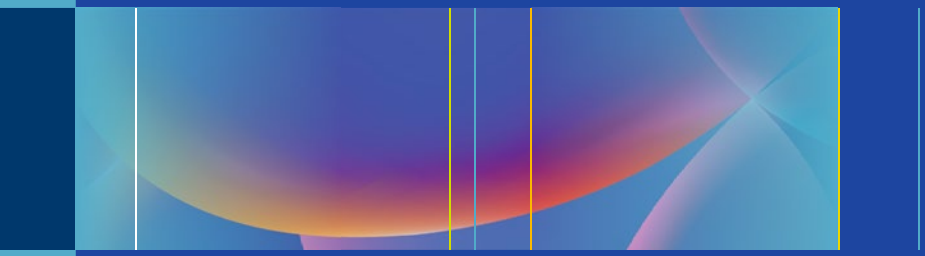
Paula C. Brady



Handbook of Consult and Inpatient Gynecology

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For my teachers

Preface

This book is designed to help residents and medical students anticipate and recognize varying levels of acuity in gynecologic care. The ability to differentiate between "sick" and "not sick" is absolutely vital in the management of a patient population that spans the spectrum of health and disease. Gynecology patients are most often young women who can seem deceptively stable until the moment that decompensated hemorrhagic or septic shock sets in. This manual is designed to be a reference and reminder to gynecology trainees of the worst-case scenarios in every chief complaint and reviews the management of both common and acute conditions.

Handbook of Consult and Inpatient Gynecology is a concise guide to gynecology in the inpatient and emergency settings and is designed to optimize patient safety and outcomes. It reflects the changing landscape of modern gynecologic practice and encompasses both advanced imaging techniques and minimally invasive surgery and interventions. The book focuses solely on gynecology with purpose. Unlike obstetrics, which usually involves several trainees in a team, and outpatient practice, which allows time for preparation and reference, gynecology "consult" or "night float" rotations require trainees to function on their own, balancing several pressing clinical demands at once.

This book is organized to address calls and consults in two general arenas: emergency care, and inpatient and postprocedural care. In addition to describing common gyneco-

logic issues such as vaginal bleeding, ectopic pregnancy, adnexal masses and torsion, spontaneous abortion, and sexual assault, this guide explores postoperative complications that are relevant to benign gynecology, gynecologic oncology, family planning, urogynecology, and reproductive endocrinology. Each chapter offers definitions of core concepts, differential diagnoses, actions to take upon receiving the consult and assessing the patient, and key points for the history, physical, diagnostic work-up, and management.

This book would not have been possible without the support of many clinicians and educators at the Brigham and Women's Hospital and Massachusetts General Hospital. Thank you to the authors who generously gave their time and expertise in writing these chapters, and the many colleagues who further reviewed the manuscript. I am particularly grateful to Elizabeth S. Ginsburg, MD, for her guidance and mentorship, and to Robert L. Barbieri, MD, Daniel J. Kaser, MD, Brian W. Walsh, MD, Daniela Carusi, MD, MSc, Amy R. Stagg, MD, Joan M. Bengtson, MD, and Ruth E. Tuomala, MD, for their support and advice at various stages of the project, which began as a clinical handbook within the Brigham and Women's Hospital and Massachusetts General Hospital Integrated Residency Program in Obstetrics and Gynecology. This book is the direct product of this training program and the values shared by its trainees, faculty and staff: A commitment to education, innovation, research and exemplary patient care.

Boston, MA, USA — Paula C. Brady, MD

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Part I
Emergency Care

Chapter 1
Acute Pelvic Pain

Paula C. Brady and Daniela Carusi

Definitions

Peritoneal Signs Evidence of peritonitis (irritation of the peritoneum, which lines the abdomen) on physical exam includes rebound (pain on the abrupt release of abdominal palpation), involuntary guarding of the abdomen, or tenderness with gentle shaking of the patient's abdomen or the bed. Peritonitis is often a response to intra-abdominal infection or inflammation or intra-abdominal hemorrhage [1]. A patient with ovarian torsion may also present with an acute abdomen, due to ovarian inflammation and necrosis.

Hemodynamic Instability Definitions vary but include a heart rate over 100 beats per min and a systolic blood pressure (SBP) below 90 millimeters of mercury (mmHg) or 20 % or more below a patient's baseline [2, 3]. In severely decompensated patients, the presence of a carotid pulse, reflecting an SBP of at least 60 mmHg, and a femoral pulse (SBP of

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60–70 mmHg), can be used as a quick estimate of blood pressure [4]. Other signs include tachypnea (over 20 breaths per minute) [5]. Tachycardia and any degree of hypotension in young healthy women, in particular, require immediate attention and aggressive resuscitation, as these can mark the onset of decompensated shock. Diagnostic criteria of hemorrhage shock and severe sepsis are shown in Tables 1.1 and 1.2.

Table 1.1 Stages of hemorrhagic shock

Class I: blood volume lost <15 %	**Class II**: blood volume lost 15–30 %
Heart rate <100 beats per minute	Heart rate >100 beats per minute
Blood pressure normal	Blood pressure normal
Respiratory rate 14–20 breaths per minute	Respiratory rate 20–30 breaths per minute
Urine output >30 mL/h	Urine output 20–30 mL/h
Mental status normal	Mental status mildly anxious
Class III: blood volume lost 30–40 %	**Class IV**: blood volume lost >40 %
Heart rate >120 beats per minute	Heart rate >140 beats per minute
Blood pressure decreased	Blood pressure decreased
Respiratory rate 30–40 breaths per minute	Respiratory rate >35 breaths per minute
Urine output 5–15 mL/h	Urine output negligible
Mental status anxious/ confused	Mental status confused/ lethargic
Often marks the onset of decompensated hypovolemic shock	

Committee on Trauma [5]

Table 1.2 Clinical criteria of sepsis and severe sepsis

Sepsis	Severe sepsis
Suspected source plus two or more: 1. Temperature >38.3 °C (101 °F) or <36 °C (96.8 °F) 2. Heart rate >90 beats per minute 3. Tachypnea (>20 breaths/minute) 4. WBC >12,000 μ/L or <4000 μ/L or normal with >10 % immature (band) forms	Sepsis plus one or more: 1. Systolic blood pressure <90 mmHg or decrease from baseline by 40 mmHg 2. Elevated lactate (>1 mmol/L; >4 particularly concerning, sign of organ hypoperfusion) 3. Acute lung injury: PaO_2/FiO_2 <250 (in the absence of pneumonia) or <200 (with pneumonia) 4. Acute oliguria: <0.5 mL/kg/h despite fluid resuscitation 5. Creatinine >2 mg/dL 6. INR >1.5 7. Platelets <100,000/uL 8. Bilirubin >2 mg/dL

Adapted from Fischerova [6] and Dellinger et al. [7]

Differential Diagnosis

Please refer to Chap. 2, Vaginal Hemorrhage, for the diagnosis and management of patients with vaginal bleeding as their primary complaint.

The most dangerous conditions are those resulting in hemodynamic compromise, including:

1. Sepsis due to tubo-ovarian abscess or other pelvic abscess, septic abortion, or post-procedural complication leading to infection, including visceral injury.
2. Intra-abdominal hemorrhage due to ruptured ectopic pregnancy or ruptured ovarian cyst.

Postoperative Complications

Please refer to Chaps. 16, Complications of Minimally Invasive Gynecologic Surgery, and 18, Gynecologic Oncology, for more information on the following conditions:

- *Postoperative infection*, including infection of abdominal or vaginal incisions, the vaginal cuff, or pelvic abscess.
- *Endomyometritis*: Polymicrobial infection of the endometrial cavity, which can occur after any uterine instrumentation.
- *Necrotizing fasciitis*: A rare and rapidly advancing wound complication, known colloquially as "flesh-eating bacteria."
- *Toxic shock syndrome*: A rare, life-threatening syndrome caused by bacterial enterotoxins, initially recognized in menstruating women and attributed to tampon use; TSS is now diagnosed most commonly in nonmenstruating women, often in the days following a procedure or in the postpartum period [8–10].
- *Genitourinary tract injury.*
- *Urinary retention.*
- *Bowel injury* or *obstruction*.
- *Anastomotic* or *stoma complications*.
- *Bowel herniation* through an incision or port site.
- *Dehiscence* of vaginal cuff or abdominal wound.
- *Uterine perforation.*
- *Nerve injury* or *entrapment*.
- *Septic pelvic thrombophlebitis* (SPT): Inflammation of the pelvic vessels may occur in the postpartum or postoperative setting, with thrombus and bacterial infection [11].
- *Ovarian vein thrombosis.*

Infections

Relatively common and potentially highly morbid etiologies of patient presentations for acute pain. Please see Chap. 6, Pelvic Inflammatory Disease and Tubo-ovarian Abscesses, for more information.

Pelvic Inflammatory Disease (PID) Infection and inflammation of the upper genital tract in women, including inflammation of the endometrium (endometritis), fallopian tube(s) (salpingitis), pelvic peritoneum, and adnexa [12]. Risk factors include multiple sexual partners, non-use of barrier contraception, smoking, illicit drug use, infection with *Neisseria gonorrhoeae* and *Chlamydia trachomatis*, and prior episodes of PID [13, 14]. In addition to pelvic pain, patients may present with chills, abnormal vaginal bleeding or discharge, and/or dyspareunia [15].

Tubo-Ovarian Abscess (TOA) Abscess(es) involving the adnexa, including the fallopian tube and/or ovary. Risk factors for TOA are similar risk to factors for PID, and abscesses are usually polymicrobial [16]. Patients may present similarly to those with PID, though patients may also have high fever and sepsis.

Associated with Pelvic Masses or IUD

Adnexal Torsion Rotation of the ovary, fallopian tube, and the associated infundibulopelvic ligament, most often occurring with adnexal masses in adults, resulting in significant pain and eventual necrosis [17]. Please see Chap. 5, Adnexal Torsion, for diagnosis and management of adnexal torsion.

Ovarian Cyst The differential diagnosis of an ovarian mass detected by physical examination or imaging includes simple (follicular) cyst, paraovarian or paratubal cyst, corpus luteum, hemorrhagic cyst, ectopic pregnancy, endometrioma, benign cystic teratoma, cystadenoma, theca lutein cyst, hydrosalpinx (fluid filled fallopian tube) or pyosalpinx, tubo-ovarian abscess or other pelvic abscess, polycystic ovaries, ovarian hyperstimulation syndrome, uterine anomaly, broad ligament or pedunculated fibroid, peritoneal inclusion cyst, ovarian malignancy (germ cell, sex cord or stromal, or epithelial), metastatic implants on the ovary, and nongynecologic causes such as diverticular abscess, appendicitis, nerve sheath tumor,

or urologic pathology (pelvic kidney, ureteral or bladder diverticulum) [18]. Please see Chap. 4, Adnexal Masses and Ovarian Cyst Rupture, for more information on the diagnosis and management of adnexal masses.

Ruptured Ovarian Cyst Please see Chap. 4, Adnexal Masses and Ovarian Cyst Rupture, for more information on the diagnosis and management of ovarian cyst rupture.

Degenerating Fibroid The most common neoplasm in reproductive age women, fibroids are smooth muscle tumors that produce symptoms of pelvic pain, menorrhagia, and/or infertility in 25 % of women [19]. Acute pain can occur when a fibroid outgrows its blood supply and degenerates, causing necrosis and inflammation [20]. Rarely, torsion of a pedunculated fibroid can also occur [19]. Fibroids may also prolapse through the cervical os, into the vagina, causing pain and irregular bleeding; patients with prolapsing fibroids are frequently anemic [21, 22].

Fibroids are optimally visualized by ultrasound or MRI [23]. By ultrasound, a degenerating fibroid may have cystic spaces and peripheral color Doppler flow, while a necrotic fibroid may have diminished Doppler flow. Cystic spaces may also be seen within degenerating fibroids visualized by MRI, and fibroids in the later stages of degeneration may appear calcified (Fig. 1.1) [25]. By MRI, degenerating or torsing fibroids may not enhance with gadolinium, due to compromised blood supply [24]. In hemodynamically stable patients without signs of infection or acutely declining hemoglobin, treatment is supportive. Prolapsing fibroids are usually removed, often vaginally, for diagnostic purposes, though in stable patients without severe anemia, surgery can be planned as an outpatient [21].

Malpositioned IUD Patients with malpositioned IUDs may present with symptoms of pelvic pain, cramping, or irregular vaginal bleeding, though many malpositioned IUDs are detected incidentally [26]. On pelvic examination, the IUD strings should be visible protruding from the cervical os; when the strings are not visible, a Cytobrush used for pap

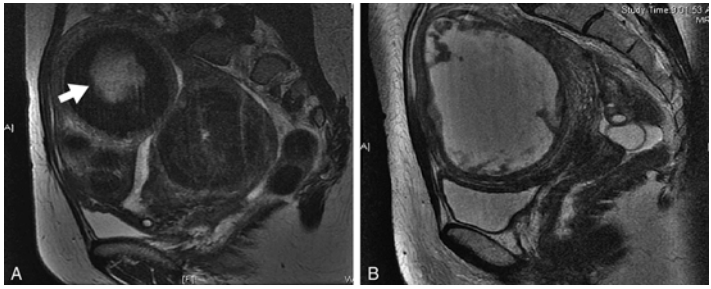

Fig. 1.1 Degenerating leiomyomas seen by T2-weighted magnetic resonance imaging (MRI; **a**; *arrow*) and by T1-weighted MRI (**b**) with gadolinium contrast (From Laughlin and Stewart [24], with permission of the American College of Obstetricians and Gynecologists)

smears can be used to try to sweep the strings out of the cervical canal [27]. While absent strings are concerning for IUD malpositioning, pelvic ultrasounds are necessary to confirm IUD location (Fig. 1.2). Patients should have a beta-human chorionic gonadotropin (hCG) checked to ensure unintended pregnancy has not occurred.

Regardless of presentation, malpositioned copper IUDs should be removed as the risk of pregnancy is increased; malpositioned levonorgestrel IUDs likely still provide adequate contraception but should be removed if the patient's pain is attributed to IUD malpositioning [26, 29]. A patient's pain should improve following removal of a malpositioned IUD; always consider the possibility of concomitant infection, including pelvic inflammatory disease, particularly in patients with persistent pelvic pain and/or fever. Please refer to Chap. 6, Pelvic Inflammatory Disease and Tubo-ovarian Abscess, for more information. If the IUD is not visualized on ultrasound, an abdominal radiograph can be obtained to assess for IUD perforation; if the IUD is not visualized in the abdominal cavity, it is assumed to have been expelled [26, 27]. Consider the possibility of visceral injury if an IUD is located in the pelvis or abdomen, outside of the uterus.

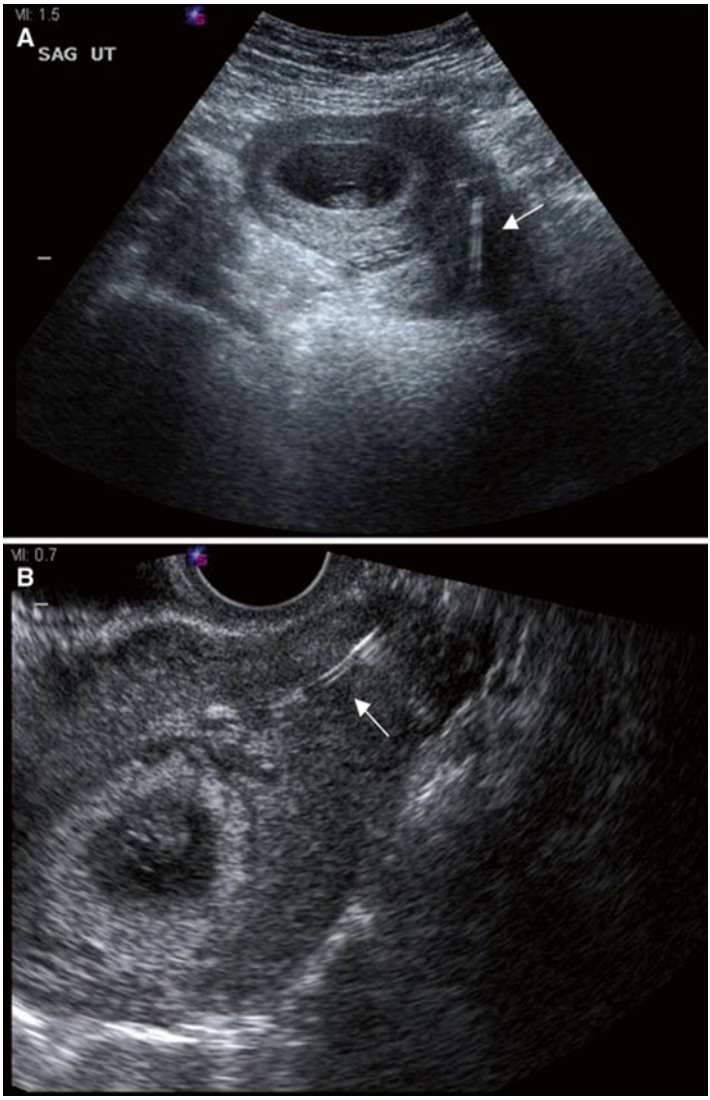

FIG. 1.2 Malpositioned IUD. (**a**) This sagittal transabdominal image shows an IUP above the malpositioned IUD (*arrow*) in the cervix. (**b**) Sagittal transvaginal image of the same patient, showing the malpositioned IUD (*arrow*) in the endocervical canal. *IUD* intrauterine device, *IUP* intrauterine pregnancy (Reprinted from Moschos and Twickler [28], with permission from Elsevier)

In patients presenting with pain and an IUD in place with a positive hCG, the pelvic ultrasound should be used to assess not only IUD location but also pregnancy location. If no pregnancy is identified, the patient should be followed for a pregnancy of unknown location (see Chap. 3, Pregnancy of Unknown Location and Ectopic Pregnancy, for more information). A patient with an intrauterine pregnancy with an IUD in place is at increased risk of first and second trimester spontaneous abortion, septic abortion, and preterm delivery [28, 30]. The IUD should be removed if the strings are visible at the cervix, though removal in itself carries a small risk of spontaneous abortion [30]. If the IUD strings are not visible at the cervix, and the IUD cannot be removed easily with ultrasound guidance, it should be left in place in patients wanting to continue their pregnancies. Patients with ongoing pregnancy with an IUD in place should be carefully counseled to present for pain, abnormal bleeding, fevers, or any other signs of infection.

Functional

Many functional causes of pelvic pain can be managed with hormonal medications, as detailed below. Contraindications to estrogen therapy include, but are not limited to, migraines with aura; smoking (in women over 35 years of age); prior deep vein thrombosis or pulmonary embolism; known thrombophilia; cerebrovascular disease; ischemic cardiac disease; severe hypertension; complicated vascular disease; peripartum cardiomyopathy within the last 6 months or with impaired cardiac function; severe cirrhosis; liver malignancy; active breast cancer; and lupus with positive antiphospholipid antibodies [31]. Contraindications to progesterone therapy include but are not limited to current breast cancer and severe liver dysfunction. Please refer to the Centers for Disease Control and Prevention U.S. Medical Eligibility for Contraception Use for further details.

Dysmenorrhea Pelvic pain during menses. Primary dysmenorrhea is defined as menstrual pain in the absence of identifiable pathology, while secondary dysmenorrhea is attributable to an underlying cause, such as endometriosis, adenomyosis, or fibroids [32]. Episodes of dysmenorrhea begin around the onset of menses and usually last 2–3 days [33]. Patients describe repetitive cramping, sometimes characterized as labor pain, potentially severe enough to necessitate absence from school or work. Patients may have accompanying backache, nausea, vomiting, and diarrhea [33]. On physical examination, patients may have mild uterine tenderness, but usually no other significant findings; laboratory assessment and pelvic ultrasound will usually be similarly unrevealing [33]. Nonsteroidal anti-inflammatory drugs and combined oral contraceptive pills have been shown to be effective in the treatment of dysmenorrhea [34, 35].

Mittelschmerz Pelvic pain preceding the rupture of the ovarian follicle (ovulation), likely occurring in 50 % of women in their lifetimes [36]. Ovulation usually occurs 2 weeks before menses begin; in patients with approximately monthly cycles, the pain will occur midcycle. Pain is usually sudden in onset; on ultrasound, patients may have a small amount of simple or complex free fluid [37]. This pain may last up to 48 h. Management is supportive, though ovulation suppression with combined oral contraceptive pills or injected or implantable progestins can be considered for patients with recurrent episodes of Mittelschmerz.

Endometriosis The presence of endometrial glands and stroma outside of the uterus, which causes inflammation and scarring [38]. Endometriosis is estimated to be present in 6–10 % of reproductive age women [39]. Patients may experience painful menses, though some also report chronic pain throughout the menstrual cycle; bladder, bowel, and/or musculoskeletal dysfunction may also contribute to endometriosis-related pain [39, 40]. Endometriosis may be suspected by transvaginal ultrasound or MRI. A pelvic ultrasound may reveal endometriomas, and by MRI, endometriosis implants

may appear as thickening of the uterine ligaments, peritoneal nodules, obliteration of the anterior or posterior cul-de-sacs, or ovarian endometriomas [41]. Please see Chap. 4, Adnexal Masses and Ovarian Cyst Rupture, for more information on the diagnosis of endometriomas. The gold standard method of diagnosis is detection of endometriosis lesions by laparoscopy.

Maintenance therapy for endometriosis chiefly involves hormonal medications, including but not limited to combined oral contraceptive pills, progesterone-only pills, injections, implant or intrauterine device, or gonadotropin-releasing hormone agonists, and some patients require surgical resections of their endometriotic implants [40]. Patients with severe chronic pain may be managed by pain specialists.

Patients with endometriosis may present with acute exacerbations of their pelvic pain, often in the context of disruption of their hormonal medications. It can be helpful to ask patients whether the quality and distribution of their current pelvic pain is consistent with their baseline endometriosis-related pain. Physical examination may reveal thick or nodular uterosacral ligaments, a nonmobile uterus, or tender adnexa. A pelvic ultrasound can be obtained if a patient does not have recent pelvic imaging, and may reveal endometriomas. In patients whose acute pain is attributed to endometriosis, treatment is supportive; nonsteroidal anti-inflammatory drugs and application of heating pads can be helpful.

