clindamycin	300 mg orally twice daily for 7 days
Clindamycin ovules[a] (Cleocin)	100 mg intravaginally at bedtime for 3 days

[a]Clindamycin cream and ovules are oil-based and might weaken latex condoms and diaphragms for 5 days after use.
[b]These granules are mixed with applesauce, yogurt, or pudding and are not chewed.
From the Centers for Disease Control and Prevention, 2015; Schwebke, 2017.

Importantly, biopsy is mandatory if carcinoma is suspected, and Figure 4-2 (p. 94) illustrates technique.

Most young sexually active women in the United States who have genital ulcers will have herpes simplex virus (HSV) infection or syphilis. Rarely, some will have chancroid, lymphogranuloma venereum, or granuloma inguinale. Essentially all are sexually transmitted and are associated with higher risk for HIV transmission.

As a general rule, females diagnosed with one STD are offered testing for others. This typically includes testing for syphilis, gonorrhea, and HIV, chlamydial, and hepatitis B infections. Sexual contacts require evaluation, and both require reassessment following treatment.

Herpes Simplex Virus Infection

Genital herpes is the most prevalent genital ulcer disease and is a chronic viral infection. After crossing an epithelial barrier, the virus enters sensory nerve endings and undergoes retrograde axonal transport to the dorsal root ganglion. Here, the virus develops lifelong latency. Spontaneous reactivation by various events results in anterograde transport of virus to the surface. The virus is shed, with or without lesion formation. It is postulated that immune mechanisms control latency and reactivation.

There are two types of herpes simplex virus, HSV-1 and HSV-2. HSV-1 is the predominant cause of oral lesions and often is acquired in childhood. Additionally, HSV-1 is now the most frequent agent of genital lesions in Hispanic and white women (Bernstein, 2013). This rise in the prevalence of HSV-1 genital disease may stem from an increase in oral–genital sexual practices. Another explanation is that HSV-1 acquisition has declined in childhood as a result of improved living conditions and hygiene. Without prior exposure, this renders people without HSV-1 antibodies susceptible to genital acquisition of HSV-1 or -2. HSV-2 causes primarily genital lesions and is the most common source of genital disease in black women (Fanfair, 2013). Of all females aged 14 to 49 years in the United States, 16 percent have suffered a genital HSV-2 infection, and nearly 55 percent are seropositive to HSV-1 (Bradley, 2014).

Most women who have been infected with either HSV-1 or HSV-2 lack a formal diagnosis because of mild or unrecognized infections. Infected patients can shed infectious virus while asymptomatic, and most infections are transmitted sexually by patients who are unaware of their infection. Compared with men, women have more severe symptoms with primary and recurrent infection.

Symptoms

Patient symptoms at initial presentation will depend primarily on whether a patient during the current episode has antibody from previous exposure. If a patient has no antibody, the attack rate in an exposed person approaches 70 percent. The mean incubation period is approximately 1 week. Up to 90 percent of those who are symptomatic with their initial infection will have another episode within a year.

The virus infects viable epidermal cells, the response to which is erythema and papule formation. With cell death and cell wall lysis, blisters form (Fig. 3-2). The covering then disrupts, leaving a usually painful ulcer. These lesions develop crusting and heal but may become secondarily infected. The three stages of lesions are: (1) vesicle with or without pustule formation, which lasts approximately a week; (2) ulceration; and (3) crusting. Virus is predictably shed during the first two phases.

Burning and severe pain accompany initial vesicular lesions. With ulcers, urinary frequency and/or dysuria from direct contact of urine with ulcers may be complaints. Rarely, local swelling can result from vulvar lesions and cause urethral obstruction. Alternatively or additionally, herpetic lesions can involve the vagina, cervix, bladder, anus, and rectum. Commonly, low-grade fever, headache, and myalgias are noted.

Viral load undoubtedly contributes to the number, size, and distribution of lesions. Normal host defense mechanisms inhibit viral growth, and healing starts within 1 to 2 days. Early treatment with an antiviral medication decreases the viral load. Immune-deficient patients have greater susceptibility and display diminished immune response and delayed healing.