Adenomyosis The presence of endometrial glands and stroma within the myometrium. Less commonly, adenomyosis may also present as a focal mass, called an adenomyoma [38]. Adenomyosis can be associated with menorrhagia, irregular bleeding, dysmenorrhea, or chronic pelvic pain. On examination, patients may have an enlarged or globular uterus [42]. Adenomyosis may be diagnosed using transvaginal ultrasound, though the reported sensitivity and specificity varies and is operator dependent (Fig. 1.3); MRI has higher sensitivity for the diagnosis of adenomyosis [44–46]. By ultrasound, adenomyosis may appear as heterogeneity in the uterine myometrium; small myometrial cysts may also be noted [43].

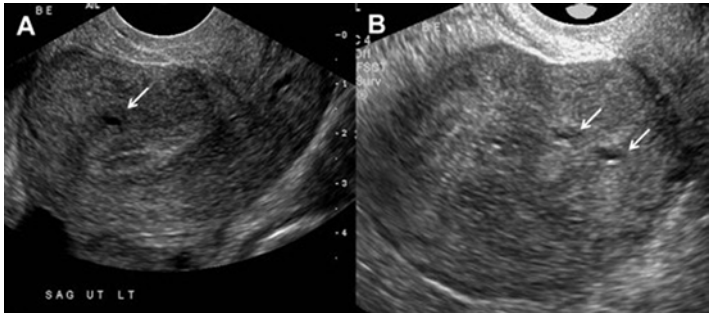

FIG. 1.3 Adenomyosis. (**a**) Transvaginal sagittal image of the uterus demonstrates a subendometrial myometrial cyst (*arrow*). (**b**) Additional cysts (*arrows*) were seen in a parasagittal plane, in the region of the junctional zone (Reprinted from Amirbekian and Hooley [43], with permission from Elsevier)

Acute interventions are not required for adenomyosis; symptoms of adenomyosis are generally treated with similar hormonal treatment regimens as endometriosis, namely, oral contraceptive pills, progesterone-only methods including levonorgestrel IUDs, and gonadotropin-releasing hormone agonists, with variable success [47, 48]. The only definitive management is hysterectomy.

Pregnancy Related

Septic Abortion An ascending polymicrobial infection of the upper genital tract following spontaneous, medical, or surgical abortions and commonly presenting with fever, bleeding, and/or pain. These infections may quickly evolve into fulminant sepsis [49]. Please see Chap. 8, Spontaneous Abortion, for more information.

Spontaneous Abortion Also known as a miscarriage, occurring in pregnancies less than 20 weeks of gestational age, and usually presenting with pain and bleeding. Please see Chap. 8, Spontaneous Abortion, for more information.

Ectopic Pregnancy A pregnancy implanted outside of the uterine cavity. Rupture of tubal ectopic pregnancies can result in acute pain and intra-abdominal hemorrhage. Please see Chap. 3, Pregnancy of Unknown Location and Ectopic Pregnancy, for more information.

Other obstetrical issues, including labor, placental abruption, uterine rupture, and chorioamnionitis, are discussed in Chap. 12, Obstetrics in the Emergency Room.

Other

Sexual Trauma or Domestic Violence Please see Chap. 9, Sexual Assault, for more information.

Ovarian Hyperstimulation Syndrome (OHSS) An iatrogenic condition resulting from ovarian stimulation, resulting in pain (usually due to ovarian enlargement), nausea, electrolyte abnormalities, ascites, oliguria, pleural effusions, and thromboembolism [50]. Please see Chap. 20, Reproductive Endocrinology and Infertility, for more information.

Pediatrics

For assessment and management of acute pelvic pain specifically in pediatric patients, please see Chap. 10, Acute Pelvic Pain in Pediatric and Adolescent Patients.

Nongynecologic Etiologies

- Cardiovascular: dissecting aortic aneurysm or other ruptured aneurysm (including splenic artery aneurysm, particularly in pregnancy)
- Urologic: urinary tract infection (cystitis or pyelonephritis), nephrolithiasis, and acute urinary retention
- Musculoskeletal: myofascial pain, pelvic floor or abdominal muscular pain
- Neurologic/pain: chronic pain syndromes
- Endocrine: diabetic ketoacidosis

- Gastrointestinal: constipation, gastroenteritis, appendicitis, colitis, diverticulitis, bowel obstruction, mesenteric ischemia, and inflammatory bowel disease
- Hematologic: porphyria and sickle cell crisis
- Psychiatric: somatization, conversion disorder, factitious disorder, and malingering

When You Get the Call Ask for the most recent full set of vital signs to assess for hemodynamic stability. Of note, tachycardia is often a first sign of sepsis or hemorrhagic shock; hypotension, even a brief episode, requires emergent assessment. Ask whether a pregnancy test has been performed and, if not, request one; a urine pregnancy test provides a more rapid result than a serum test, which is particularly important in a patient with severe pain or hemodynamic changes.

If the patient is postoperative, review the operative report, including whether any intraoperative complications occurred. Note whether extensive lysis of adhesions was performed, which may potentially increase the risk of visceral injury or other postoperative complications.

When You Arrive Review all available vital signs to determine hemodynamic stability. Assess whether the patient is in distress, including whether she is alert, visibly uncomfortable, pale, and diaphoretic. Ask whether the patient has received any pain medications, which may affect the patient's physical exam findings.

History

The history provided by the patient may be abbreviated in the setting of clinical instability, namely, abnormal vital signs or altered mental status.

In a stable patient, review her full medical, surgical, obstetrical, and gynecologic history, including prior ovarian cysts, pelvic infections, or ectopic pregnancy. Record the date of her last menstrual period and inquire whether she is currently pregnant, using reliable contraception or undergoing fertility treatment. Review whether the patient recently had surgery.

Ask the patient about the onset of her pain, whether it occurred acutely or developed over days or longer. Review the location and quality of her pain, including aching, sharp, continuous, or episodic. Ask whether it was incited by an event such as intercourse, exercise, heavy lifting, or abdominal trauma, which may indicate (depending on the patient's history) vaginal cuff or wound dehiscence, rupture of ovarian cyst or ectopic pregnancy, ovarian torsion, or musculoskeletal injury. Identify associated symptoms, including fever, nausea, vomiting, diarrhea, or new or different vaginal bleeding or discharge. Review whether she has ever had this pain before or suffers from chronic pain.

Physical Examination

Observe the patient's degree of discomfort with her pain, as evidenced by posture or inability to settle into a comfortable position. Note whether the patient is pale or diaphoretic, and whether she is alert and oriented. Check for capillary refill by pressing on the fingernails; delayed reperfusion of the fingernail beds is evidence of decreased perfusion, associated with sepsis or anemia [7]. Examine the patient's abdomen for distention, rebound (pain with quickly withdrawing pressure from the abdomen), or involuntary guarding. An abdominal exam may also reveal a mass. Assess for right-sided abdominal pain suggestive of appendicitis or right-sided adnexal pathology, flank pain suggestive of nephrolithiasis, or suprapubic pain suggestive of cystitis.

If the patient is having vaginal bleeding or complains of purulent vaginal discharge, perform a speculum exam to quantify any bleeding and collect a cervical swab for nucleic acid amplification testing (NAAT) for *Neisseria gonorrhoeae* and *Chlamydia trachomatis*. A wet prep (a slide of vaginal discharge prepared with potassium hydroxide and saline, separately) or gram stain of the vaginal discharge to check for white blood cells may be helpful in diagnosing pelvic inflammatory disease or acute cervicitis. Perform a bimanual exam to assess for cervical motion tenderness, and adnexal

enlargement or tenderness. In a patient who is suspected of having an ectopic pregnancy—with a positive hCG and pelvic pain—a bimanual exam is not strictly necessary and may risk rupture of the ectopic pregnancy.

Diagnosis

A temperature of 100.4 °F (38 °C) on two occasions more than 4 h apart or a single temperature of 101 °F (38.3 °C) constitutes a fever in non-neutropenic patients. Take note of tachycardia and hypotension (even transient), which can herald impending septic or hemorrhagic shock. In patients with hemodynamic instability or altered mental status, begin resuscitation in parallel with the diagnostic workup. Hemodynamic and laboratory findings in patients with hemorrhagic or septic shock are shown in Tables 1.1 and 1.2, respectively.

All reproductive aged women—from menarche to menopause—should have an hCG checked, either by serum or by urine. Bladder catheterization can be performed to obtain this sample if necessary. Urine pregnancy tests have a lower limit of hCG detection of 20–50 milli-international units per milliliter (mIU/mL) [51].

A complete blood count with differential should be obtained in all patients with acute pelvic pain, which may reveal anemia and/or leukocytosis. Of note, hemoglobin may underestimate acute anemia due to an ongoing hemorrhage. A blood type and antibody screen should be obtained for any pregnant patient or any patient who is suspected to have sepsis or significant bleeding. Obtain coagulation studies (prothrombin time (PT), activated partial thromboplastin time (aPTT), and fibrinogen) in patients with known bleeding diathesis, taking anticoagulant medications, or those with hemorrhage or sepsis (to assess for disseminated intravascular coagulation). In patients with possible sepsis, also obtain a lactate, liver function tests, electrolytes, and creatinine. Blood, urine, sputum, wound, and/or drain cultures (as applicable)

should be obtained in any patient with a temperature above 38.3 °C (101 °F) and/or concern for sepsis. Consider sending stool studies for *Clostridium difficile* in patients with diarrhea, recent antibiotic exposure and/or prior *C. difficile* infection. In well-appearing patients with just mild pelvic discomfort, a urinalysis and nucleic acid amplification testing (NAAT) of a cervical swab for *N. gonorrhoeae* and *C. trachomatis* are often good starting points.

In patients with peritoneal signs, mental status changes, and/or hemodynamic instability, waiting for a formal ultrasound may not be prudent; a focused assessment with sonography for trauma (FAST) scan should be performed for the rapid assessment of hemoperitoneum, potentially due to ruptured ovarian cyst or ectopic pregnancy. The FAST scan is a bedside ultrasound assessing for free fluid in the perihepatic, perisplenic, and pelvic space (Fig. 1.4); the full trauma assessment includes the pericardial space [52]. Of note, a FAST scan will not reliably reveal retroperitoneal hemorrhage, which is

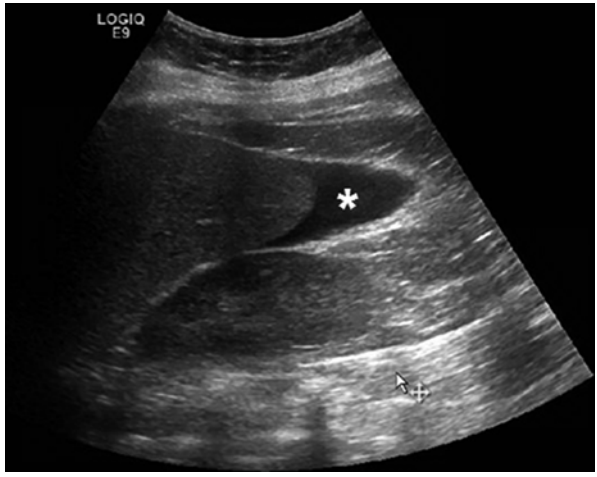

Fig. 1.4 Hemoperitoneum by abdominal ultrasound. Abdominal ultrasound revealed hemoperitoneum, indicated with an asterisk (*), extending from the pelvis to the liver edge

generally best visualized by CT scan. Most patients are sufficiently stable for formal imaging, and a transvaginal ultrasound is preferable as a first step in women with acute pelvic pain.

In patients with signs of sepsis, imaging should be obtained to identify the source. A pelvic ultrasound may suggest a tubo-ovarian abscess, while a CT scan may be useful in better characterizing a pelvic abscess while also allowing visualization of the gastrointestinal and urinary tracts, and such pathology as diverticulitis, appendicitis, bowel obstruction, nephrolithiasis, and postoperative surgical complications. A patient who is hemodynamically unstable, however, may need to move straight to surgical exploration without obtaining a CT scan, unless she responds immediately to resuscitative measures.

Management

Please see Fig. 1.5 for a diagnostic and management algorithm for patients with pelvic pain, focusing on emergent or life-threatening causes of pelvic pain. An important branch point in the assessment and management of acutely ill patients with pelvic pain is to determine whether an infection is present.

Noninfectious

In hemodynamically unstable patients with pain and without evidence of sepsis, hemorrhage is a frequent cause. In patients who are not hemorrhaging vaginally (Chap. 2), intra-abdominal hemorrhage should be suspected; intraperitoneal (but not retroperitoneal) hemorrhage can be confirmed with a FAST scan. Hemodynamic changes in patients with hemorrhagic shock are shown in Table 1.1.

The more common gynecologic etiologies of hemoperitoneum include a ruptured ectopic pregnancy and a ruptured

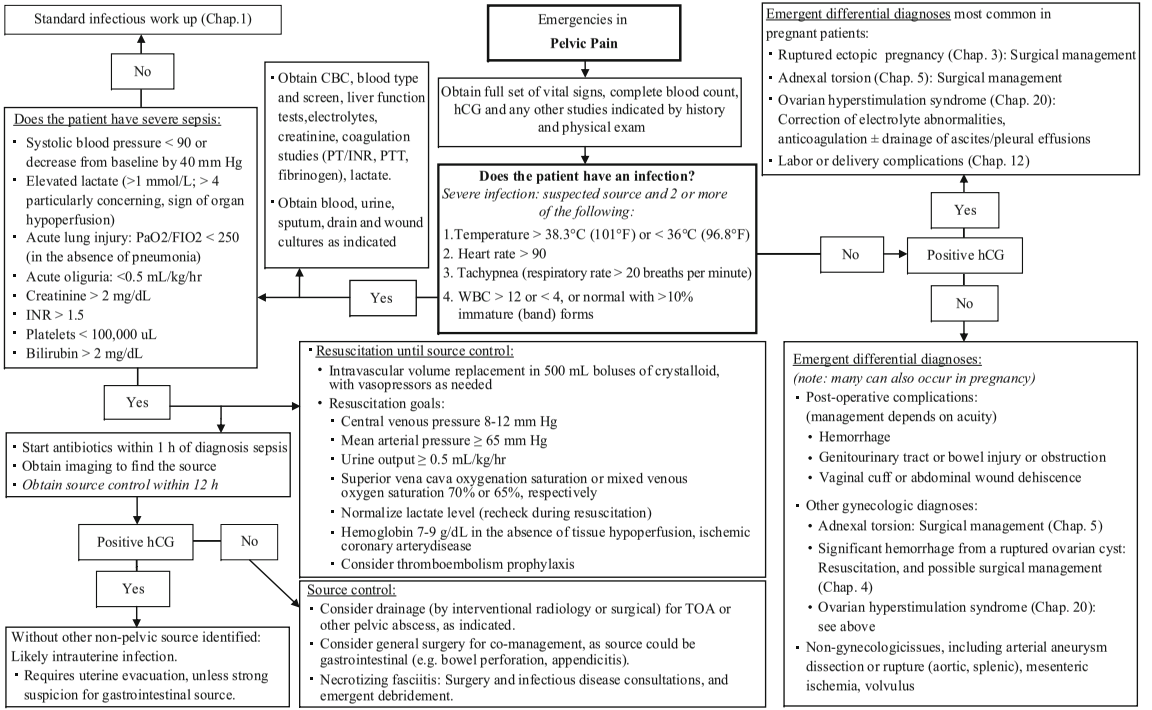

FIG. 1.5 Diagnostic and management algorithm for acute pelvic pain

ovarian cyst. In patients with a positive hCG (without intrauterine pregnancy), pain, and hemodynamic compromise, immediate operative management is indicated with the presumed diagnosis of ruptured ectopic pregnancy. A caveat is in patients who have recently undergone in vitro fertilization. Patients may rarely have significant hemoperitoneum following oocyte retrieval (particularly in the first 24 h), with residual positive serum hCG due to their treatment medications. Additionally, patients with severe OHSS (who may also be pregnant) may have large ascites by FAST exam, as well as tachycardia, oliguria, and hypotension. Please refer to Chap. 20, Reproductive Endocrinology and Infertility, for more information on the diagnosis and management of these complications. Please see Chap. 3, Pregnancy of Unknown Location and Ectopic Pregnancy, for the diagnosis and management of ectopic pregnancy. Please see Chap. 4, Adnexal Masses and Ovarian Cyst Rupture, for diagnosis and management of ruptured ovarian cysts.

While resources are being mobilized for a patient with suspected intra-abdominal hemorrhage, resuscitation should be started for patients with estimated blood loss of 500 cc or more and/or hemodynamic changes. In acutely unstable patients, uncrossed O-negative blood can be ordered. Resuscitation goals include a heart rate below 100 beats per min, hemoglobin of at least 7 g per deciliter (dL), platelets above 50,000 per microliter (uL), fibrinogen above 100 mg/dL, and an INR less than 1.5 [53, 54]. These laboratory values should be rechecked frequently during resuscitation and transfusion, in addition to blood pH and electrolytes (particularly calcium and potassium). Hypothermia should be avoided.

Please see Chap. 13, Preparing for Urgent or Emergent Surgery, for more information on resuscitation and transfusion. Patients with acute intra-abdominal or vaginal hemorrhage, particularly those requiring surgery, may require reversal of anticoagulant medications, also discussed in Chap. 13. Management of patients with disseminated intravascular coagulation and von Willebrand disease is discussed in Chap. 2, Vaginal Hemorrhage.

Non-hemorrhagic causes of acute pelvic pain without infection include ovarian torsion, which is a surgical emergency and is discussed in further detail in Chap. 5, Adnexal Torsion. Pregnancy-related issues (including labor, placental abruption, and uterine rupture) are discussed in Chap. 12, Obstetrics in the Emergency Room. OHSS can also cause significant pelvic pain and distention, in addition to metabolic and hematologic perturbations; OHSS is discussed in Chap. 20, Reproductive Endocrinology and Infertility. Non-gynecologic causes of acute pelvic pain include, but are not limited to, abdominal arterial aneurysm dissection or rupture, mesenteric ischemia, bowel obstruction or volvulus, and nephrolithiasis. Bowel obstruction is discussed in Chaps. 16 and 18.

Infectious

This chapter will focus on emergent infectious causes of pelvic pain, namely, conditions leading to sepsis (Table 1.2). Infections without sepsis are addressed in Chap. 6, Pelvic Inflammatory Disease and Tubo-ovarian Abscesses, and Chap. 16, Complications of Minimally Invasive Gynecologic Surgery, and neutropenic fever is discussed in Chap. 18, Gynecologic Oncology. Furthermore, potentially morbid noninfectious sources of fever specific to gynecologic patients include ovarian torsion, ovarian cyst rupture, venous thrombosis, medication reactions, alcohol withdrawal, tumor fever, and some blood transfusion reactions (though sepsis from a blood transfusion is also possible).

The patient's vital signs and laboratory results can be used to diagnose sepsis; the clinical criteria for the diagnosis of sepsis are shown in Table 1.2 [6, 7]. The suspected source of infection is usually suggested by the patient's history, including recent surgical procedure, physical examination, and/or imaging.

For acutely unstable patients, including those with hypotension and mental status changes, additional support personnel should be called to assist. Initial management of severe sepsis/shock includes the placement of two large-bore IVs, IV

crystalloid for blood pressure support, and supplemental oxygen by high-flow facemask as needed [7]. As resuscitation continues using intravenous fluid, oxygen, and vasopressors as needed, goals include a central venous pressure of 8–12 mmHg; a mean arterial pressure >65 mmHg; urine output of at least 0.5 mL/kg/h; superior vena cava oxygenation saturation or mixed venous oxygen saturation 70 % or 65 %, respectively; a normalized lactate level; and a hemoglobin level of 7–9 g/dL in patients without tissue hypoperfusion or ischemic coronary artery disease [7]. Thromboembolism prophylaxis should be considered.

If not obtained earlier, a complete blood count, blood type and antibody screen, liver function tests, coagulation studies (PT, aPTT, and fibrinogen), and lactate should be obtained. A complete blood count, electrolytes, lactate, and coagulation studies (as indicated) should be rechecked frequently during resuscitation to assess progress. An arterial blood gas should be obtained if the patient is in distress. Blood, urine, sputum, and/or wound cultures should be collected as indicated; 1,3 [beta]-D-glucan, mannan, and anti-mannan antibody assays can be obtained in immunocompromised or chronically ill patients at risk for disseminated candidiasis. Antibiotics should be started within 1 h of diagnosis of sepsis [7].

Antibiotic selection is dictated by the suspected source and recent antibiotic exposure. Please refer to Chap. 16, Complications of Minimally Invasive Gynecologic Surgery, for antibiotic recommendations for specific sources. In patients with sepsis from an unknown source, a broad-spectrum regimen can include vancomycin (15 mg/kg IV every 12 h, in patients with normal renal function) and piperacillin-tazobactam (3.375–4.5 g IV every 6 h); cefepime (2 g IV every 8 h) and ceftazidime (2 g every 8 h) are alternatives to piperacillin-tazobactam [55]. Antibiotic regimens for neutropenic fever are discussed in Chap. 18, Gynecologic Oncology.

The source of infection must be identified and addressed quickly. Infectious collections must be addressed as soon as possible, through uterine evacuation, abscess drainage (by

interventional radiology, laparotomy or laparoscopy, as indicated), or repair of visceral injury or vaginal cuff dehiscence. If a patient has an intrauterine pregnancy and no other source can be identified, a septic abortion is diagnosed and uterine evacuation must be performed. Patients with suspected necrotizing fasciitis (postpartum or postoperatively) based on fever, laboratory parameters, imaging and exquisite pain require urgent, aggressive surgical debridement. For management of septic abortion, please see Chap. 8, Spontaneous Abortion. For management of tubo-ovarian abscess, please see Chap. 6, Pelvic Inflammatory Disease and Tubo-ovarian Abscess. For the management of postoperative complications including bowel and urinary tract injuries, necrotizing fasciitis, pelvic abscesses, and vaginal cuff cellulitis, please see Chap. 16, Complications of Minimally Invasive Gynecologic Surgery. For management of bowel anastomotic leaks, abdominal wound dehiscence, and neutropenic fever, please see Chap. 18, Gynecologic Oncology.

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Chapter 2
Vaginal Hemorrhage

Paula C. Brady and Daniela Carusi

Definitions

Disseminated Intravascular Coagulation (DIC) Systematic activation of coagulation pathways causing diffuse fibrin deposition, leading to consumption of coagulation factors and platelets, which can result in hemorrhage and/or thrombosis [1]. Conditions leading to DIC include sepsis, malignancy, trauma, obstetrical complications (amniotic fluid embolism, placental abruption, intrauterine fetal demise), liver failure, and ABO incompatibility [1].

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Differential Diagnosis [2]

Spontaneous

In any group:

- Bleeding diathesis or other hematologic abnormality including thrombocytopenia or DIC
- Malignancy: uterine, cervical, vaginal, or gestational trophoblastic neoplasia
- Anticoagulation therapy

Nonpregnant:

- Endometrial polyps
- Uterine fibroids
- Adenomyosis
- Primary menorrhagia (heavy menses)
- Anovulatory bleeding, such as in polycystic ovarian syndrome, perimenopause, or hypothyroidism

Early pregnancy:

- Complete, incomplete, threatened abortion, or early pregnancy failure
- Subchorionic hematoma
- Placenta previa (overlying the cervical os)
- Placental abruption
- Retained products of conception
- Gestational trophoblastic neoplasia
- Ectopic pregnancy

Pregnancy at 20 weeks of gestation or more:

- Uterine rupture
- Placental abruption
- Placenta previa
- Cervical dilation

(continued)

(continued)

Postpartum:

- Atony
- Cervical or vaginal lacerations
- Uterine inversion
- Retained products of conception, including abnormally adherent placenta (i.e. placenta accreta)

Traumatic

- Vaginal laceration from intercourse, assault, or sexual trauma
- Surgical site bleeding (such as following a hysterectomy, vaginal surgery, loop electrosurgical excision procedure (LEEP), or cone biopsy)
- Any uterine instrumentation leading to retained products of conception, perforation, atony, or uterine, vaginal, or cervical lacerations

This chapter will focus on the diagnosis and management of vaginal bleeding in nonpregnant women, attributed to anovulatory bleeding, menorrhagia, uterine pathology (such as fibroids), anticoagulation, or bleeding diatheses. For diagnosis and management of ectopic pregnancies, which can result in vaginal bleeding (particularly cervical or cesarean scar ectopic pregnancies), please refer to Chap. 3, Pregnancy of Unknown Location and Ectopic Pregnancy. For diagnosis and management of hemorrhage from a spontaneous abortion, please refer to Chap. 8, Spontaneous Abortion. For diagnosis of management of bleeding due to intrauterine pregnancies in the second or third trimesters, please see Chap. 12, Obstetrics in the Emergency Room. For diagnosis and management of bleeding complications of medical or surgical abortion, please see Chap. 17, Induced Abortion. Vaginal hemorrhage due to gynecologic malignancies is discussed in Chap. 18, Gynecologic Oncology.

When You Get the Call Ask for a full set of the patient's vital signs. As a means of triaging the acuity of the patient's bleeding, consider asking the caller to describe the volume of bleeding, including whether the source of the vaginal bleeding could be visualized or if too much bright red bleeding was present. Ensure that a pregnancy test has been performed in any premenopausal patient, and request that the patient be moved to a private room on bed or stretcher equipped for gynecologic exams (i.e., with stirrups).

When You Arrive Review the full vital sign flow sheet to assess for hemodynamic instability and hemorrhagic shock (Table 2.1). Assess the patient's distress, including whether she is pale or diaphoretic and whether she is alert and oriented. Confirm that the patient has IV access. If there is evidence of significant bleeding or vital sign changes, order a second IV to be placed. Tachycardia, hypotension, and/or lethargy requires immediate resuscitation. Request that blood products be cross-matched, and consider requesting delivery of emergency release, O-negative blood to the beside for clinically unstable patients.

History

The history may be abbreviated in clinically unstable patients. In these patients, the history may consist of a brief review of medical problems, medications (including anticoagulants and contraception), allergies, prior surgeries, and possible causes for her bleeding, such as recent surgery, pregnancy, fibroids, anovulation, and known bleeding diathesis.

In stable patients, the history of present illness includes when the bleeding started and how many maxi pads or tampons she is using per day. Soaking two thick maxi pads or tampons per hour for 2 h is a rough estimate of potentially excessive bleeding. Record the date of her last menstrual period. Ask the patient whether she has any associated symptoms of pain, fever, bowel, or bladder dysfunction. Review whether any activities—such as intercourse—precipitated the bleeding, which may sug-

Table 2.1 Stages of hemorrhagic shock

Class I: blood volume lost <15 %	**Class II**: blood volume lost 15–30 %
Heart rate <100 beats per minute	Heart rate >100 beats per minute
Blood pressure normal	Blood pressure normal
Respiratory rate 14–20 breaths per minute	Respiratory rate 20–30 breaths per minute
Urine output >30 mL/h	Urine output 20–30 mL/h
Mental status normal	Mental status mildly anxious
Class III: blood volume lost 30–40 %	**Class IV**: blood volume lost >40 %
Heart rate >120 beats per minute	Heart rate >140 beats per minute
Blood pressure decreased	Blood pressure decreased
Respiratory rate 30–40 breaths per minute	Respiratory rate >35 breaths per minute
Urine output 5–15 mL/h	Urine output negligible
Mental status anxious/ confused	Mental status confused/ lethargic
Often marks the onset of decompensated hypovolemic shock	

Committee on Trauma [4]

gest a laceration, or vaginal cuff injury or dehiscence in a patient who has undergone total hysterectomy (particularly within the last 6–8 weeks). If the patient underwent recent gynecologic surgery, review the operative report.

Review the patient's full medical history, including her obstetrical history, whether her menses are regular (occurring roughly every 21 to 35 days), and whether she has menorrhagia or any known uterine lesions including fibroids, polyps,

Table 2.2 History suggestive of bleeding diathesis

One of the following:
Menorrhagia (particularly since menarche)
Postpartum hemorrhage
Peri- or postoperative hemorrhage
And/or two of more of the following:
Easy bruising (at least once or twice per month)
Epistaxis (at least once or twice per month)
Bleeding from the gums
Family history of excessive bleeding

American College of Obstetricians and Gynecologists [2]

or adenomyosis. Review whether the patient has a current or prior gynecologic malignancy, a known bleeding diathesis, or history suggestive of a bleeding problem (Table 2.2) [2]. Review the patient's medications, particularly whether she is taking anticoagulant or hormonal medications.

Physical Examination

Assess the patient's alertness and orientation. Check for capillary refill by pressing on the fingernails; delayed reperfusion of the fingernail beds is evidence of decreased perfusion, associated with sepsis or anemia [3]. Perform an abdominal examination, noting the presence of peritoneal signs, including rebound (pain when abdominal pressure is quickly withdrawn), involuntary guarding, or shake tenderness (pain when shaking the patient's abdomen or bed), which may indicate intra-abdominal infection, inflammation, or hemorrhage.

If bleeding is heavy, prepare to use wall suction, which is available in most emergency room bays and hospital rooms, for the speculum exam in order to enhance visualization. Localize the source of bleeding, and assess for cervical or vaginal lacerations. In a patient likely having a spontaneous abortion, if products of conception are visualized extruding

from the cervical os, remove these and send them to pathology for confirmation. Of note, if the tissue cannot be easily extracted, abort efforts to remove it. This could represent a cervical (or other abnormal) implantation, and extraction could lead to severe hemorrhage. Similarly, cervical or vaginal polyps or other masses (including possible malignancy) should not be removed or biopsied in the emergency room, as hemorrhage may result. On bimanual exam, note the uterine size, which may indicate the presence of pregnancy, adenomyosis, or fibroids; also note uterine tenderness.

Diagnosis

Hemorrhagic shock can be diagnosed clinically, shown in Table 2.1 [4]. Hypotension is defined as systolic blood pressure (SBP) below 90 millimeters of mercury (mmHg) or 20 % or more below a patient's baseline [5, 6]. In severely decompensated patients, the presence of a femoral pulse can be used for reference, reflecting an SBP of 60–70 mmHg; alternatively, the presence of a carotid pulse represents an SBP of at least 60 mmHg [7]. Notably, tachycardia is the first sign of hemorrhagic shock, and hypotension may not appear until 30–40 % of a patient's blood volume has been lost. These findings require immediate, aggressive resuscitation, which should begin alongside diagnosis. Resuscitation is discussed under "Management" below.

In patients with vaginal bleeding, a complete blood count and blood type and antibody screen should be ordered. A human chorionic gonadotropin (hCG) should be ordered in any patient who is not menopausal, defined as 1 year without menses, occurring at a mean age of 51 years [8]. Complicating this definition are some women with over a year of amenorrhea who are premenopausal but anovulatory, which is a risk factor for endometrial hyperplasia and malignancy and heavy bleeding.

In patients using anticoagulant medications, and those with major hemorrhage, possible or known bleeding diathesis, pregnancy-related bleeding, or possible disseminated

intravascular coagulation, order coagulation studies (prothrombin time (PT) and activated partial thromboplastin time (aPTT)) and a fibrinogen [1].

The diagnosis of DIC is both clinical and by laboratory criteria (usually thrombocytopenia, low fibrinogen and/or prolonged PT/aPTT); serial laboratory testing may reveal worsening parameters. In patients with possible bleeding diathesis, particularly von Willebrand disease, check a von Willebrand factor, ristocetin cofactor assay, and factor VIII level, which are less helpful acutely; pregnancy, thyroid dysfunction, and use of hormonal medication affect these levels [9, 10]. In patients with irregular periods or baseline menorrhagia, consider checking a thyroid-stimulating hormone (TSH) if not recorded in the past year.

If a patient is sufficiently stable to be sent for imaging, a pelvic ultrasound should be obtained, which may reveal uterine pathology such as polyps or fibroids.

In patients who are perimenopausal, anovulatory or oligoovulatory, obese and/or receiving hormone replacement therapy, or any woman over 45 years with irregular bleeding, endometrial sampling is recommended to assess for endometrial hyperplasia or malignancy [2]. This is ideally performed prior to initiating any hormones, though sampling should be performed in a setting in which the results can be reliably followed up. For patients with significant anovulatory bleeding, uterine evacuation (with curettage or manual vacuum extraction) can be both diagnostic and therapeutic.

Management

Management is determined according to the patient's clinical stability; hemodynamically unstable patients require intervention (detailed below), while stable patients can be managed medically. The goal of management of vaginal hemorrhage is to significantly reduce or stop a patient's bleeding.

Resuscitation

In hemodynamically unstable patients, resuscitation should begin alongside the assessment. In recommendations drawn from the trauma literature, patients receiving massive transfusion (>10 units of packed red cells), red blood cells, fresh frozen plasma (FFP), and platelets should be administered in a ratio of 1:1:1, meaning 6 units of pooled random donor platelets (which equals one apheresis platelet unit) should be given for every 6 units of red blood cells and 6 units of FFP [11–13].

For non-massive, goal-oriented resuscitation, goals include (1) hemoglobin greater than 7 g per deciliter (dL), though higher thresholds are advisable in elderly patients and those with cardiopulmonary disease; (2) platelets above 50,000 per uL, particularly if surgery is planned; (3) an international normalized ratio (INR) less than 1.5; and (4) a fibrinogen level above 100 milligrams (mg) per dL [14, 15]. A patient's goal heart rate should generally be less than 100 beats per minute, with urine output at least 0.5 milliliters (mL) per kilogram per hour.

Please refer to Chap. 13, Preparing for Urgent or Emergent Surgery, for further information regarding specific blood products and fibrinogen concentrates.

Medical Management of Vaginal Hemorrhage

In the acute setting, medical management is preferable in hemodynamically stable patients with vaginal bleeding attributed to anovulatory bleeding, menorrhagia, or uterine pathology such as fibroids and may be helpful in subacute bleeding attributed to anticoagulation or bleeding diatheses. Commonly used medications are shown in Table 2.3.

Medical management alone has a limited role in the management of unstable patients, though intravenous estrogen, in

Table 2.3 Medical management of vaginal bleeding

Premarin® (conjugated equine estrogen)	25 mg IV every 4–6 h, effect should be seen in 6–8 h
Monophasic oral contraceptive pills	1 pill PO, up to every 6 h, then tapered
Tranexamic acid, as adjunct	IV: 10 mg/kg up to 1 g (or 1 g presumptively) over 10 min, repeated every 8 h as needed
	PO: 1 g PO every 6 h, or 1.3 g every 8 h.
Medroxyprogesterone acetate	20 mg PO every 8 h (up to 80 mg per day)
Norethindrone acetate	5–15 mg per day

American College of Obstetricians and Gynecologists [2], James et al. [9]
Please refer to the text for contraindications and side effects of these medications
PO by mouth, *IV* intravenous

conjunction with resuscitative efforts, can be an effective intervention for vaginal hemorrhage, with improvement in bleeding within 6 h [16]. In many unstable patients, medical management—such as correction of DIC, reversal of anticoagulation, treatment of bleeding diathesis, or adjunctive treatment with tranexamic acid—may be used, while the underlying cause of bleeding (such as retained products of conception or severe intrauterine infection) is addressed surgically.

Medical management of severe vaginal hemorrhage

For acute vaginal bleeding unrelated to pregnancy, intravenous conjugated equine estrogen (Premarin®, Wyeth Pharmaceuticals, Philadelphia, PA, 25 mg IV every 4–6 h) can

be used [9, 16]. Improvement is usually seen in 1–2 doses; continuation should be reevaluated at 48 h at the latest. This medication is highly thrombogenic; contraindications to estrogen therapy include, but are not limited to, migraines with aura, smoking (in women over 35 years of age), prior deep vein thrombosis or pulmonary embolism, known thrombophilia, cerebrovascular disease, ischemic cardiac disease, severe hypertension, complicated vascular disease, peripartum cardiomyopathy within the last 6 months or with impaired cardiac function, severe cirrhosis, liver malignancy, active breast cancer, and lupus with positive antiphospholipid antibodies [17]. Ultimately, the thrombogenic risks of the medication must be weighed against the severity of the bleeding and the risks to the patient of alternative management such as surgery.

Once bleeding has improved with IV estrogen, a patient should be transitioned to monophasic combined oral contraceptive pills (COC) with 50 micrograms (μg) of ethinyl estradiol every 6 h until the bleeding is much improved; a suggested downtitration protocol involves decreasing pill frequency to every 8 h for 2–7 days and then every 12 h for 2–7 days, followed by daily administration going forward [9]. Lower doses of ethinyl estradiol and more rapid downtitration should be considered in patients whose bleeding is much improved, particularly patients over age 35 years and/or with comorbidities such as diabetes and hypertension [17]. Side effects of high-dose estrogen therapy include nausea, and antiemetics should be prescribed as needed.

As an adjunct to treatment of acute bleeding, intravenous tranexamic acid can be used. Tranexamic acid is an antifibrinolytic medication, administered in a dose of 10 mg/kg for a maximum of 1 g, or 1 g presumptively (extrapolating from the trauma literature) intravenously over 10 min and repeated every 8 h as needed [18–20]. Tranexamic acid can also be administered orally in the acute setting, 1 gram every 6 h. Oral tranexamic acid (1.3 g every 8 h), administered for the 5 days of menses, is used for chronic menorrhagia and may reduce blood loss by up to half [21]. Contraindications

include, but are not limited to, acquired defective color vision and active intravascular clotting. The risk of thromboembolism associated with tranexamic acid is controversial, though in general, this medication should be used with caution in patients at high risk for thromboembolism, including those with known thrombophilia or a history of venous thromboembolism [22]. Dosing should be adjusted in patients with renal dysfunction.

Medical management of subacute vaginal bleeding

For patients without severe hemorrhage or hemodynamic instability, upfront use of oral medications can be considered. Contraindications to estrogen apply to the use of combined oral contraceptive pills and can be found in the Centers for Disease Control and Prevention's U.S. Medical Eligibility Criteria for Contraceptive Use [17]. The patient's risk of thromboembolism must be balanced with the severity of her bleeding.

For patients with severe bleeding and anemia, a monophasic COC containing 30–50 μg ethinyl estradiol can be administered at a dose of 1 tab orally every 6–8 h until the bleeding slows significantly, at which point the interval can be downtitrated over a week to one pill per day [9]. In patients with stable bleeding, a daily COC can be prescribed.

Oral progestins are a useful alternative for the management of vaginal bleeding in nonpregnant patients who are not appropriate candidates for estrogen-containing medications. Options suggested by a European consensus group include medroxyprogesterone acetate (20 mg every 8 h, up to 80 mg per day) or norethindrone acetate (up to 15 mg per day) [9, 23, 24]. These medications can be continued until bleeding improves, at which point the doses can be titrated down over a week to daily or twice daily administration. Contraindications to progesterone therapy include, but are not limited to, current breast cancer and severe liver dysfunction [17].

Gonadotropin-releasing hormone agonists, such as leuprolide acetate, are also effective in gradually reducing vaginal bleeding, as well as fibroid volume, but are not helpful in the acute setting. A 3-month course of treatment with monthly 3.75 mg intramuscular leuprolide injections is associated with a median reduction in fibroid volume of 47 %, and amenorrhea is 89 % of women [25]. Side effects include vasomotor symptoms and decreased bone density [26]. Gonadotropin-releasing hormone agonists should be administered in the luteal phase of the menstrual cycle to avoid a flare effect [27].

DIC For patients with DIC, the patient's bleeding should be managed by both addressing the underlying cause and correcting the coagulopathy. Patients with platelets less than 50,000/μL who will undergo a procedure should receive a platelet transfusion [1]. In patients with bleeding and prolonged PT or aPTT, fresh frozen plasma (FFP) can be administered, for a goal INR of 1.5 [28]. Fibrinogen levels less than 100 mg/dL not improved with FFP should be treated with cryoprecipitate or commercially available fibrinogen concentrates. Please see Chap. 13, Preparing for Urgent or Emergent Surgery, for more information on blood products and fibrinogen concentrates.

Von Willebrand Disease In patients with type 1 von Willebrand disease and severe bleeding, a ristocetin cofactor assay and factor VIII level should be drawn at baseline and 1 h after administration of desmopressin (DDAVP, 0.3 ug/kg IV in 50 mL of saline over 30 minutes) [29]. Risks of DDAVP include vasodilation and hyponatremia. Consult hematology for monitoring treatment response and determining ongoing management. In patients with type 2 or type 3 disease, DDAVP is less likely to be helpful; von Willebrand factor-containing products or concentrates can be used (dosing varies) [29]. Additional medical management options for patients with von Willebrand disease also include aminocaproic acid (50–60 mg/kg PO or IV, every 4–6 h) or tranexamic

acid (10–15 mg/kg IV every 8–12 h); doses of these medications must be adjusted in patients with renal dysfunction [29].

Anticoagulants In patients with bleeding exacerbated by anticoagulant medications, assessment of the acuity of the patient's bleeding is vital to deciding whether her medications should be stopped or reversed, in consultation with the prescribing physician. At other times, these medications are absolutely crucial, such as in patients with mechanical cardiac values or active venous thromboses, and solutions to a patient's vaginal bleeding must be found in parallel. Please see Chap. 13, Preparing for Urgent or Emergent Surgery, for information on reversing anticoagulant medications.

Interventional/Surgical Management of Vaginal Hemorrhage

Lacerations of the vagina or cervix leading to significant ongoing bleeding, either due to sexual activities, trauma, or postoperative complications, should be repaired and may require an exam under anesthesia to allow for adequate visualization. In patients with hemorrhage due to a laceration, vaginal packing can be placed while mobilizing resources to the operating room; the number of sponges or vaginal packs should be recorded, to ensure complete removal later. When addressing injuries sustained due to sexual activities, patients should be asked about sexual abuse or assault, which is addressed in further detail in Chap. 9, Sexual Assault.

As a specific note, patients with recent LEEP and cone biopsy may also present with postoperative bleeding. For these patients, ferric subsulfate solution (Monsel's solution) can be applied, with or without a vaginal packing [30]. If a vaginal packing is placed with plans to observe the patient overnight, a Foley catheter should be placed in the bladder. Any refractory bleeding will require an exam under anesthesia.

For acute hemorrhage attributed to uterine bleeding, consider **uterine tamponade**, which can be performed in parallel with resuscitation and medical management, and/or while preparing for operative management or uterine artery embolization by interventional radiology. Tamponade is achieved by carefully placing one of the following into the uterine cavity using a ring clamp: (1) a 30 mL Foley catheter inflated with up to 60 mL of saline and (2) a Bakri® balloon (Cook Medical, Bloomington, IN), which can hold up to 500 mL of saline, which is usually too large to place into a uterine cavity that is neither postabortion nor postpartum [31]. If these techniques are successful, the device can stay in place for 12–24 h, with or without antibiotic prophylaxis [32]. If a Foley or a Bakri balloon is not available, laparotomy sponges or vaginal packing can be placed into a postpartum or postabortion uterus (i.e. one sufficiently enlarged to accommodate them); a sponge count should be recorded to ensure that all are eventually removed.

For patients with acute vaginal bleeding, surgical management is indicated for those who are clinically unstable and who have failed or declined medical or less invasive management. **Dilation and curettage** is a common approach to vaginal bleeding in a hemodynamically unstable patient. This procedure is both diagnostic and therapeutic, allowing for analysis of the endometrium by pathologists for signs of hyperplasia or malignancy. Manual vacuum aspiration, known to be effective for surgical abortions up to 10 weeks of gestational age and endometrial sampling for hyperplasia or malignancy, is an easily accessible method of uterine evacuation that can potentially be performed in the emergency room with a paracervical block or light systemic sedation. Studies are lacking, however, regarding the efficacy of manual vacuum aspiration in addressing acute vaginal bleeding outside of the abortion setting [33, 34]. Appropriate hormonal medication should be continued after surgical intervention to further decrease bleeding and prevent recurrence of acute hemorrhage.