For a previously uninfected patient, the period of new lesion formation and time to healing are both longer. Pain persists for

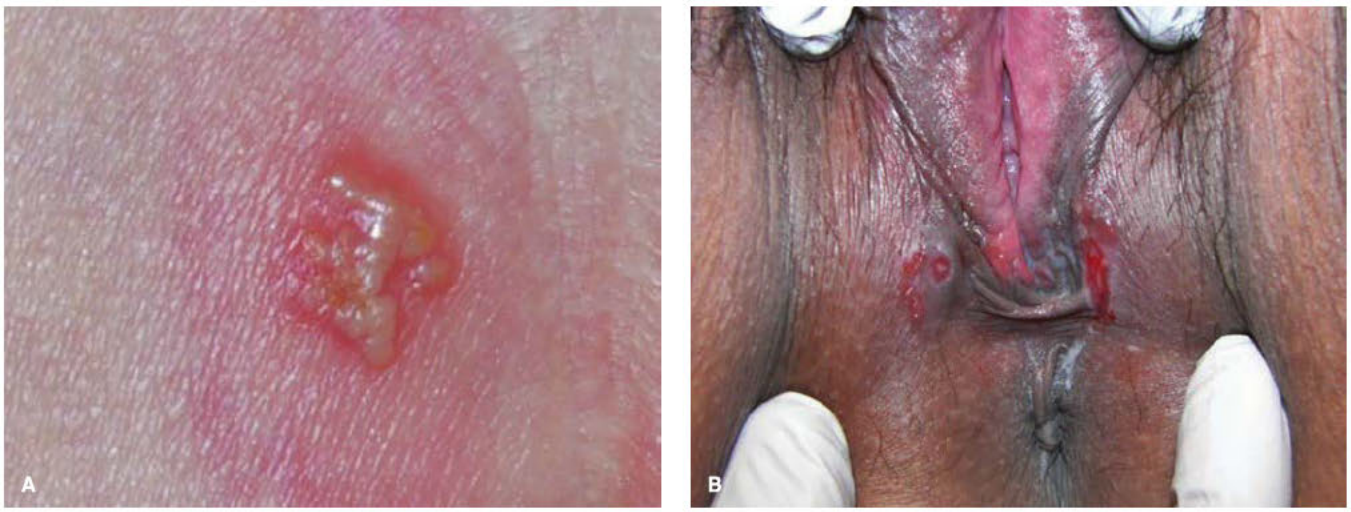

FIGURE 3-2 Genital herpetic ulcers. **A.** Vesicles prior to ulceration. **B.** Punctate (*left*) or "knife-cut" (*right*) ulcers are common lesions. (Reproduced with permission from Dr. William Griffith.)

the first 7 to 10 days, and lesions heal by 2 to 3 weeks. If a patient has had prior exposure to HSV-2, their initial episode is significantly less severe, and time to healing approximates 2 weeks.

Recurrence following HSV-2 infection is common, and almost two thirds of patients have a prodrome prior to lesion onset. Heralding paresthesias are frequently described as pruritus or tingling in the area prior to vesicle formation. However, prodromal symptoms may develop without actual lesion formation. Clinical manifestations for women with recurrences are more limited, with only approximately 1 week of symptoms.

Diagnosis

The gold standard for diagnosing genital herpes was previously cell culture. Specificity is high, but sensitivity is low and declines as lesions heal. Nucleic acid amplification test (NAAT) testing is many times more sensitive than culture and can detect HSV DNA shed from epithelia without vesicular lesions (LeFoff, 2014). Moreover, results generally are available in 1 to 2 days. Importantly, a negative culture or polymerase chain reaction (PCR) result does not mean that there is no herpetic infection. In contrast, false-positive results are rare.