In patients in whom fertility is not desired, or for whom more conservative measures have failed, emergent endometrial ablation, uterine artery embolization (UAE), or hysterectomy may be required. None of these methods are recommended for women desiring future fertility, and endometrial ablation is contraindicated in the setting of known or suspected uterine malignancy (and endometrial sampling beforehand is mandatory) [35]. **Endometrial ablation** entails the transvaginal destruction of the endometrium, performed using a variety of methods, including hysteroscopic resection, bipolar radiofrequency, microwave energy, and heat, among others [36–38]. **Uterine artery embolization**, performed by interventional radiology, involves the cannulation of the femoral artery followed by catheter-guided delivery of embolic particles to the uterine arteries (Fig. 2.1) [39]. UAE is used for the management of fibroids and uterine arteriovenous malformations and can be considered for the urgent management of refractory acute uterine or cervical hemorrhage due to other causes [40, 41]. Contraindications include current pregnancy or severe coagulopathy in which femoral puncture and intravascular procedure would be very high risk for bleeding. Overall, UAE is a relatively low-risk and well-tolerated procedure, though it can result in significant cramping and fevers; complications include groin puncture site infection or hematoma, contrast allergy, arterial trauma, or accidental embolization of nontarget vessels [42]. Though not recommended in women desiring future fertility, UAE may be required for severe vaginal hemorrhage that would otherwise require hysterectomy. Successful pregnancies after UAE have been reported [43].

Hysterectomy is the most invasive and definitive method of control of vaginal bleeding, requiring the longest recovery time and associated with the highest morbidity [44]. The method of approach, by laparoscopy or laparotomy, depends on the patient's stability, uterine size, surgical history, and physician preference.

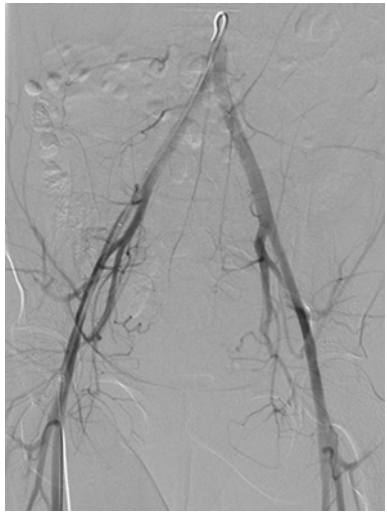

Fig. 2.1 Uterine artery embolization. Pelvic angiogram during bilateral uterine artery embolization, performed in a 24-year-old with refractory anovulatory uterine bleeding, not adequately addressed with IV conjugated equine estrogen

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Chapter 3
Pregnancy of Unknown Location and Ectopic Pregnancy

Paula C. Brady

Definitions

Pregnancy of Unknown Location Positive serum beta-human chorionic gonadotropin (hCG) without evidence of an intrauterine or ectopic pregnancy by pelvic ultrasound. Approximately 30 % of these pregnancies will develop into intrauterine pregnancies, while the remainder will be diagnosed as miscarriages or ectopic pregnancies [1].

Protocols to diagnose pregnancy location vary by clinician preference and institutional guidelines. An important concept is the **discriminatory zone**, or the serum hCG level at which evidence of an intrauterine pregnancy is expected by transvaginal ultrasound. Due to improvements in ultrasound technology, the current discriminatory zone is 1500–2000 milli-international units per milliliter (mIU/mL) [2]. Of note, uterine visualization may be compromised by fibroids or

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uterine position; the absence of a visualized pregnancy in patients with serum hCG above 2000 mIU/mL is concerning for ectopic pregnancy but not diagnostic, as intrauterine pregnancies (particularly multiple pregnancies) have been diagnosed in patients with initially negative pelvic ultrasounds despite serum hCG levels above the discriminatory zone [3].

Serial serum hCG levels, measured at 2-day intervals, are used to clarify pregnancy prognosis. The expected hCG rise over 2 days has been defined for normally progressing intrauterine pregnancies; ectopic pregnancies and miscarriages demonstrate slower hCG rises or declines. Of note, clinical findings may often deviate from these guidelines, requiring close follow up and careful patient counseling. While older guidelines advocated for a doubling of hCG in 2 days for normal intrauterine pregnancies, a more recent study suggests the minimum expected hCG rise may be as low as 35 % in 2 days [4]. In stable asymptomatic patients with pregnancies of unknown location, checking additional values at 2-day intervals adds to the accuracy of this diagnostic technique.

Spontaneous abortions will demonstrate a decline in hCG, dependent on the starting value [5]. A decline of at least 12 % in 2 days is expected for a starting hCG of 50 mIU/mL, as compared to a decline of at least 21 % in 2 days for a starting hCG of 500 mIU/mL, and a decline of at least 35 % in 2 days in patients with a starting hCG of 5000 mIU/mL. Serial hCG values not rising or declining according to these cutoffs are considered "plateaued" and are concerning for ectopic pregnancy, requiring further assessment.

A **serum progesterone level** is sometimes used to clarify pregnancy prognosis, as nonviable pregnancies—ectopic pregnancies or miscarriages—often have abnormally low levels, though a progesterone level is less sensitive and specific than serial hCG testing. A serum progesterone level below 10 nanograms per milliliter (ng/mL) following a spontaneous conception is suggestive of nonviable pregnancy [6]. A progesterone threshold has not been identified in patients using assisted reproductive technologies, who also often receive progesterone supplementation [7].

Endometrial sampling can be used to clarify pregnancy location in patients with abnormal hCG trends and nondiagnostic pelvic ultrasounds [8]. Identification of chorionic villi (gestational tissue) by pathologic analysis of endometrial curettings and/or a decline in serum hCG by 15–20 % the day after endometrial sampling is consistent with a failing intrauterine pregnancy, while pregnancies with neither identification of villi nor adequate decline in hCG are diagnosed as ectopic pregnancies [10]. Endometrial sampling can be performed by dilation and curettage (D&C) or manual vacuum aspiration, using handheld suction attached to a Karman cannula; endometrial biopsy pipelle is insufficient for this purpose [9, 10]. Patients diagnosed with failing intrauterine pregnancies following endometrial sampling require just weekly serum hCG levels until the value is negative [9]. The assessment of pregnancies of unknown location is shown in Fig. 3.1.

Ectopic Pregnancy The implantation of one or more embryos outside of the uterus, occurring in 1–2 % of all pregnancies and up to 5 % of pregnancies conceived using assisted reproductive technology [5, 11]. Ectopic pregnancy can lead to intra-abdominal hemorrhage (or vaginal hemorrhage, in patients with cervical or cesarean scar ectopic pregnancies) due to separation or rupture of the ectopic gestation.

Ectopic pregnancies implant most commonly in the ampulla of the fallopian tube; rupture of tubal ectopic pregnancies usually occurs around 6–7 weeks of gestational age [12]. Ten percent of ectopic pregnancies implant in locations other than the fallopian tube, including the cervix, ovary, myometrium, cesarean section scar, interstitial portion of the fallopian tube (within the muscular wall of the uterus), or abdominal cavity [5]. One in 4000–30,000 women in the general population may have both an intrauterine and ectopic pregnancy, called a **heterotopic pregnancy** [5, 13]. Furthermore, though not uniformly referred to as an "ectopic pregnancy," a pregnancy may also implant in the rudimentary or hypoplastic uterine horn of a patient with this

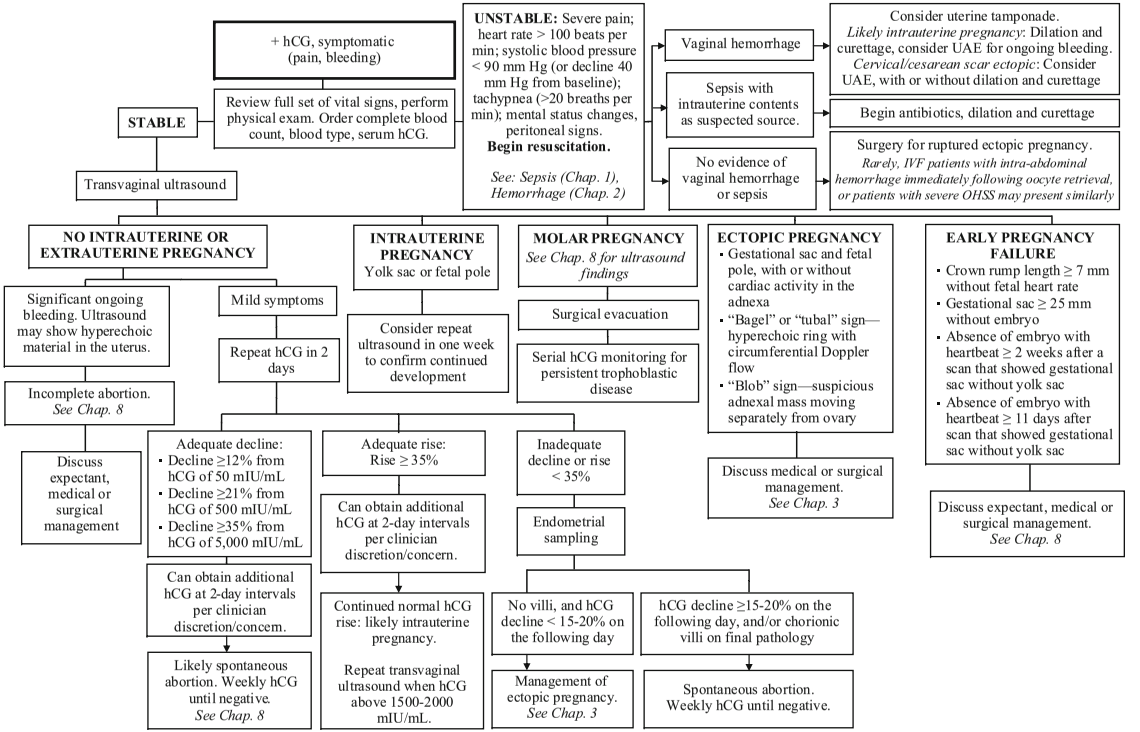

FIG. 3.1 Management algorithm for patients presenting with positive pregnancy tests and pain and/or bleeding

müllerian anomaly, occurring in an estimated 1 in 100,000–140,000 pregnancies [14]. Fifty percent of rudimentary uterine horns containing pregnancies will rupture, most prior to the third trimester [15]. Patients with ectopic pregnancies in any of these locations may present with pelvic pain and/or vaginal bleeding.

Risk factors for a tubal ectopic pregnancy include age over 35 years, smoking, prior ectopic pregnancy, prior tubal surgery, prior pelvic infection (including *Chlamydia trachomatis* and pelvic inflammatory disease), and pregnancy conceived by assisted reproduction, particularly in patients with infertility attributed to fallopian tube obstruction [11, 16–19].

Patients presenting with pregnancy in the setting of a prior tubal ligation or current use of an intrauterine device for contraception are at high risk of ectopic pregnancy. The failure rate across all methods of tubal sterilization is estimated at 18.5 per 1000, one-third of which are ectopic pregnancies [20]. Current IUD use does not predispose to ectopic pregnancy; pregnancies conceived with an IUD in place are simply more likely to be ectopic. In pregnant patients with an IUD in place, one-half of pregnancies are ectopic with a levonorgestrel device in place, compared to 1 out of 16 with a copper IUD in place [21].

When You Get the Call Ask for a full set of the patient's vital signs. Ensure that an hCG has been checked, either by blood or urine (which is faster). In patients with hemodynamic changes or extreme pain, request IV access, a complete blood count, blood type and antibody screen, and proceed immediately to assess the patient.

When You Arrive Review the patient's vital signs in detail to assess for tachycardia or hypotension, and assess the patient's general appearance for signs of distress, including altered mental status or extreme pain. In such patients, confirm that IV access is present, and request a second IV. Tachycardia, hypotension, and/or lethargy requires immediate resuscitation and likely surgical planning.

History

The history may be abbreviated in clinically unstable patients. Ask the patient for the date of her last menstrual period, whether her menses occur regularly (roughly every 21-35 days, indicating whether menstrual dating is reliable), and whether the pregnancy was conceived using assisted reproduction. Inquire whether the patient is currently using a contraceptive method, namely, tubal ligation or an IUD. Review with the patient the time course of her presenting complaint (usually pain or vaginal bleeding) and any associated symptoms or inciting events.

The patient's obstetric history should be reviewed, including prior deliveries, miscarriages, ectopic pregnancies, and whether management of prior ectopic pregnancies was medical or surgical. The patient's medical history should be reviewed, including infertility, prior sexually transmitted infections, and endometriosis, which may result in pelvic adhesions. Review her surgical history, including prior tubal surgery.

Physical Examination

On abdominal examination, note the presence of peritoneal signs—including rebound (pain when abdominal pressure is quickly withdrawn), involuntary abdominal guarding, or shake tenderness (pain when shaking the patient's abdomen or bed)—which may indicate the presence of hemoperitoneum (blood in the abdomen), intra-abdominal inflammation or infection. A gentle bimanual exam can be performed to assess for laterality of pain, though a bimanual exam is not necessary in cases highly suspicious for ectopic pregnancy, as the ectopic pregnancy can rupture. A bimanual exam may also reveal an open cervical os, which, in conjunction with heavy vaginal bleeding, is suggestive of an ongoing miscarriage.

Diagnosis

Hemodynamic Instability

Occasionally, a gynecology consult will be called before any clinical data has been obtained, in patients who report pregnancy and are hemodynamically unstable or have severe abdominal pain. Diagnosis of hemorrhagic shock is shown in Table 3.1. The first signs of hemorrhagic shock are often

TABLE 3.1 Stages of hemorrhagic shock

Class I: blood volume lost <15 %	**Class II**: blood volume lost 15–30 %
Heart rate <100 beats per minute	Heart rate >100 beats per minute
Blood pressure normal	Blood pressure normal
Respiratory rate 14–20 breaths per min	Respiratory rate 20–30 breaths per min
Urine output >30 mL/h	Urine output 20–30 mL/h
Mental status normal	Mental status mildly anxious
Class III: blood volume lost 30–40 %	**Class IV**: blood volume lost >40 %
Heart rate >120 beats per minute	Heart rate >140 beats per minute
Blood pressure decreased	Blood pressure decreased
Respiratory rate 30–40 breaths per minute	Respiratory rate >35 breaths per min
Urine output 5–15 mL/h	Urine output negligible
Mental status anxious/confused	Mental status confused/ lethargic
Often marks the onset of decompensated hypovolemic shock	

Committee on Trauma [22]

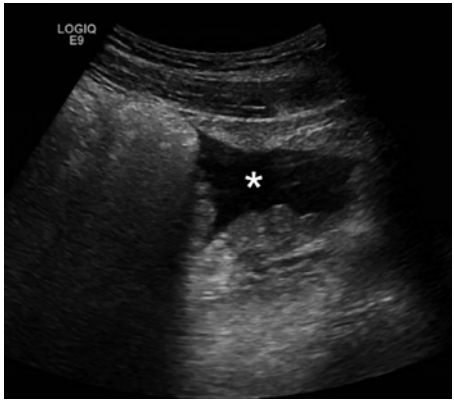

Fig. 3.2 Focused assessment with sonography for trauma (FAST) scan. Transabdominal ultrasound reveals moderate complex free fluid in the right lower quadrant, indicated with an *asterisk* (*), in a patient with a ruptured tubal ectopic pregnancy

tachycardia or anxiety; hypotension only occurs once 30–40 % of the patient's blood volume has been lost, often marking the onset of decompensated hypovolemic shock [22].

Pregnancy can be most quickly confirmed with a urine hCG test; the bladder can be catheterized to expedite this test result. In patients with an acute presentation, a focused assessment with sonography for trauma (FAST) scan can be performed, for the rapid assessment of hemoperitoneum. For gynecologic purposes, the FAST scan is a bedside ultrasound assessing for free fluid in the perihepatic, perisplenic, and pelvic spaces [23]. Pelvic free fluid is shown in Fig. 3.2. The combination of a confirmed positive hCG by urine or serum and suspected hemoperitoneum by FAST scan or other ultrasound in a patient with significant pain and/or hemodynamic changes requires expeditious surgical management, usually with diagnostic laparoscopy.

Rarely, alternative explanations for this presentation arise (which should be readily identified by the patient history), with differing management. Patients may present with acute pain and hemoperitoneum following oocyte retrieval for in vitro fertilization (usually in the first 24 hours); their positive

hCG is due to exogenous hCG administration, not pregnancy. Furthermore, patients in early pregnancy with severe ovarian hyperstimulation syndrome may present similarly with pain, hemodynamic changes and large ascites (though ectopic pregnancies are also possible in these patients). Please refer to Chap. 20, Reproductive Endocrinology and Infertility, for the diagnosis and management of these issues.

Stable Patients

In stable patients, a serum hCG, complete blood count, liver function tests, basic metabolic panel, and blood type and antibody screen should be obtained, in addition to a transvaginal ultrasound.

Ultrasound is a vital tool in the diagnosis of a patient in early pregnancy with pain or bleeding. An intrauterine pregnancy may be diagnosed by the presence of a gestational sac and a yolk sac, with or without a fetal pole. Identification of a gestational sac alone is insufficient, as patients with ectopic pregnancies may have a small fluid collection or "pseudosac" in the uterus, mimicking an intrauterine gestational sac (Fig. 3.3) [24].

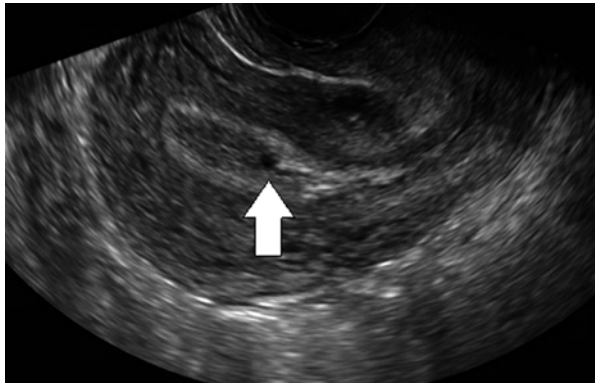

FIG. 3.3 Intrauterine pseudosac. The *arrow* indicates a small intrauterine fluid collection that was called a gestational sac, in a patient with a subsequent surgery-proven ectopic pregnancy

For reference, a normally progressing intrauterine pregnancy for which pregnancy dating is known—either by use of assisted reproduction or a reliable last menstrual period—is associated with ultrasound findings at certain gestational ages, though diagnosis of a failed pregnancy cannot be made by these guidelines [25]. At 5 weeks of gestation, an intrauterine gestational sac is expected, usually 2–3 millimeters (mm) in diameter at this point, while at 5.5 weeks of gestation, a yolk sac becomes visible. At 6 weeks of gestation, the embryo becomes visible, usually 1–2 mm in length.

Early pregnancy failure can be diagnosed by certain ultrasound criteria [26]. These include one of the following: (1) a fetal crown-rump length of 7 mm or greater without fetal cardiac activity, (2) gestational sac 25 mm or greater without presence of a fetal pole, (3) absence of an embryo with cardiac activity 2 weeks or more after an ultrasound documenting a gestational sac without a yolk sac, and (4) absence of embryo with cardiac activity 11 days or more after an ultrasound that showed a gestational sac and yolk sac [27]. Please see Chap. 8, Spontaneous Abortion, for more information on the diagnosis of early intrauterine pregnancies.

Evidence of a **tubal ectopic pregnancy** by transvaginal ultrasound includes (1) visualization of a gestational sac and fetal pole—with or without cardiac activity—in the adnexa; (2) a hyperechoic ring in the adnexa with circumferential Doppler flow, called the "bagel" or "tubal" sign (Fig. 3.4); or (3) the "blob" sign, in which a suspicious mass moves separately from the ovary with application of pressure with the transvaginal ultrasound probe [25, 28]. Patients with ruptured ectopic pregnancies are likely to have complex free fluid on imaging, reflecting hemoperitoneum; a small amount of simple free fluid in the pelvis is normal (Fig. 3.5).

Rarely, ectopic pregnancies implant in locations other than the fallopian tube and are associated with ultrasound findings specific to each location. A **cervical ectopic pregnancy** will appear as a gestational sac within the cervical canal, below a closed internal cervical os, and with circumferential Doppler flow [29]. A **cesarean scar ectopic pregnancy** will appear as a gestational sac within a prior cesarean sec-

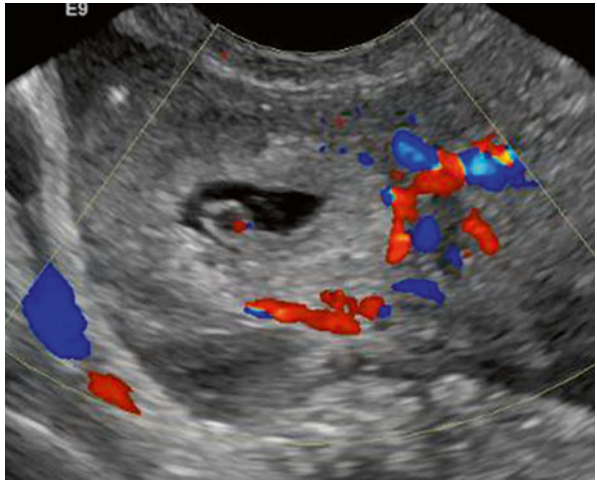

FIG. 3.4 Tubal ectopic pregnancy by transvaginal ultrasound. Transvaginal ultrasound shows a hyperechoic ring containing a gestational sac in the right adnexa, with circumferential Doppler flow

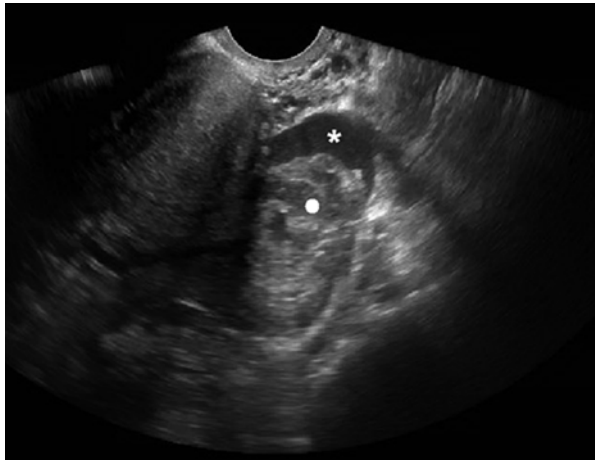

FIG. 3.5 Adnexal complex free fluid. Transvaginal ultrasound showing complex free fluid (*) around an adnexa (●) in patient with a ruptured tubal ectopic pregnancy

tion scar with very thin overlying myometrium (<3 mm) and an empty intrauterine cavity [30]. Cervical and cesarean scar ectopic pregnancies must be differentiated from spontaneous miscarriages, which may slide down into the lower uterine segment; unlike a miscarriage, these ectopic pregnancies will not move when pressure is applied with the transvaginal probe. An **interstitial ectopic pregnancy**—implanted in the most proximal/intramuscular portion of the fallopian tube—will appear as an eccentrically located gestational sac in the cornual region with a thin (<5 mm) overlying myometrial layer [31]. An **intramural ectopic pregnancy** will appear completely surrounded by myometrium, with no pregnancy in the uterine cavity [32]. An **ovarian pregnancy** may appear as an echogenic ring in the ovary with peripheral Doppler flow and will not move separately from the ovary when pressure is applied with a transvaginal probe; these pregnancies can be difficult to differentiate from ovarian cysts, and definitive diagnosis is often made by laparoscopy [32, 33]. An **abdominal pregnancy** may appear as an extrauterine gestational sac or fetus without overlying myometrium, often surrounded by loops of bowel [34]. A heterotopic pregnancy is an ectopic pregnancy in any location coexisting with an intrauterine pregnancy.

In women with a unicornuate uterus and a rudimentary uterine horn, pregnancies implanted in the rudimentary uterine horn may be misdiagnosed as tubal, interstitial, or abdominal pregnancies by ultrasound. A pregnancy in a rudimentary horn may also be misdiagnosed as an intrauterine pregnancy in a bicornuate uterus; the latter can be expectantly managed with close follow-up by an obstetrician [35]. In a pregnant patient with a müllerian anomaly that has not been definitively diagnosed prior to pregnancy, an MRI should be obtained to clarify the patient's uterine anatomy. A pregnancy in a rudimentary horn may be suspected when the myometrium of the horn containing the pregnancy is thinner than the other horn, and the horns are at a marked distance from one another; furthermore, the endometrial canal of the rudimentary horn is often not continuous with the cervical canal [36]. Please see Chap. 10, Acute Pelvic Pain in Pediatric

and Adolescent Patients, for more information on the diagnosis of müllerian anomalies.

Management

Please see Fig. 3.1 for a flowchart of the diagnosis of patients with positive serum hCG and pain and/or bleeding. For management of spontaneous abortions, please refer to Chap. 8.

In general, in patients with significant pain and/or hemodynamic changes, with a confirmed positive hCG by urine or serum and hemoperitoneum by FAST scan or other ultrasound, expeditious surgical management is required. Resuscitation of severe intra-abdominal hemorrhage due to a ruptured ectopic pregnancy should be started while proceeding to the operating room. Please refer to Chap. 13, Preparing for Urgent or Emergent Surgery, for more information on emergent resuscitation of intra-abdominal hemorrhage. Patients presenting with vaginal hemorrhage attributed to cesarean scar or cervical ectopic pregnancies may require uterine artery embolization (UAE) and/or surgical management; please refer to Chap. 2, Vaginal Hemorrhage, for management of vaginal hemorrhage [37, 38].

Medical Management of Ectopic Pregnancy

Medical management of ectopic pregnancy is appropriate in hemodynamically stable, carefully selected, and well-counseled patients. Medical management entails use of methotrexate, a dihydrofolate reductase inhibitor, which targets rapidly dividing cells [39].

Before administration of methotrexate, a complete blood count, liver function tests, and creatinine should be obtained; a patient's Rhesus factor (Rh) status should be verified, as Rh-negative women should receive Rho(D) immune globulin [11]. Patients with active pulmonary disease should have a chest radiograph.

Patients receiving methotrexate for treatment of ectopic pregnancy should be clearly counseled regarding the need for

Table 3.2 Strict contraindications to medical management of ectopic pregnancy (EP)

Clinical instability or significant pain suggestive of ruptured EP
Heterotopic pregnancy
Liver function tests > two times the upper limit of normal
White blood cell count <1500/uL
Platelet count <100,000/uL
Creatinine >1.5 mg/dL
Significant anemia
Current breastfeeding
Active peptic ulcer disease
Active pulmonary disease

Pisarska et al. [73], Practice Com-mittee of the American Society for Reproductive Medicine [11]

close clinical follow-up, ongoing risk of rupture of tubal ectopic pregnancy, and signs and symptoms—namely, worsening abdominal pain—concerning for rupture of ectopic pregnancy. Side effects of methotrexate include abdominal and pelvic pain, nausea, headaches, dermatitis, and less commonly alopecia and mucositis [40, 41].

Strict contraindications to the medical management of ectopic pregnancy are listed in Table 3.2. Relative contraindications include the presence of fetal cardiac activity or suspected ectopic pregnancy mass greater than 4 cm, serum hCG level greater than 5000 mIU/mL, patient refusal of blood transfusion, or patient inability to adhere to close outpatient follow-up [11].

The most common regimen is a single weight-based dose of methotrexate (50 mg/m^2 of body surface area), as shown in Table 3.3 [42]. Success is defined as a decline in hCG of 15 % or more between day 4 and day 7, calculated as the difference between the two values divided by the day 4 value. The

Table 3.3 Single-dose methotrexate (MTX) regimen for management of ectopic pregnancy

Protocol day	Testing	Action
Day 1	hCG	Administer methotrexate (MTX) (50 mg/m^2 of body surface area IM)
Day 4	hCG	
Day 7	1. hCG 2. Repeat complete blood count, liver function testing, creatinine	1. hCG decline <15 %, day 4 to day 7: return to day 1 of protocol and administer MTX (50 mg/m^2 of body surface area IM) 2. hCG decline >15 %: repeat hCG weekly until negative

Stovall et al. [42], Practice Committee of the American Society for Reproductive Medicine [11]

Table 3.4 Successful management of ectopic pregnancy with methotrexate by serum hCG

Serum hCG (mIU/mL)	Success rate (%)
Less than 1000	98.5
1000–1999	94.4
2000–4999	96.2
5000–9999	85.7
10,000–150,000	81.8

Adapted from Menon et al. [43], with permission from Elsevier

regimen may be repeated up to three more times if the serum hCG level does not decline adequately, provided that the patient's physical symptoms, complete blood count, liver function tests, and creatinine remain stable. If the hCG level does decline adequately, patients should have hCG levels checked weekly until the value is negative. The success rates of single-dose methotrexate vary by starting hCG value and are listed in Table 3.4 [43].

Table 3.5 Two-dose methotrexate (MTX) regimen for management of ectopic pregnancy

Protocol day	Testing	Action
Day 0	hCG	Administer MTX (50 mg/m^2 of body surface area IM)
Day 4	hCG	Administer MTX (50 mg/m^2 of body surface area IM)
Day 7	1. hCG 2. Repeat complete blood count, liver function tests, and creatinine	1. hCG decline <15 %, day 4 to day 7: administer MTX 2. hCG decline >15 %: stop protocol; weekly hCG until negative
Day 11	hCG	1. hCG decline <15 %, day 7 to day 11: administer MTX 2. hCG decline >15 %: stop protocol; weekly hCG until negative
Day 14	1. hCG 2. Repeat complete blood count, liver function tests, and creatinine	1. hCG decline <15 %, day 11 to day 14: surgical management 2. hCG decline >15 %: repeat hCG weekly until negative

As described in Barnhart et al. [40]

Alternative regimens include a two-dose regimen (Table 3.5) and a multiple-dose regimen (Table 3.6). The multiple-dose regimen utilizes leucovorin—a folic acid derivative—to counteract side effects of the methotrexate [44, 45]. Comparisons of single- and two-dose regimens have shown similar success; studies have variably shown increased efficacy of the multiple-dose regimen as compared to the single-dose regimens, though side effects are more common with the multiple-dose regimen [40, 46–48].

Patients receiving methotrexate should stop folate supplementation (present in multivitamins and enriched foods), nonsteroidal anti-inflammatory medications, and alcohol and

Table 3.6 Multiple-dose methotrexate (MTX) regimen for management of ectopic pregnancy

Protocol day	Testing	Action
Day 1	hCG	Administer MTX (1.0 mg/kg IM)
Day 2		Administer leucovorin (0.1 mg/kg IM or PO)
Day 3	hCG	1. hCG decline <15 %, day 1 to day 3: administer MTX 2. hCG decline >15 %: stop protocol; weekly hCG until negative
Day 4		Administer leucovorin (0.1 mg/kg IM or PO)
Day 5	hCG	1. hCG decline <15 %, day 3 to day 5: administer MTX 2. hCG decline >15 %: stop protocol; weekly hCG until negative
Day 6		Administer leucovorin (0.1 mg/kg IM or PO)
Day 7	hCG	1. hCG decline <15 %, day 5 to day 7: administer MTX 2. hCG decline >15 %: stop protocol; weekly hCG until negative
Day 8		Administer leucovorin (0.1 mg/kg IM or PO)

Goldstein et al. [45], Ory et al. [44]

avoid vigorous physical activity, including intercourse and bimanual exams [49]. Following resolution of the ectopic pregnancy, patients are generally counseled to avoid conception for three months after exposure to methotrexate, which is a teratogen, though data are lacking for this recommendation [11].

Hemodynamically stable patients with **nontubal ectopic pregnancies** may be eligible for medical management. Cervical, cesarean scar, interstitial, or intramural ectopic pregnancies may be managed with single- or multiple-dose systemic methotrexate, with or without methotrexate or potassium chloride injection into the ectopic gestation, particularly in the presence of fetal cardiac activity; uterine

artery embolization may be used prophylactically or in the event of hemorrhage [51, 55]. The use of single- or multiple-dose methotrexate for management of ovarian ectopic pregnancies has also been described, though management is most commonly surgical, in part because laparoscopy is often required for definitive diagnosis [11, 56]. Treatment of heterotopic pregnancies depends on the location, and potassium chloride injections into these ectopic gestations have been described; methotrexate, which is a teratogen, should not be used for heterotopic pregnancies if the patient wishes to preserve the intrauterine pregnancy, though the risk of miscarriage is overall higher in these patients [57, 58].

Surgical Management of Ectopic Pregnancy

Patients with **tubal ectopic pregnancies** who have failed medical management, are not candidates for medical management, prefer surgical management, or present with acute clinical instability as evidenced by unstable vital signs or severe pain, should be managed surgically.

Laparoscopy is the most common approach in stable patients with tubal ectopic pregnancy, with equal success but less blood loss and pain and shorter hospital stay as compared to laparotomy [59]. The tubal ectopic pregnancy can be removed either by salpingostomy (an incision in the fallopian tube) or salpingectomy, which entails excision of the fallopian tube [60]. Subsequent intrauterine and ectopic pregnancy rates are similar between the two methods, in the presence of a remaining contralateral fallopian tube [61]. Salpingostomy may be preferable in patients with prior contralateral salpingectomy. Salpingectomy is preferable in patients with extensive tubal damage or uncontrolled bleeding, prior tubal sterilization, or an ectopic gestation 5 cm or more in diameter [60]. Following salpingostomy, patients require weekly serum hCG measurements to monitor for persistent trophoblastic tissue, which occurs in approximately 7 % of cases and may require methotrexate [62]. Following salpingectomy, patients

do not strictly require further hCG monitoring once the trophoblastic tissue is confirmed by pathology.

In patients with **nontubal ectopic pregnancies**, surgery may similarly be required in patients who have failed or cannot receive medical management, prefer surgical management, or present with evidence of bleeding from their ectopic pregnancies. Surgical management of nontubal ectopic pregnancy is tailored to the ectopic pregnancy location; uterine artery embolization may be performed preemptively or in the event of hemorrhage [51, 55]. For **cervical and cesarean scar ectopic pregnancies**, dilation and curettage alone is not recommended as first-line therapy given the high risk of hemorrhage; blood loss may be limited by injection of potassium chloride or methotrexate into gestations with fetal cardiac activity beforehand [37, 63]. In patients with cesarean scar implantations, laparoscopic resection of the cesarean scar ectopic pregnancy and scar revision has also been reported [64]. **Ovarian ectopic pregnancies** are commonly managed surgically, most commonly with ovarian wedge resection [65, 66]. Cornuostomy or cornual resection is the most common surgical procedure for **interstitial ectopic pregnancies**, particularly for ectopic gestations greater than 3–4 cm [67, 68]. **Abdominal pregnancies** are most commonly managed surgically, either by laparoscopy or laparotomy, with a high risk of hemorrhage; depending on implantation site, the placenta may be left in situ and treated with methotrexate, particularly in advanced pregnancies [69, 70]. If surgery is required, **heterotopic tubal pregnancies** are removed by laparoscopic salpingectomy; salpingostomy is not recommended as patients cannot be monitored for persistent trophoblastic tissue in the setting of an ongoing intrauterine pregnancy [7]. Patients with pregnancies diagnosed within a **rudimentary horn** should be counseled for prompt excision of the rudimentary uterine horn, given the high risk of uterine rupture and maternal morbidity and mortality [35, 71]. Laparotomy or laparoscopy is acceptable, depending on the patient's clinical stability and surgeon preference [72].

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Chapter 4
Adnexal Masses and Ovarian Cyst Rupture

Paula C. Brady and Daniel J. Kaser

Definitions

Simple Cyst Usually a functional cyst resulting from an unruptured Graafian follicle. These are the most common type of ovarian cysts in premenopausal women [1]. The risk of malignancy is less than 1 % [2].

Paraovarian or Paratubal Cyst Simple-appearing cystic structures separate from the ovary, arising from the broad ligament, fallopian tube, or surface of the ovary [3]. Like simple ovarian cysts, the risk of malignancy is very low, particularly in paraovarian or paratubal cysts measuring less than 5 centimeters (cm) [4].

Corpus Luteum Following ovulation, the collapsed follicle becomes a functional endocrine gland known as a corpus luteum, which secretes estrogen and progesterone to prepare the endometrial lining for implantation [5]. These cysts are typically less than 3 cm and regress spontaneously in the absence of pregnancy.

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Hemorrhagic Cyst These common ovarian cysts result from bleeding into a follicular cyst or corpus luteum and can produce abrupt onset of pain [6].

Endometrioma Also called "chocolate cysts," endometriomas are growths of endometriosis—endometrial glands and stroma implanted outside of the uterus—on the ovary. Endometriosis is present in 6–10 % of reproductive age women [7]. Patients with endometriosis may be asymptomatic, though others report dysmenorrhea, dyspareunia, dysuria, dyschezia, and cyclic or acyclic abdominopelvic pain. Endometriomas may produce pelvic pain or pressure symptoms as they enlarge. Rarely, deep infiltrating endometriosis can lead to hydronephrosis or renal insufficiency due to ureteral involvement. Endometriosis may also be associated with elevation with cancer antigen 125 (CA-125), a serum biomarker commonly associated with epithelial ovarian cancer [8].

Mature Cystic Teratoma Also called dermoids, mature cystic teratomas are the most common benign ovarian germ cell tumor in adolescence and during the reproductive years [1]. These tumors may contain elements from the three germ cell layers, including adipose tissue and hair, teeth, and thyroid tissue [9]. Rarely, these can be associated with paraneoplastic syndromes; for example, teratomas with monodermal differentiation can lead to symptoms of hyperthyroidism or anti-*N*-methyl D-aspartate (NMDA)-receptor-mediated encephalitis, which presents with psychiatric disturbances, seizure, or coma [10, 11].

Cystadenoma Benign epithelial tumors of serous or mucinous subtypes. These are the most common benign ovarian neoplasm in postmenopausal women [1]. Patients commonly present with large masses (>10 cm), increased abdominal girth, pelvic pain, or pressure symptoms. These masses may also be detected incidentally [3].

Theca-Lutein Cyst A rare type of functional ovarian cyst that is often bilateral and multilocular in appearance, these develop in the setting of elevated serum human chorionic gonadotropin (hCG). These cysts develop most often in patients with gestational trophoblastic disease such as hydatidiform moles or

choriocarcinomas, but can also be diagnosed in normal pregnancy (in particular, with multifetal gestation) [12, 13]. Theca-lutein cysts may be found incidentally or may present as pelvic pain or pressure due to their size [14]. Occasionally, ascites develops with these tumors. Patients may also develop signs of virilization [15].

Hydrosalpinx Fluid accumulated in a fallopian tube that appears anechoic, serpiginous, and adjacent to the ovary on ultrasound. Hydrosalpinges may occur in up to 10 % of patients with pelvic inflammatory disease (PID) or endometriosis [3]. These also may result from adhesive disease from appendicitis or prior abdominal or pelvic surgery.

Tubo-Ovarian Abscess (TOA) An abscess of the adnexa, involving the fallopian tube and/or ovary. TOAs occur in one-third of patients with PID and may also be secondary to appendicitis, diverticulitis, inflammatory bowel disease, or postoperative infection [16]. Patients may present with fever, abdominal pain, chills, abnormal vaginal bleeding, dyspareunia, and/or vaginal discharge, while some patients may be asymptomatic; over 30 % may be afebrile [17, 18]. Risk factors include multiple sexual partners, young age at coitarche, nonuse of barrier contraception, smoking, illicit drug use, infection with *Neisseria gonorrhoeae* and *Chlamydia trachomatis*, prior episodes PID, and potentially immunosuppression, such as chronic steroid use or infection with human immunodeficiency virus (HIV) [19–21]. Ruptured TOAs represent a surgical emergency and may present as sepsis and hemodynamic instability. Please see Chap. 6, Pelvic Inflammatory Disease and Tubo-Ovarian Abscesses, for more information on the diagnosis of management of TOA. Please see Chap. 16, Complications of Minimally Invasive Gynecologic Surgery, for the diagnosis and management of pelvic abscesses other than TOA, related to postoperative complications.

Ectopic Pregnancy The implantation of an embryo outside of the uterus, occurring in 1–2 % of all pregnancies [22]. Ectopic pregnancies occur most commonly in the ampulla of the fallopian tube, though pregnancies can also implant in the cervix, ovary, myometrium, cesarean section scar, interstitial (intramuscular) portion of the fallopian tube, or abdominal cavity in 10 % of cases. Risk factors for ectopic pregnancy include age over

35 years, smoking, prior ectopic pregnancy, prior tubal surgery, prior pelvic infection, and pregnancy conceived by assisted reproduction [22–25]. Patients with ectopic pregnancies commonly present with pelvic pain and/or vaginal bleeding. All patients of reproductive age with abnormal vaginal bleeding, particularly in the presence of an adnexal mass, require a pregnancy test even if abstinent or on highly effective contraception. Please see Chap. 3, Pregnancy of Unknown Location and Ectopic Pregnancy, for more information on the diagnosis and management of ectopic pregnancy.

Polycystic Ovarian Syndrome (PCOS) The diagnosis of PCOS requires at least two of the following: (1) oligo- or anovulation; (2) clinical or laboratory evidence of hyperandrogenism (such as hirsutism); or (3) polycystic ovaries by ultrasound, defined as one or both ovaries with increased ovarian volume (>10 mL) and/or containing 12 or more antral follicles each, measuring 2–9 mm [26]. This syndrome in itself does not cause pain, but an enlarged, polycystic ovary may torse, and these patients are at higher risk of ovarian hyperstimulation syndrome (OHSS) while undergoing infertility treatment [27].

Ovarian Hyperstimulation Syndrome (OHSS) An iatrogenic condition resulting from excessive ovarian stimulation with exogenous gonadotropins [28]. Risk factors include age less than 33 years, low body weight, a history of PCOS or hypothalamic amenorrhea, high antral follicle count or anti-müllerian hormone levels (above 3.3 ng/mL), a large number of oocytes retrieved (>15), significantly elevated serum estradiol (>5,000–6,000 pg/mL), or prior episodes of OHSS [27, 29–32]. Symptoms of OHSS most often begin 48 h after administration of an hCG trigger injection to induce final oocyte maturation or ovulation during infertility treatment and peak in 7–10 days [33]. There is also a late phase of OHSS that can occur if the patient becomes pregnant, likewise driven by serum hCG. Patients may present with increased abdominal girth, pelvic pain, nausea, vomiting, shortness of breath, or chest pain; patients with severe OHSS may develop hypotension, tachycardia, oliguria, ascites, pleural and pericardial effusions, thromboembolism, and/or renal failure. Hyperstimulated

ovaries are prone to torsion, so any infertility patient with pelvic pain requires an ultrasound for evaluation. Please see Chap. 20, Reproductive Endocrinology and Infertility, for more information on the diagnosis and management of OHSS.

Müllerian Anomalies Congenital defects of uterine development, which may result in a variety of malformations, as shown in Fig. 4.1. These occur in approximately 5 % of all women and up to 25 % of patients with prior pregnancy loss and infertility; septate uterus is the most common malformation [34, 35]. Approximately 30 % of women with uterine anomalies will also have renal anomalies, such as renal agenesis, duplication, or a pelvic kidney [36]. By ultrasound, some anomalies—such as a rudimentary horn—may appear as a pelvic mass. These anomalies may cause pelvic pain due to endometriosis from retrograde menstruation or hematometra from obstructed menstrual egress or in the presence of pregnancy, which may result in spontaneous abortion or rupture of a rudimentary uterine horn [37].

Leiomyomata Also known as fibroids, these smooth muscle tumors are the most common neoplasm in reproductive age women and arise from monoclonal expansion of cells in the uterine myometrium. Fibroids may be asymptomatic or produce symptoms of pelvic pressure, menorrhagia, and/or infertility in 25 % of women [38]. Similar to some müllerian anomalies, pedunculated, broad ligament fibroids and those with cystic degeneration may be mistaken for complex adnexal masses by ultrasound and are better delineated using magnetic resonance imaging (MRI). Like endometriosis, fibroids can also cause elevated CA-125 values [39]. Fibroids generally do not cause pain unless torsing or degenerating; please see Chap. 1, Acute Pelvic Pain, for further information on the diagnosis and management of painful fibroids.