HSV is surrounded by envelope glycoproteins, and glycoprotein G is the antigen of interest. Serologic assays are available to detect antibodies formed against the HSV type-specific glycoproteins, namely glycoprotein G2 (HSV-2) or glycoprotein G1 (HSV-1). Assay specificity is ≥96 percent, and the sensitivity of HSV-2 antibody testing ranges from 80 to 98 percent. Importantly, with serologic screening, only immunoglobulin G (IgG) antibody assays are ordered. Although these tests may be used to confirm herpes simplex infection, seroconversion following initial infection takes approximately 3 weeks (Ashley-Morrow, 2003). Immunoglobulin M (IgM) testing is not recommended. This can lead to ambiguous results as the IgM assays are not type-specific and also may be positive during a recurrent outbreak. Thus, in clinically obvious cases, immediate treatment and additional STD screening can be initiated following physical examination alone.

Serologic screening for HSV in the asymptomatic general population is not recommended. However, HSV serologic testing can be considered for HIV-infected individuals or for women presenting for an STD evaluation, especially for those with multiple partners and for those in demographics with high prevalence (Fanfair, 2013). It can also add management information for couples thought but not confirmed to be discordant for infection (Centers for Disease Control and Prevention, 2015).

Treatment

The CDC provides and regularly updates guidelines for the treatment of all STDs. These are found on the CDC website at: www.cdc.gov/std/tg2015/default.htm. For HSV, currently available antiviral therapy is listed in Table 3-2. Although these agents may hasten healing and improve symptoms, therapy does not eradicate latent virus or affect future rates of recurrent infection. Analgesia with nonsteroidal antiinflammatory drugs or, if severe, a mild narcotic such as acetaminophen with codeine may be prescribed. In addition, topical anesthetics such as lidocaine ointment may provide relief. Local hygiene to prevent secondary bacterial infection is important.

For women with established HSV-2 infection, therapy may not be necessary if symptoms are mild and tolerable. Episodic therapy for recurrent disease is ideally initiated at least within 1 day of lesion outbreak or during the prodrome. Patients may be given a prescription ahead of time so that medication is available to begin therapy with prodrome onset.

If episodes recur at frequent intervals, a woman may elect daily suppressive therapy, which reduces recurrences by 70 to 80 percent (Centers for Disease Control and Prevention, 2015). Suppressive therapy may eliminate recurrences and decreases sexual transmission. Once-daily dosing may result in enhanced compliance and lower cost.

Patient education is mandatory, and specific topics include prodrome recognition, recurrence triggers, methods to reduce sexual transmission, and obstetric consequences. Acquisition of this infection may have significant psychological impact, and several websites provide patient information and support. A useful CDC website is www.cdc.gov/std/Herpes/STDFact-Herpes.htm.

TABLE 3-2. Oral Agents for Genital Herpes Simplex Infection

First clinical episode
Acyclovir 400 mg three times daily for 7–10 days
or
Acyclovir 200 mg five times daily for 7–10 days
or
Famciclovir (Famvir) 250 mg three times daily for 7–10 days
or
Valacyclovir (Valtrex) 1 g twice daily for 7–10 days

Episodic therapy for recurrent disease
Acyclovir 400 mg three times daily for 5 days
or
Acyclovir 800 mg twice daily for 5 days
or
Acyclovir 800 mg three times daily for 2 days
or
Famciclovir 125 mg twice daily for 5 days
or
Famciclovir 1 g twice daily for 1 day
or
Famciclovir 500 mg once, then 250 mg twice daily for 2 days
or
Valacyclovir 500 mg twice daily for 3 days
or
Valacyclovir 1 g once daily for 5 days

Suppressive therapy
Acyclovir 400 mg twice daily
or
Famciclovir 250 mg twice daily
or
Valacyclovir 0.5 or 1 g once daily

From the Centers for Disease Control and Prevention, 2015.