Peritoneal Inclusion Cysts Pelvic adhesions distended with peritoneal fluid. Peritoneal inclusion cysts are most often diagnosed in patients with prior pelvic surgery, pelvic inflammatory disease, endometriosis, or inflammatory bowel disease [3, 40]. Peritoneal inclusion cysts are also more commonly diagnosed in reproductive-aged women as compared to postmenopausal women or men [40]. Often

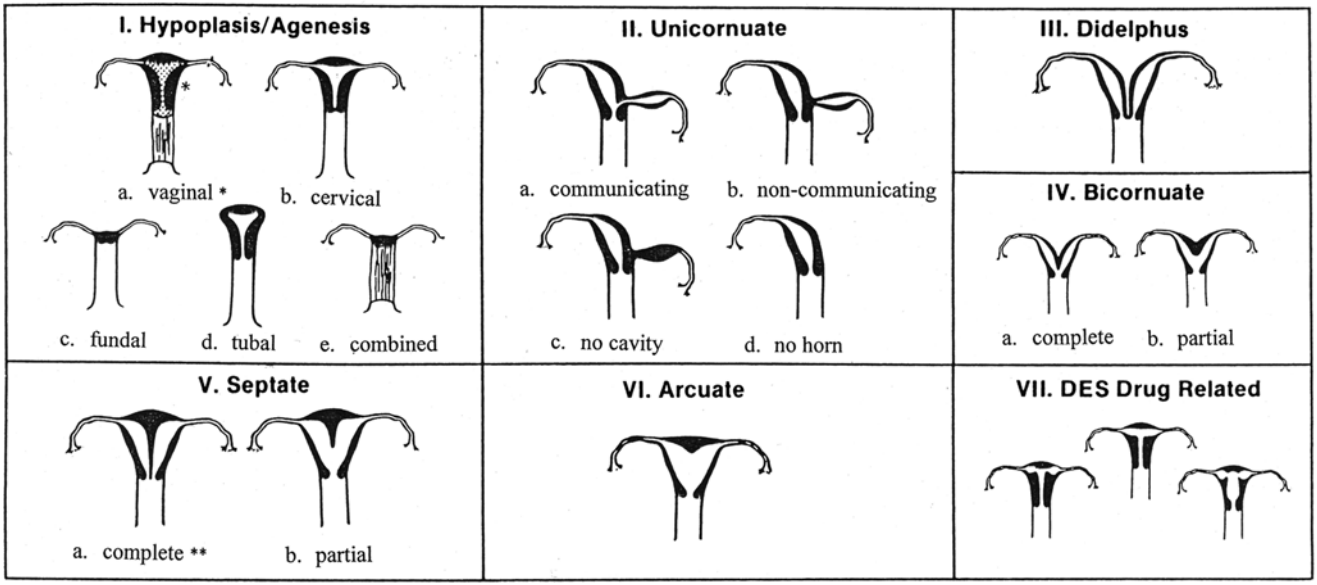

FIG. 4.1 Müllerian anomalies. * Uterus may be normal or take a variety of abnormal forms. ** May have two distinct cervices (Reprinted by permission from the American Society for Reproductive Medicine (*Fertility and Sterility* [83]))

discovered incidentally, these cysts may produce pelvic pressure or pain if they enlarge.

Ovarian Malignancy Primary ovarian malignancies occur in 1.3 % of women in their lifetimes [41]. Risk factors include nulliparity, advancing age, a family history of breast or ovarian cancer, and hereditary cancer syndromes, due to germline mutations in tumor suppressor genes (BRCA1, BRCA2) or mismatch repair genes (MLH1, MSH2, MSH6, or PMS2) [42, 43]. Epithelial ovarian cancers, the most common type, are diagnosed most often in postmenopausal women [6]. Germ cell tumors are often diagnosed in younger women, while sex-cord stromal tumors can present in any age group [6]. Non-epithelial ovarian cancers are generally associated with very favorable prognosis [6]. Patients with ovarian malignancies may present with abdominal distention, pain or pressure, changes in appetite (anorexia or early satiety), urinary symptoms, or gastrointestinal symptoms including bowel obstruction [44].

Of note, less than 10 % of malignant tumors of the ovary represent metastatic implants of nongynecologic primary tumors, most commonly of the gastrointestinal tract (colon or stomach) or breast [45, 46]. Metastases of appendiceal, pancreatic, thyroid, lung, and gallbladder cancers and melanoma, among others, may also occur [46]. Metastatic tumors on the ovary are most often bilateral [45]. As a result, reviewing a patient's full medical history is crucial, and if surgery is performed, survey of the entire abdomen for other suspicious masses is prudent.

Ruptured Ovarian Cyst Rupture of an ovarian cyst wall, leading to the spread of cyst contents and/or blood into the peritoneum. Ruptured ovarian cysts constitute the most common cause of spontaneous hemoperitoneum [47]. Many types of ovarian cysts can rupture, including simple cysts, cystadenomas, endometriomas, TOAs, and dermoids [48–50]. While unruptured ovarian cysts can result in dull pelvic pain due to stretching of the ovarian capsule and mass effect, ovarian cyst rupture often results in the acute onset of pain [51]. Patients may report that their pelvic pain began after physical activity or intercourse or, if specifically asked, may report rectal pressure if blood has pooled in the posterior cul-de-sac, which may be seen on speculum exam as a bulge in the posterior fornix.

Differential Diagnosis

Differential Diagnosis of an Adnexal Mass

- Simple (follicular) cyst
- Paraovarian or paratubal cyst
- Corpus luteum
- Hemorrhagic cyst
- Ectopic pregnancy
- Endometrioma
- Benign cystic teratoma (also referred to as a dermoid)
- Cystadenoma
- Theca-lutein cyst
- Hydrosalpinx (fluid-filled fallopian tube) or (fallopian tube filled with purulent material)
- Tubo-ovarian abscess or other pelvic abscess
- Polycystic ovaries
- Ovarian hyperstimulation syndrome
- Uterine anomaly
- Broad ligament or pedunculated fibroid
- Peritoneal inclusion cyst
- Other ovarian neoplasms (benign or malignant; germ cell, sex-cord or stromal, or epithelial)
- Metastatic gastrointestinal or breast cancer
- Nongynecologic causes such as diverticular abscess, appendicitis, nerve sheath tumor, and urologic pathology (pelvic kidney, ureteral or bladder diverticulum) [52].

When You Get the Call Ask for a full set of vital signs to assess hemodynamic stability. Ensure that a pregnancy test and ultrasound have been performed, and the patient is located in a private room on bed or stretcher equipped for gynecologic exams (i.e., with stirrups).

When You Arrive Review all available vital signs to assess for fever, hypotension, or tachycardia. Assess whether the patient is in distress due to pain. Quickly review any available clinical data, particularly an hCG level or ultrasound.

History

Review the patient's onset of symptoms (gradual or acute) and any associated symptoms, including fever, nausea, vomiting, or diarrhea. Inquire whether she is on any hormonal medications which might suppress ovulation, such as combined oral contraceptive pills, Depo-Provera, or a gonadotropin-releasing hormone agonist. Review the patient's last menstrual period and whether she is undergoing ovulation induction. Review whether she has a history of polycystic ovarian syndrome, PID, ovarian cysts, ovarian torsion, or a family history of breast or ovarian cancer. As always, review the patient's full obstetrical, gynecologic, medical, and surgical history, including whether she is on anticoagulation medications or has a bleeding disorder.

Physical Examination

Before examining a patient with pain, always review when she last received narcotics, which may mask clinically significant findings. Examine the patient's abdomen to assess for peritoneal signs—including rebound (pain on the abrupt release of abdominal palpation), involuntary abdominal guarding, or shake tenderness (pain with shaking the patient's abdomen or bed)—which may indicate the presence of infection or intraperitoneal blood from an ovarian cyst rupture or ruptured ectopic pregnancy. On bimanual exam, make note of enlarged adnexae, cervical motion tenderness, and any nodularity of the uterosacral ligaments or immobility of the uterus.

Diagnosis

A complete blood count, serum human chorionic gonadotropin (hCG) and pelvic ultrasound should be obtained in patients suspected to have adnexal masses based on their symptoms or physical exam. Other imaging studies, such as a computed tomography (CT) scan, may have already been performed by the emergency department or primary team, but ultrasound should be requested for further characterization, as this is the modality of choice for evaluation of pelvic masses. In patients who may be pregnant or have peritoneal signs on abdominal exam, collection of a blood type and antibody screen is prudent. In patients taking anticoagulation with possible cyst rupture or possible need for operative management, obtain coagulation studies (prothrombin time (PT) and activated partial thromboplastin time (aPTT)).

Management

Overall, management of ovarian masses in the emergent setting is driven by the patient's clinical stability and report of pain. Most noninfectious pelvic masses in hemodynamically stable patients with pain controlled on oral agents do not require intervention. Patients with presentations highly suspicious for ruptured ectopic pregnancy or adnexal torsion—which is more common for cysts over 5 cm—require diagnostic laparoscopy; please see Chap. 3, Pregnancy of Unknown Location and Ectopic Pregnancy, and Chap. 5, Adnexal Torsion, for more information [53]. For patients with suspected adnexal or pelvic abscess, antibiotics and potentially abscess drainage are indicated. Please see Chap. 6, Pelvic Inflammatory Disease and Tubo-Ovarian Abscesses, for more information on the diagnosis of management of TOA. Please see Chap. 16, Complications of Minimally Invasive Gynecologic Surgery, for the diagnosis and management of pelvic abscesses other than TOA, usually related to postoperative complications.

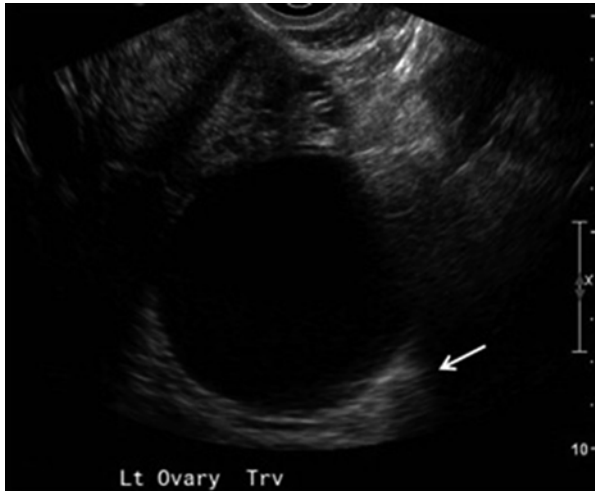

FIG. 4.2 Simple/follicular ovarian cyst. Transvaginal ultrasound demonstrates an anechoic 6-cm cyst with a thin wall and posterior acoustic enhancement (*arrow*) (Reprinted from Amirbekian and Hooley [51], with permission from Elsevier)

Simple Cyst Transvaginal ultrasound is usually sufficient to characterize simple cysts, though cysts greater than 7 cm may be difficult to completely visualize, for which MRI may be useful [54]. Simple cysts are thin-walled, anechoic structures with no complex features, such as thick septations, mural nodularity, papillary excrescences, or hypervascularity (Fig. 4.2). In asymptomatic premenopausal women, simple cysts less than 5 cm are very low risk for malignancy and do not strictly require follow-up [54]. Simple cysts up to 1 cm can be seen in postmenopausal women and confer very low risk for malignancy; follow-up is not strictly necessary but is at the discretion of the clinician [54]. In premenopausal and postmenopausal women, larger simple cysts, measuring up to 10 cm, are generally followed with serial ultrasounds; a repeat ultrasound within 3 months is prudent, as two-thirds will resolve over time [2]. Stable cysts less than 10 cm can be followed with an annual repeat ultrasound, unless patients

become symptomatic or sonographic features concerning for malignancy develop [54].

Paraovarian or Paratubal Cyst Pelvic ultrasound is sufficient to characterize these cysts and allows for observation of cyst movement separate from the ovary to confirm the diagnosis. Simple paraovarian or paratubal cysts are benign in the vast majority of patients and can be followed like simple ovarian cysts [54]. Simple-appearing paraovarian or paratubal cysts only require intervention if greater than 10 cm or if patients have pain. The presence of papillary structures in a paraovarian or paratubal cyst is more concerning for borderline or malignant neoplasm; such cysts must be followed more closely and may require operative management to confirm pathology, though not emergently [4].

Corpus Luteum Pelvic ultrasound reveals a small cyst, usually less than 3 cm, with thickened walls, internal echoes, crenulated (collapsing) margins, and peripheral color Doppler flow (Fig. 4.3) [6]. Follow-up for a corpus luteum measuring 3 cm or less is not required, as these most often resolve unless pregnancy occurs, at which point the corpus luteum is "rescued" to secrete progesterone that supports the pregnancy [55]. If the corpus luteum enlarges, hemorrhage into the cyst may occur, resulting in a hemorrhagic cyst (see below).

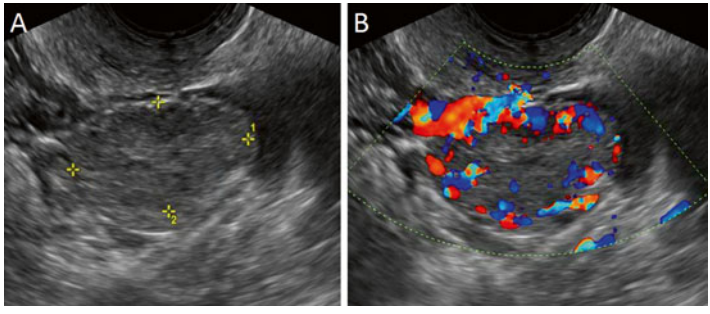

FIG. 4.3 Corpus luteum. (**a**) Transvaginal ultrasound reveals a 3-cm corpus luteum (*calipers*) with internal echoes; (**b**) peripheral flow is seen by color Doppler

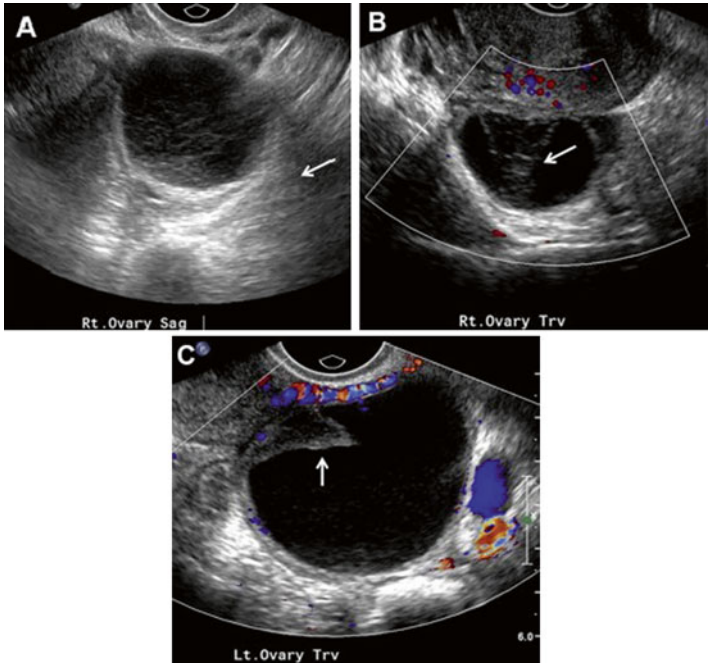

Fig. 4.4 Hemorrhagic ovarian cysts. (**a**) Transvaginal ultrasound demonstrates a thin-walled hypoechoic cyst with a "lacelike" pattern of internal low-level echoes representing fibrin formation from lysis of RBCs (*arrow*). (**b**, **c**) Transvaginal ultrasound demonstrating a later stage of hemorrhagic cysts, which contain retractile clot seen as heterogeneous iso-echoic to hypoechoic irregular-shaped mural foci (*arrows*) without Doppler flow (Reprinted from Amirbekian and Hooley [51], with permission from Elsevier)

Hemorrhagic Cyst By ultrasound, hemorrhagic cysts may have fluid-fluid levels, internal echoes, and/or a mural thrombus; these cysts usually have circumferential flow without internal color Doppler flow (Fig. 4.4) [51, 54]. An internal reticular and lacy pattern due to fibrin may be noted, but do not cross the whole cyst, unlike septations [6]. The sonographic appearance of a hemorrhagic cyst may mimic

that of an endometrioma, or vice versa. In premenopausal women, hemorrhagic cysts are expected to resolve and can be followed with a repeat ultrasound in 6–8 weeks to ensure resolution. Conversely, a cyst which appears hemorrhagic in a postmenopausal woman is potentially concerning for neoplasia and require close follow-up, as ovulation is no longer occurring in these women [54].

Endometrioma Physical examination may reveal an adnexal mass; thickened or nodular uterosacral ligaments or rectovaginal septum and a fixed (non-mobile) uterus may also be appreciated, consistent with intraperitoneal scarring due to endometriosis. Transvaginal ultrasound will demonstrate a mass with homogenous "ground-glass" echoes, smooth walls and without internal color Doppler flow (Fig. 4.5); the sensitivity and specificity for the diagnosis of endometrioma by ultrasound is high (77–98 %), but occasionally these can be mistaken for hemorrhagic cysts [56]. Repeat ultrasound should be performed in 6–8 weeks to differentiate an endometrioma from a hemorrhagic cyst, as the latter should resolve [54].

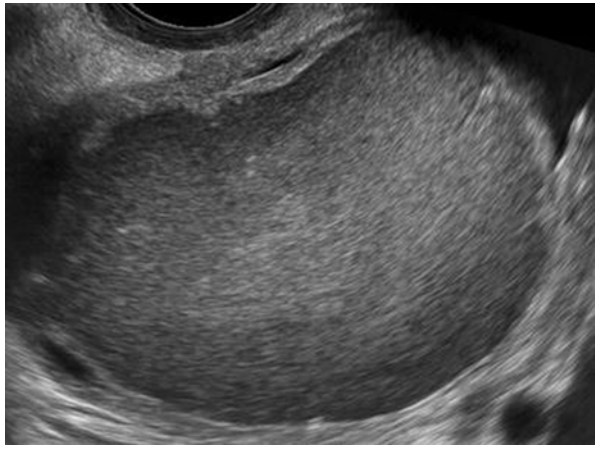

Fig. 4.5 Endometrioma by transvaginal ultrasound (Reprinted from Coccia et al. [74], Figure 3, with kind permission from Springer Science and Business Media)

Malignant transformation occurs in 1 % of endometriomas; malignant transformation is more common in endometriomas over 6 cm and in women over 45 years of age [57]. Urgent management is indicated only for evidence of torsion or, rarely, superinfection, which may occur following percutaneous drainage or oocyte retrieval for in vitro fertilization [58]. Please see Chap. 1, Acute Pelvic Pain, for more information on the management of endometriosis; see Chap. 20, Reproductive Endocrinology and Infertility, for management of superinfected endometriomas.

Mature Cystic Teratoma By ultrasound, mature teratomas often have cystic and solid components, along with acoustic shadowing, calcifications from bone or teeth, or thin bands (also known as "dermoid mesh") from strands of hair (Figs. 4.6 and 4.7) [3, 9, 59]. Cyst contents may appear to float within the

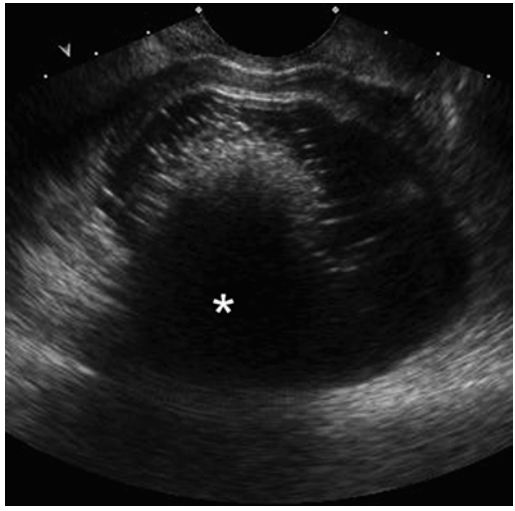

FIG. 4.6 Ovarian teratoma on transvaginal ultrasound. The cystic adnexal mass has a central dense echogenic nodule (the Rokitansky nodule) causing posterior acoustic shadowing (*). The Rokitansky nodule is composed of the fat, bone, and hair (Reprinted from Heilbrun et al. [3], with permission)

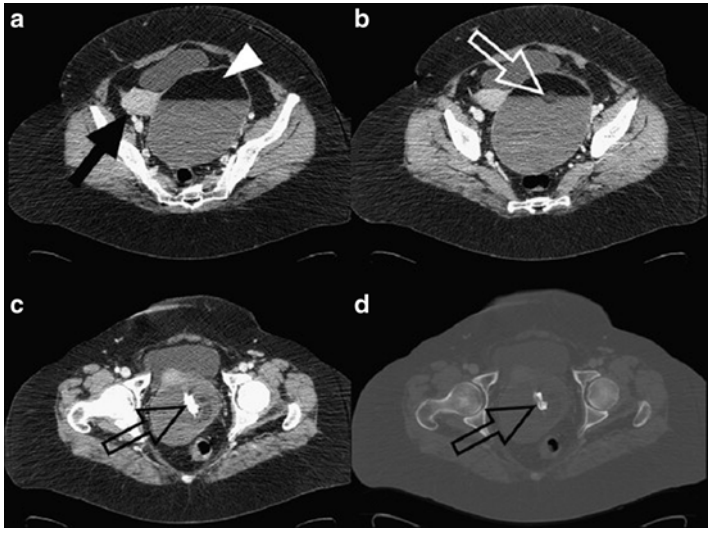

FIG. 4.7 Ovarian teratoma. Contrast-enhanced CT scan (**a**, **b**) shows well-defined ovarian tumor with fat-fluid level (*white arrowhead*), round mass of matted tuft of hair (*white open arrow*), and enhancing lobulated soft-tissue component (*black arrow*) in lateral wall. A toothlike calcification in inferior wall is visible (*black open arrow*) in (**c**, **d**) scans (Reprinted from Saba et al. [59], with permission from Elsevier)

cyst. An echogenic "plug," called a Rokitansky tubercule, is often seen projecting into the cyst cavity [3]. The sensitivity and specificity for the diagnosis of a teratoma by ultrasound is high (86–99 %) [56]. Peripheral color Doppler flow is often seen by ultrasound; central flow may be more concerning for malignancy [54]. Mature teratomas are also well-characterized by CT scan and MRI. The vast majority of these masses are benign; malignant transformation occurs in less than 1 % of cases [60]. In asymptomatic patients, mature teratomas can be followed by ultrasound, to monitor for an increase in diameter or characteristics concerning for malignancy; once the mass reaches 4–5 cm, surgical removal is advisable given the risk for torsion [54].

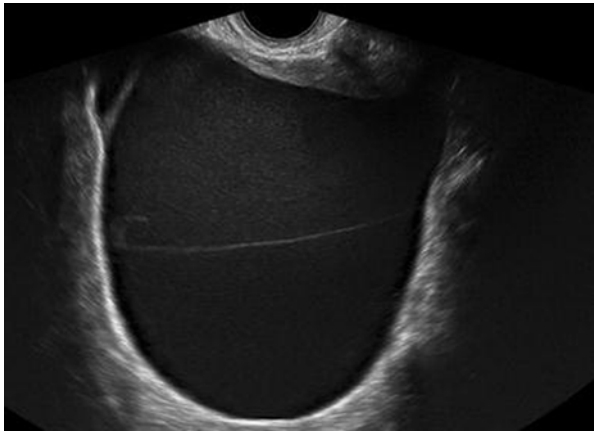

FIG. 4.8 Mucinous cystadenoma by transvaginal ultrasound (Reprinted from Coccia et al. [74], Figure 9, with kind permission from Springer Science and Business Media)

Cystadenoma By ultrasound, serous cystadenomas are simple and thin-walled in appearance, resembling simple cysts, although they are often much larger (10 cm or more) [3]. Mucinous cystadenomas are similarly large, but may have internal echoes, septations, or locules (Fig. 4.8) [61]. On MRI, cystadenomas typically have a low T1 signal and a high T2 signal. The T1 signal in a mucinous cystadenoma may be higher than in a serous cystadenoma, and correspondingly, the T2 signal may be comparatively lower and vary among locules [3]. These neoplasms will not resolve on serial ultrasounds. A variant of the cystadenoma, a cystadenofibroma, will have solid components, usually without vascularity [62]. Differentiating cystadenomas from low malignant potential or malignant tumors by imaging can be challenging, and as a result, surgical excision is often pursued, though not emergently in hemodynamically stable patients without signs of torsion.

Theca-Lutein Cyst On examination, patients may have abdominal distention and pain. Patients may also have signs of virilization including hirsutism, though, if pregnant, patients can be advised that female fetuses are exceedingly rarely

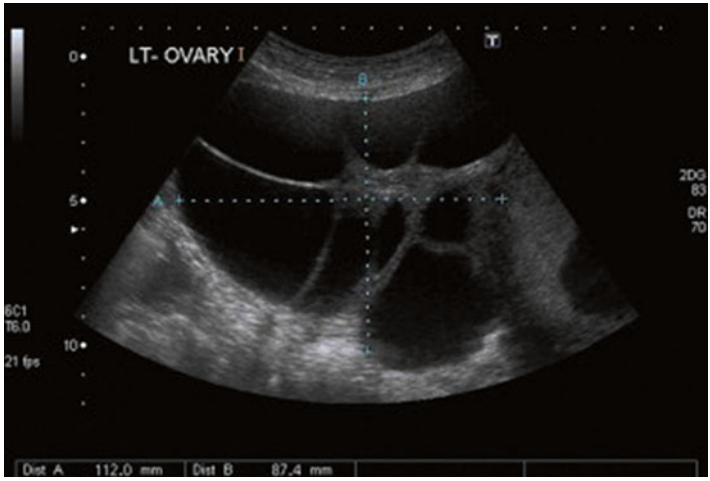

Fig. 4.9 Hyperreactio luteinalis by transvaginal ultrasound, with a spoke-wheel appearance (Reprinted from Amoah et al. [14], with permission from Elsevier and the American Society of Reproductive Medicine)

affected [63, 64]. On transvaginal ultrasound, theca-lutein cysts are usually bilateral and multilocular, measuring 6–12 cm in diameter [3]. These cysts have thin walls without nodularity, often with a classic "spoke-wheel" appearance (Fig. 4.9) [14]. Ascites may also be present. Theca-lutein cysts can resemble mucinous neoplasms but are distinguished by the uniform size of each locule [65]. The cysts will resolve with withdrawal of the hCG or gonadotropin source [64].

Hydrosalpinx Patients with hydrosalpinges are often asymptomatic, and a mass is variably detectable by physical examination. The sensitivity and specificity for the diagnosis of a hydrosalpinx by ultrasound is high (86–98 %) [56]. By ultrasound, hydrosalpinges are anechoic and notable for the presence of incomplete septations, resulting from the fallopian tube folding on itself (Fig. 4.10) [66]. A hydrosalpinx must be differentiated from a tubo-ovarian abscess; the latter is distended with debris and echogenic material (Fig. 4.11) [66]. Unlike a woman with a hydrosalpinx, a patient with a pyosalpinx would likely have an elevated white blood cell

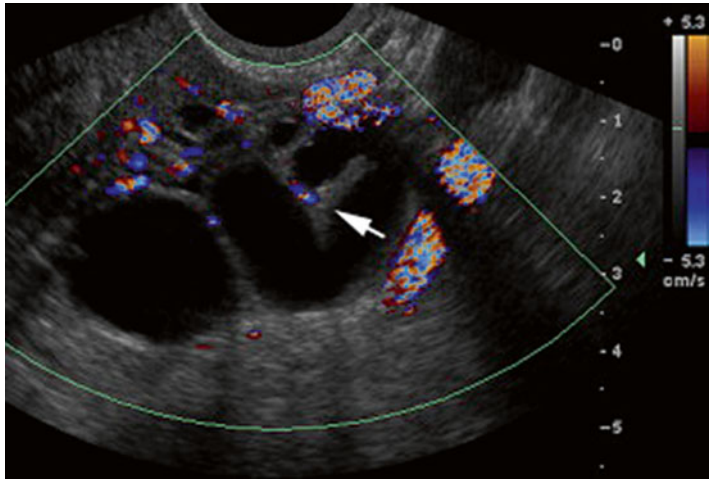

FIG. 4.10 Hydrosalpinx. Color Doppler coronal image shows a serpiginous anechoic tubular structure in the adnexa. Real-time imaging helps differentiate this tubular structure from complex adnexal cystic mass. Note the incomplete septation sign (*arrow*) (Reprinted from Chu et al. [66], with permission from Elsevier)

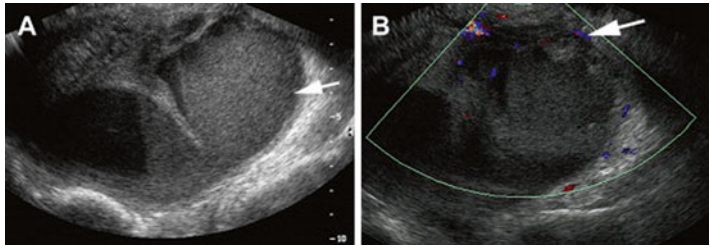

FIG. 4.11 Pyosalpinx. (**a**) Transvaginal ultrasound shows serpiginous tubular structure (*arrow*) in the adnexa with low-level internal echoes, consistent with pyosalpinx. (**b**) Color Doppler sagittal ultrasound image shows peripheral vascularity along the inflamed fallopian tube (*arrow*) (Reprinted from Chu et al. [66], with permission from Elsevier)

count, fever, and cervical motion tenderness; infection should be carefully excluded in patients whose pain is attributed to their hydrosalpinges. Please see Chap. 6, Pelvic Inflammatory Disease and Tubo-Ovarian Abscess, for more information on the management of TOAs. Furthermore, as a hydrosalpinx is not expected to cause pain, tubal torsion should be considered; a torsed fallopian tube occurs rarely but has a pathognomonic ultrasound appearance of a midline, cystic mass sometimes with intraluminal debris [67]. Please see Chap. 5, Adnexal Torsion, for more information.

TOAs Please see Chap. 6, Pelvic Inflammatory Disease and Tubo-Ovarian Abscess, for more information on the management of TOAs.

Ectopic Pregnancy Please see Chap. 3, Pregnancy of Unknown Location and Ectopic Pregnancy, for more information on the management of ectopic pregnancies.

Polycystic Ovaries Pelvic ultrasounds in patients with PCOS will reveal multiple peripheral follicles and an overall volume greater than 10 mL (Fig. 4.12); enlargement is usually bilateral,

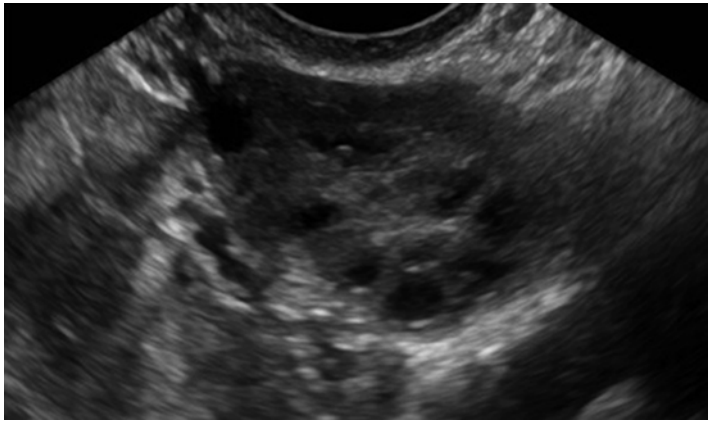

Fig. 4.12 Polycystic ovarian syndrome. Transvaginal ultrasound of a 21-year-old patient with PCOS reveals several small, peripherally located follicles with a "string of pearls" appearance

but can be unilateral [68]. The ovarian stroma may also be increased and echogenic, though use of oral contraceptive pills may normalize the appearance of the stroma [69]. Urgent intervention is not indicated, except in cases of suspected torsion; patients can be followed by gynecologists in the outpatient setting for management of oligo-ovulation and hirsutism, as needed.

OHSS Please see Chap. 20, Reproductive Endocrinology and Infertility, for more information on the diagnosis and management of OHSS.

Müllerian Anomalies MRI is the recommended study to clarify the anatomy in patients with suspected müllerian anomalies (Fig. 4.13) [70]. For the management of pregnancy in a patient with a müllerian anomaly, please see Chap. 3, Pregnancies of Unknown Location and Ectopic pregnancy.

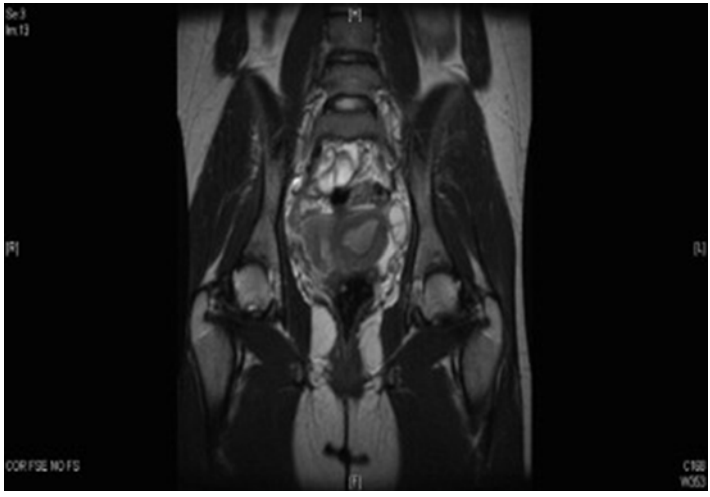

FIG. 4.13 MRI indicating significant myometrial connection between unicornuate uterus and functional, noncommunicating uterine horn (Reprinted from Spitzer et al. [37], with permission from Elsevier and the North American Society for Pediatric and Adolescent Gynecology)

For the management of müllerian anomalies resulting in obstructed menstrual flow, please see Chap. 10, Acute Pelvic Pain in Pediatric and Adolescent Patients.

Leiomyoma Please see Chap. 1, Acute Pelvic Pain, for further information on the diagnosis and management of painful fibroids.

Peritoneal Inclusion Cysts Peritoneal inclusion cysts can vary widely in size and appearance. By ultrasound, many septations are often noted. No solid components should be present, though the ovary may be involved in the mass and mistakenly identified as a nodule (Fig. 4.14); MRI can be useful in identifying the ovary within a peritoneal inclusion cyst [3]. Expectant management is acceptable in the absence of significant symptoms or imaging findings concerning for malignancy, such as solid areas or papillations [40]. Successful control through hormonal suppression with combined oral contraceptive pills or gonadotropin-releasing hormone agonist injections has been reported, though the cysts return

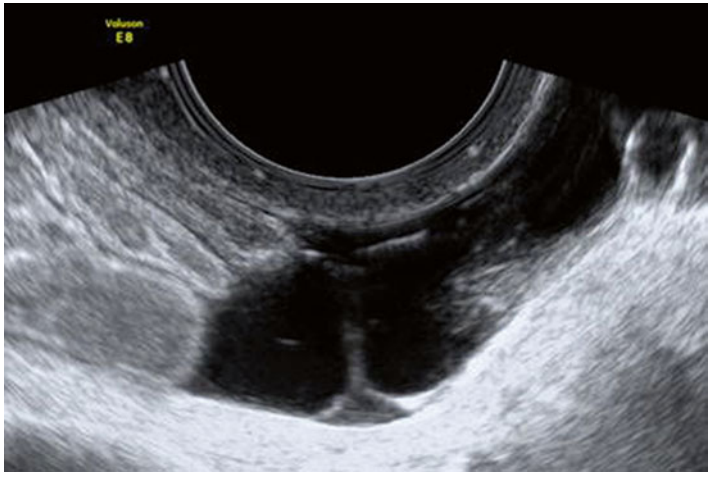

Fig. 4.14 Peritoneal inclusion cyst by transvaginal ultrasound (Reprinted from Coccia et al. [74], Figure 6, with kind permission from Springer Science and Business Media)

once those medications are stopped [71, 72]. More than half of peritoneal inclusion cysts will recur if removed surgically or drained percutaneously [72, 73]. Successful resolution using sclerotherapy (draining and chemically ablating the cyst bed) has been reported [73].

Ovarian Malignancy Features of malignant masses on transvaginal ultrasound include papillary projections, thick septations (>3 mm), and solid components with color Doppler flow (Fig. 4.15) [62, 74]. The presence of ascites is also highly concerning for malignancy, though ascites may also be identified in benign conditions as well, such as ovarian fibromas and OHSS [75]. CT scan may also be useful in characterizing pelvic masses concerning for malignancy by detecting metastatic disease and peritoneal carcinomatosis.

Serologic markers of ovarian cancers can be sent, usually for the purposes of follow-up and ongoing management in the outpatient setting; the most commonly used marker is CA-125, which may be elevated in epithelial ovarian cancer but can also be elevated in benign neoplasms, uterine fibroids, endometriosis, pregnancy, and other systemic illness [52]. Beta-hCG, lactate dehydrogenase (LDH), and alpha-

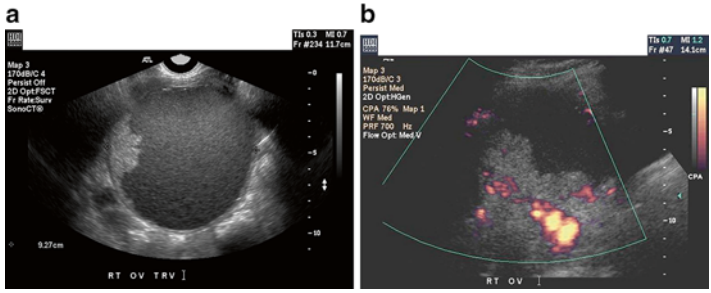

FIG. 4.15 Ovarian cancer. (**a**) A solid excrescence is present on the inner cyst wall of this complex ovarian cyst. (**b**) Doppler examination of the mass reveals multiple intermediate resistance vessels. A stage I-C epithelial ovarian cancer was found at laparotomy (Reprinted from Cohen [62], Figure. 4a, b, with kind permission from Springer Science and Business Media)

fetoprotein (AFP) may be elevated in non-epithelial ovarian cancers.

In women with a pelvic mass, referral to a gynecologic oncologist for management is recommended in any woman who also has ascites, a mass that is fixed or nodular, evidence of abdominal or distant metastases by imaging or physical examination, or a family history of breast or ovarian cancer in a first-degree relative. Furthermore, premenopausal women with CA-125 levels greater than 200 units/mL or postmenopausal women with CA-125 levels above 35 units/mL should also be referred to a gynecologic oncologist [76]. Otherwise, few suspected ovarian malignancies require admission and/or immediate intervention, though patients with evidence of bowel obstruction, ureteral obstruction, sepsis, or intraabdominal hemorrhage, in conjunction with imaging suggestive of advanced gynecologic malignancy (such as a large pelvic mass and peritoneal carcinomatosis), require admission for stabilization.

Ruptured Ovarian Cyst On physical examination, patients may have signs of peritoneal irritation due to free fluid in the abdomen, including rebound or cervical motion tenderness; patients are generally afebrile, without an elevated white blood cell count [50]. By transvaginal ultrasound, patients may have simple or complex free fluid in the pelvis, particularly the posterior cul-de-sac; the originating cyst is seldom visualized [47]. A CT scan will also reveal hemoperitoneum, but is often unnecessary with appropriate history, physical exam, and targeted ultrasound; if a CT is performed with intravenous contrast, active contrast extravasation from the ovary may rarely be visualized (Fig. 4.16).

A repeat hemoglobin value should be checked to ensure that the patient does not have ongoing bleeding. Overall, 80 % or more of patients with hemoperitoneum attributed to a ruptured ovarian cyst can be treated with analgesia and expectant management [77]. Patients should be counseled that their pain may take days to weeks to resolve, as the hemoperitoneum is gradually reabsorbed. Ovarian cyst suppression with combined oral contraceptive pills can be considered for

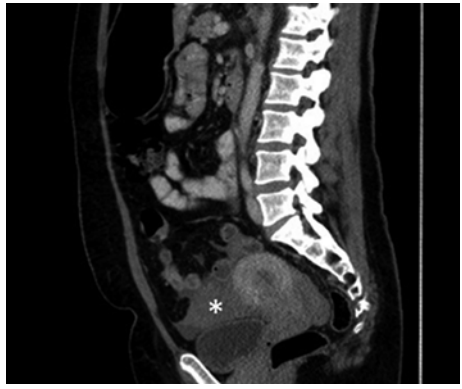

Fig. 4.16 Ovarian cyst rupture. CT scan showing moderate complex free fluid, indicated with an *asterisk* (*), consistent with hemoperitoneum due to ovarian cyst rupture

patients presenting with ruptured functional ovarian cysts (simple cysts or corpora lutea) without contraindications to estrogen therapy, which include but are not limited to migraines with aura, smoking, prior deep vein thrombosis or pulmonary embolism, hypertension vascular disease, and history of breast cancer [78, 79].

Clinically significant hemorrhage resulting in hemodynamic instability is uncommon, but rarely patients may show signs of hemodynamic compromise (please see Chap. 1, Acute Pelvic Pain, Table 1.1, for the stages of hemodynamic shock). Severe hemorrhage is more common in patients on anticoagulation therapy or those with a bleeding diathesis [80, 81]. In patients who are hemodynamically unstable or with persistently declining hemoglobin (or those in whom torsion cannot be reliably eliminated as the cause of pelvic pain), surgical exploration is indicated. Laparoscopy or laparotomy are options and depend on the patient's clinical stability and clinician preference. Please see Chap. 13, Preparing for Urgent or Emergent Surgery, for a discussion of reversing anticoagulant medications when indicated.

Intraoperatively, in patients bleeding from a ruptured ovarian cyst, fulguration or oversewing of the cyst rupture site, and/or ovarian cystectomy may be required. Rarely, oophorectomy may be required for hemostasis, though ovarian preservation in reproductive-aged women is an absolute priority.

Of note, in pregnant patients, ovarian cystectomy may result in removal of the corpus luteum, which secretes progesterone crucial for pregnancy maintenance for up to 9 weeks of gestation. At approximately 9 weeks' gestation, the luteoplacental shift occurs, and the placenta becomes the dominant source of progesterone secretion for the remainder of pregnancy; thus, removal of the corpus luteum before 9 weeks of gestation can result in spontaneous abortion. Patients who undergo ovarian surgery which may compromise the corpus luteum before 9 weeks of gestation should receive progesterone replacement, such as intramuscular progesterone in oil (50 mg per day) or micronized vaginal progesterone (200 mg three times daily), until they reach 9 weeks of gestation [82].

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Chapter 5
Adnexal Torsion

Paula C. Brady

Definitions

Adnexal Torsion Twisting of the adnexa—the ovary and/or fallopian tube—leading to occlusion of vascular outflow, resulting in pain and eventual necrosis. Ovarian torsion constitutes 3 % of gynecologic emergencies [1]. Risk factors for ovarian torsion include ovarian cysts greater than 5 cm, prior ovarian torsion (particularly torsion of a normal-appearing ovary), polycystic ovarian syndrome, treatment with gonadotropins for ovarian stimulation, ovarian hyperstimulation syndrome (OHSS), and pregnancy [2, 3]. Isolated tubal torsion is very rare and almost always associated with tubal enlargement, either with fluid or a mass; the clinical presentation is indistinguishable from ovarian torsion [4].

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Differential Diagnosis

Conditions that may present similarly to adnexal torsion include:

- Ruptured ovarian cyst
- Pelvic inflammatory disease or tubo-ovarian abscess
- Ectopic pregnancy
- Degenerating fibroid
- Appendicitis
- Nephrolithiasis
- Pyelonephritis
- Postoperative complications of gynecologic surgery

Please see Chap. 1, Acute Pelvic Pain, for a full differential diagnosis of acute-onset pelvic pain.