Prevention

Women with genital herpes should refrain from sexual activity with uninfected partners when prodrome symptoms or lesions are present. Latex condom use potentially lowers the risk for herpetic transmission (Martin, 2009). Suppressive therapy with oral valacyclovir 0.5 g daily reduces sexual transmission by almost 50 percent among couples discordant for HSV-2 (Corey, 2004). Unfortunately, preventive herpes vaccine trials have failed to demonstrate protective immunity in the genital tract (Belshe, 2012; Shin, 2013).

Syphilis

Pathophysiology

Syphilis is an STD caused by the spirochete *Treponema pallidum*, which is a slender, spiral-shaped organism with tapered ends. Women at highest risk are those from lower socioeconomic groups, adolescents, those with early onset of sexual activity, and those with many sexual partners. The number of syphilis cases has risen almost every year in the United States since 2001. In 2017, more than 100,000 cases of syphilis, which included all stages, were reported to the CDC (2018a).

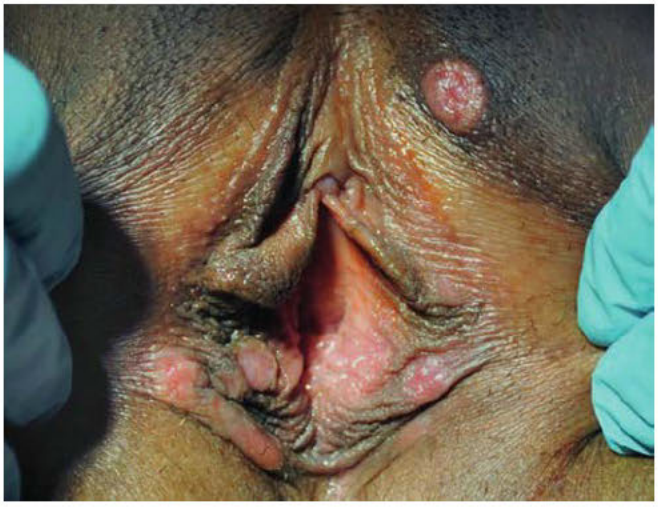

FIGURE 3-3 Several vulvar syphilitic chancres. Lesions that lie directly across the vulvar midline from each other are sometimes referred to as "kissing" lesions.

The natural history of syphilis in untreated patients can be divided into four stages. Of these, primary and secondary syphilis represent incident infection. With primary syphilis, the hallmark lesion is the *chancre*, in which spirochetes are abundant. Classically, it is an isolated, nontender ulcer with raised, rounded borders and an uninfected base (Fig. 3-3). However, it may become secondarily infected and painful. Chancres are often found on the cervix, vagina, or vulva but may also form in the mouth or around the anus. The mean incubation period is 3 weeks, but lesions can develop 10 days to 3 months after exposure. Without treatment, lesions spontaneously heal within 6 weeks.

With *secondary syphilis,* bacteremia develops 6 weeks to 6 months after a chancre appears. Its hallmark is a maculopapular rash that may involve the entire body and includes the palms, soles, and mucous membranes (Fig. 3-4). Mucosal lesions, called *mucous patches*, actively shed spirochetes. In warm, moist body areas, this rash may produce broad, pink or gray-white, highly infectious plaques called *condylomata lata*. Because syphilis is a systemic infection, other manifestations may include fever and malaise. Less commonly, cranial nerve dysfunction, meningitis, hepatitis, nephrotic syndrome, and arthritis develop.

Untreated, the manifestations of secondary syphilis resolve, and latent syphilis is diagnosed using serologic tests. During *early latent syphilis*, which is diagnosed within 1 year of infection, secondary signs and symptoms may recur. *Late latent syphilis* is defined as a period greater than 1 year after the initial infection.

Tertiary syphilis is the phase of untreated syphilis that may appear up to 20 years after latency. During this phase, cardiovascular, central nervous system, and musculoskeletal involvement become apparent. However, cardiovascular and neurosyphilis are half as common in females as in males.

Diagnosis

A definitive diagnosis requires direct detection of spirochetes within a lesion sample. However, most cases are diagnosed presumptively