When You Get the Call Ask for a full set of vital signs, and request a pelvic ultrasound if one has not already been performed. Request that the patient not receive further pain medications prior to a physical examination by gynecology, to allow for an accurate assessment.

When You Arrive Review the full vital signs flow sheet and whether the patient has received any pain medications, which may affect the patient's physical exam findings. Assess the patient's discomfort and distress.

History

Review the acuity of the patient's onset of symptoms—whether the pain began abruptly or developed over several days—and any associated symptoms, including nausea, vomiting, and diarrhea. Review the location and quality of her

pain, including aching, sharp, continuous, or episodic. Pain from adnexal torsion is usually acute in onset and unilateral, often associated with nausea and emesis [5, 6]. Review whether she has ever had this pain before or suffers from chronic pain.

Review her full medical, surgical, obstetrical, and gynecologic history, including whether she is currently pregnant or recently had surgery. Review the patient's last menstrual period and whether she is undergoing ovulation induction or controlled ovarian hyperstimulation for in vitro fertilization. Review whether she has a history of polycystic ovarian syndrome, ovarian cysts, or ovarian torsion.

Physical Examination

Before examining a patient, review when she last received narcotics, which may mask clinically significant findings. Adnexal torsion is primarily a clinical diagnosis. Observe the patient's degree of discomfort with her pain, as evidenced by posture or inability to settle into a comfortable position. Patients with adnexal torsion often have significant abdominal pain and may have peritoneal signs, including rebound (pain on the abrupt release of abdominal palpation), involuntary abdominal guarding, or shake tenderness (pain with shaking the patient's abdomen or bed). On bimanual exam, the patient usually has unilateral adnexal tenderness and may have an enlarged adnexa [6].

Diagnosis

A complete blood count, serum human chorionic gonadotropin (hCG), and pelvic ultrasound should be obtained. Up to 50 % of patients with adnexal torsion may have a leukocytosis, though this finding is nonspecific [5].

A transvaginal ultrasound can support the diagnosis of adnexal torsion. Adnexal torsion is commonly associated with adnexal masses; in the absence of a mass, a torsed ovary

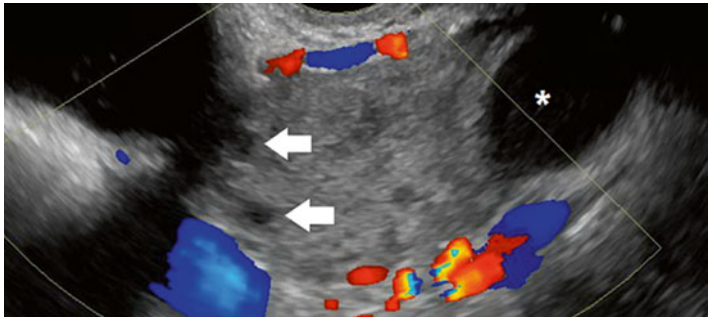

FIG. 5.1 Peripheralized follicles. In a 26-year-old patient with laparoscopy-confirmed ovarian torsion, the ovarian follicles (indicated with *arrows*) appeared peripheralized by transvaginal ultrasound. No ovarian blood flow was documented by color Doppler. An ovarian cyst is denoted with an *asterisk* (*)

may appear larger than the normal contralateral ovary [7]. Patients with ovarian torsion will often have ovarian edema (85 %), and the ovarian follicles may appear peripheralized (Fig. 5.1). Abnormal ovarian displacement may also be noted, such as into the anterior cul-de-sac. Of patients with adnexal torsion, 70 % may have free fluid around the torsed adnexa and/or in the posterior cul-de-sac (Fig. 5.2) [7]. Transvaginal ultrasound in patients with adnexal torsion may also reveal the whirlpool sign, which refers to the whirled appearance of the torsed vascular pedicle (Fig. 5.3) [8]. Tubal torsion may appear as a hydrosalpinx by ultrasound—a thick-walled tortuous cystic structure, sometimes with intraluminal debris [9].

By ultrasound, abnormal blood flow within the torsed ovary or the ovarian pedicle may be observed by Doppler evaluation. In small series, the absence of arterial and venous blood flow has been reported to have a positive predictive value of 80 % or more [7, 10]. Studies, however, conflict on the reliability of abnormal blood flow in diagnosing ovarian torsion, particularly as this ultrasound finding is operator dependent [7]. Overall, while absence of normal ovarian blood flow may increase suspicion of adnexal torsion,

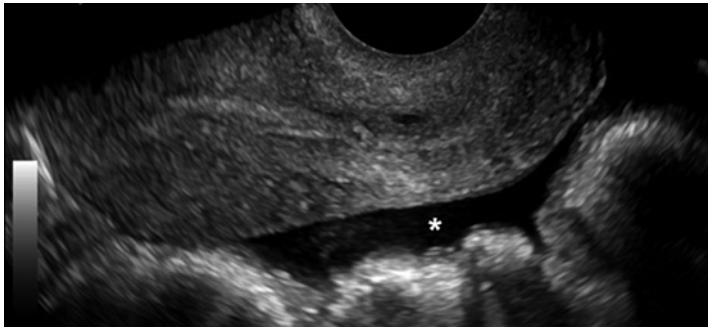

Fig. 5.2 Free fluid in the posterior cul-de-sac. In a 26-year-old patient with laparoscopy-confirmed ovarian torsion, free fluid was noted in the posterior cul-de-sac by transvaginal ultrasound, indicated with an *asterisk* (*)

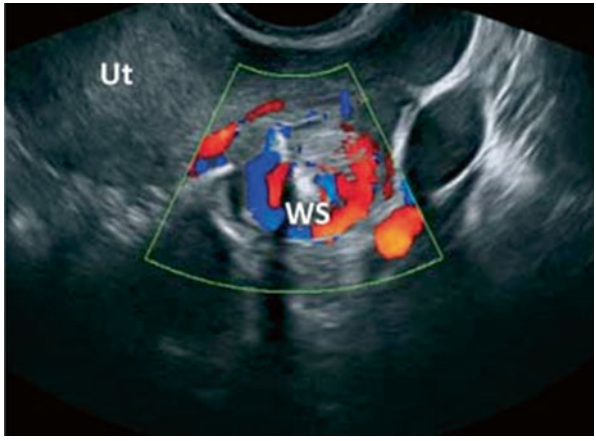

Fig. 5.3 Whirlpool sign with color Doppler. *Ut* uterus, *WS* whirlpool sign (Reprinted from Valsky et al. [8], with permission of John Wiley & Sons, Inc.)

management decisions should not be made based on the presence or absence of Doppler flow.

In patients with suspected adnexal torsion, CT and MRI are not required, but may be obtained to rule out other

diagnoses such as nephrolithiasis and appendicitis. In a patient with adnexal torsion, a CT scan with IV contrast may show an enlarged ovary with decreased enhancement, free fluid, and uterine deviation to the side of the torsion [11]. In a patient with ovarian torsion, MRI may show an enlarged ovary (relative to the normal contralateral ovary) with edema, a twisted ovarian pedicle, and ovarian hemorrhage [12].

Management

Management of ovarian torsion is surgical. Intraoperatively, a torsed ovary and/or tube will often appear dusky and sometimes necrotic or hemorrhagic. The ovary and/or fallopian tube should be untwisted. Adnexal detorsion does not confer a significant risk of thromboembolism (0.2 %) [12]. Following adnexal detorsion, the ovary and tube should be observed intraoperatively for return of normal color; significant necrosis is more common after 48 h of torsion [13]. The majority of ovaries can be left in situ, as over 94 % of discolored or hemorrhagic ovaries will regain normal ovarian function and normal appearance by ultrasound [14, 15].

At the time of surgery, any adnexal cysts potentially responsible for the torsion should be drained or removed, as deemed appropriate by the surgeon. Of note, an ovarian cystectomy in a pregnant patient may result in the removal of the corpus luteum, which secretes progesterone crucial for pregnancy maintenance for up to 9 weeks of gestation [16]. Pregnant patients who undergo ovarian cystectomies before 9 weeks of gestation should receive progesterone supplementation, such as intramuscular progesterone in oil (50 mg per day) or micronized vaginal progesterone (200 mg three times per day).

Oophoropexy, or surgical fixation of the ovary, can be considered to prevent recurrent torsion, but clear guidelines have not been established, and the practice is controversial [17]. Oophoropexy may be considered if ovarian torsion occurred in the absence of risk factors (such as an ovarian

mass), in a patient with only one ovary, or if torsion is recurrent. Techniques include truncation of the utero-ovarian ligament and fixation of the ovary to the ipsilateral round ligament, pelvic sidewall, uterosacral ligament, or posterior uterus, using absorbable or permanent suture [18, 19]. There are no randomized studies comparing recurrence rates or long-term effects on fertility of these techniques.

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Chapter 6
Pelvic Inflammatory Disease and Tubo-Ovarian Abscesses

Paula C. Brady

Definitions

Pelvic Inflammatory Disease (PID) Inflammation of the upper genital tract, including inflammation of the endometrium (endometritis), fallopian tube(s) (salpingitis), and pelvic peritoneum (peritonitis) [1]. Risk factors include multiple sexual partners, young age at coitarche, non-use of barrier contraception, smoking, illicit drug use, infection with *Neisseria gonorrhoeae* and *Chlamydia trachomatis*, or prior episodes of PID [2, 3]. Approximately 50 % of cases of PID are associated with *N. gonorrhoeae* and/or *C. trachomatis* infection; other bacteria associated with PID include anaerobes, *Gardnerella vaginalis*, *Streptococcus agalactiae, Haemophilus influenzae,* and enteric gram-negative rods [4, 5].

Patients may present with abdominal pain, chills, abnormal vaginal bleeding, dyspareunia, and/or vaginal discharge, while others may be asymptomatic [6]. Patients can also develop perihepatitis, also called Fitz-Hugh–Curtis syndrome, which

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may be associated with right upper quadrant pain and elevated liver enzymes [7].

Long-term sequelae of PID include chronic pelvic pain and infertility due to obstructed fallopian tubes [8]. Each episode of PID doubles the rate of infertility; following one, two, or three or more PID episodes, rates of infertility have been reported at 8.0 %, 19.5 %, and 40 %, respectively [9, 10].

Tubo-Ovarian Abscess An abscess of the adnexa, involving the fallopian tube and/or ovary. Tubo-ovarian abscesses are commonly considered a complication of PID, occurring in approximately one-third of cases [11]. Less commonly, TOAs may instead result from spread of infection from the bowel (such as diverticulitis) or postoperative infection in the pelvis. Risk factors for TOA and PID are similar. Immunosuppression, such an infection with human immunodeficiency virus (HIV), may expose women to higher risk of TOA [12]. The abscesses are usually polymicrobial, comprised of the same bacteria involved in PID [7]. Patients present with symptoms similar to those with PID, and up to 30 % may be afebrile [13]. Patients may also present with high fever and signs of sepsis, including hemodynamic instability, particularly in patients with ruptured TOA. Patients with hemodynamic instability and ruptured TOA require emergent surgical exploration.

When You Get the Call Ask for a full set of vital signs, to ensure hemodynamic stability. Consider requesting pelvic imaging in patients with fever, pain, prior TOA, immunosuppression, or other risk factors for pelvic abscess.

When You Arrive Review the full vital sign flow sheet for evidence of septic physiology, including tachycardia or hypotension. For diagnosis and management of sepsis, please refer to Chap. 1, Acute Pelvic Pain. Patients with TOA, hemodynamic instability and sepsis who do not respond immediately to resuscitation require emergent surgical exploration.

History

Ask the patient to describe her symptoms, including onset and severity. Review whether the patient has had symptoms of fever, pain, or vaginal bleeding or discharge. Review whether the patient has been diagnosed with sexually transmitted infections or PID in the past, and review the risk factors for PID. Ask whether she is sexually active and uses barrier contraception. The patient's medical history should be reviewed, including sources of immunosuppression, as well as her surgical history.

Physical Examination

Perform an abdominal examination, noting the presence of peritoneal signs, including rebound (pain with abdominal pressure is quickly withdrawn) or involuntary guarding. A speculum exam should be performed to assess for mucopurulent cervicitis and to allow for collection of a swab for nucleic acid amplification testing (NAAT) for *N. gonorrhoeae* and *C. trachomatis*. In patients complaining of vaginal discharge, a vaginal culture can be collected, as well as a wet prep (a slide of vaginal discharge prepared with normal saline and potassium hydroxide, separately) to assess for *Trichomonas vaginalis*, bacterial vaginosis, and *Candida*. Note the presence or absence of white blood cells on the wet prep. A bimanual exam should be performed to assess for tenderness of the gynecologic organs, including the cervix (cervical motion tenderness), uterus, and ovaries.

Diagnosis

Obtain a pregnancy test in all reproductive age women. A complete blood count with differential may be helpful, to assess for leukocytosis. To rule out other common etiologies of pelvic pain, check a urinalysis for infection.

With either PID or TOA, patients may be febrile with leukocytosis; these findings are not universal, however, as patients may also be afebrile, and only 44 % of patients with PID and 77 % of patients with TOA have elevated white blood cell (WBC) counts [7, 13].

PID

The diagnosis of PID is primarily made by physical examination. Given the potential morbidity of PID for the reproductive health of young women, the threshold for diagnosis is relatively low, shown in Table 6.1 [6]. Of note, in patients with normal vaginal discharge without leukocytes on wet mount, the diagnosis of PID is unlikely, with a negative predictive value of 94.5 % [14]. At laparoscopy, salpingitis will appear as tubal erythema or edema, potentially with peritubal adhesions, and with purulent drainage from the fimbriated end of the fallopian tube (Fig. 6.1) [7]. Laparoscopic evaluation for diagnosis is increasingly uncommon, given the cost and potential morbidity.

Imaging is not required for the diagnosis of PID, and most patients will have normal imaging. Transvaginal ultrasound in patients with PID may reveal thickened fallopian tubes [15]. Less commonly, the "cogwheel" sign may be seen, which refers to a sonolucent cogwheel structure visible on cross section of an inflamed fallopian tube, representing the swollen walls and mucosal folds projecting into the lumen (Fig. 6.2) [16, 17].

TOA

Tubo-ovarian abscesses are usually diagnosed by imaging, in a patient with the symptoms and physical exam findings of PID. A patient with TOA may also have a palpable pelvic mass or adnexal fullness on physical exam. Transvaginal ultrasound and/or computed tomography (CT) scan is often obtained for the diagnosis of TOA. The sensitivity and speci-

Table 6.1 Diagnostic criteria for pelvic inflammatory disease (PID)

Minimum diagnostic criteria
The absence of a more likely etiology of pain *and*
Cervical motion tenderness *or*
Uterine tenderness *or*
Adnexal tenderness
Increased specificity
Temperature greater than 101 °F (38.3 °C)
Mucopurulent cervical or vaginal discharge
Presence of WBC on wet mount examination of vaginal discharge
Elevated erythrocyte sedimentation rate
Elevated C-reactive protein
Positive cultures for *N. gonorrhoeae* or *C. trachomatis*
Highest specificity
Imaging (transvaginal ultrasound or magnetic resonance imaging) revealing thickened fallopian tubes filled with fluid or a tubo-ovarian abscess
Evidence of endometritis by histopathologic analysis of endometrial biopsy
Evidence of salpingitis by laparoscopy

Centers for Disease Control and Prevention [6]

ficity of transvaginal ultrasound for tubo-ovarian abscesses are greater than 90 % [18]. TOAs will appear as complex, loculated cystic masses with thickened irregular walls; internal debris may be seen (Fig. 6.3).

When the diagnosis of TOA is not clear following a pelvic ultrasound, a CT scan is recommended. CT scans can also detect gastrointestinal causes of pelvic abscess, such as diverticulitis or appendicitis, and bowel or gynecologic malignancy, which may also present as complex pelvic masses [19]. By CT

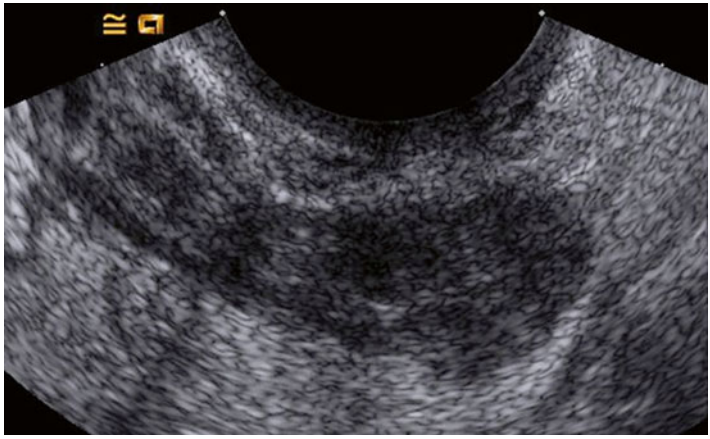

FIG. 6.1 Acute salpingitis by ultrasound, verified by laparoscopy. The sausage-shaped solid structure corresponds to the inflamed tube (Reprinted from Romosan et al. [27], by permission of Oxford University Press and The European Society of Human Reproduction and Embryology)

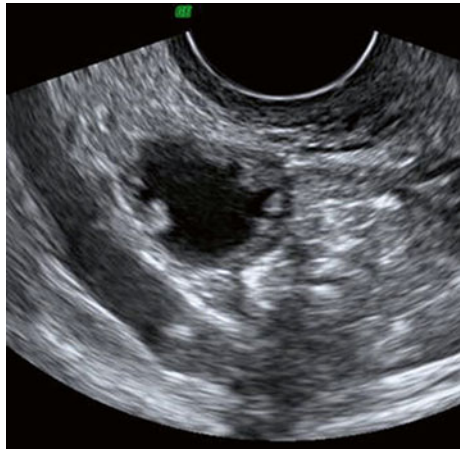

FIG. 6.2 Ultrasound image illustrating the cogwheel sign (Reprinted from Romosan and Valentin [16], Figure 3, with kind permission from Springer Science and Business Media)

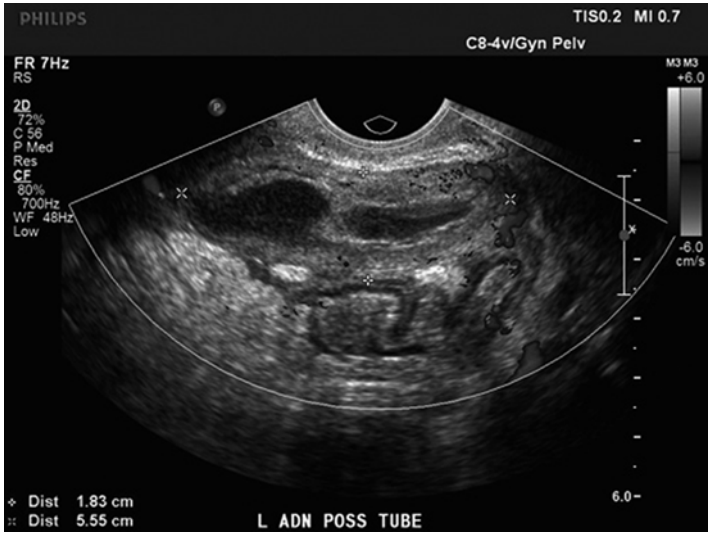

FIG. 6.3 Ultrasound image of pyosalpinx (Reprinted from Chappell and Wiesenfeld [19], with permission)

scan, a TOA appears as a thick-walled, uniformly enhancing abscess, which may be multilocular [20]. The mesosalpinx and uterosacral ligaments may also appear thickened, and pyosalpinx is noted in 50 % of patients (Fig. 6.4).

MRI is not routinely used for the diagnosis of TOA, but may similarly show a complex adnexal mass with surrounding inflammation; TOAs will commonly have a low signal intensity on T1-weighted images and high signal intensity in T2-weighted images [18, 21]. Gas bubbles within the suspected TOA are highly specific for abscess [22].

Management

While PID and TOAs are commonly managed medically or minimally invasively, a ruptured TOA can represent a life-threatening emergency. Hemodynamically unstable patients

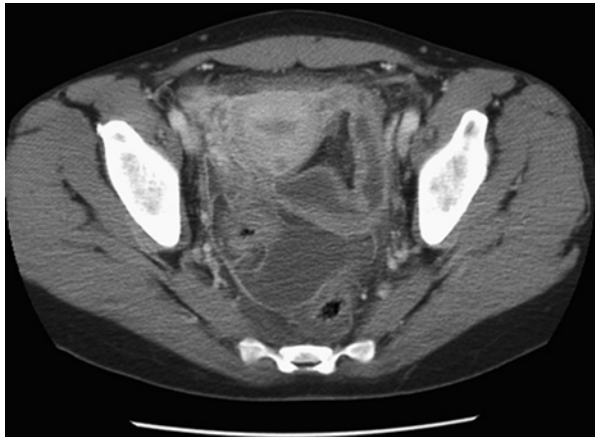

Fig. 6.4 Computed tomographic image of pyosalpinx and tubo-ovarian abscess (Reprinted from Chappell and Wiesenfeld [19], with permission)

with sepsis attributed to a ruptured TOA require emergent surgical exploration.

In stable patients eligible for medical management, intrauterine devices (IUDs) can be left in situ during PID treatment, though removal should be considered in patients without clinical improvement after 48 h of antibiotic treatment. IUDs should be removed in patients diagnosed with TOAs [6].

In general, patients who have tested positive for gonorrhea or chlamydia should be retested in 3 months given the high rate of reinfection [6, 23]. Partner treatment should be arranged for patients who tested positive for these sexually transmitted infections. Patients should abstain from intercourse with their partners until both have completed treatment.

PID

In managing PID, the decision must be made whether to admit the patient. In patients with stable vital signs and

discomfort controlled with oral medications, outpatient management may be reasonable. Inpatient treatment should be pursued in patients with (1) tubo-ovarian abscess; (2) possible surgical emergencies as the cause of their presentation, including appendicitis or ruptured pelvic abscess; (3) high fever, severe nausea, vomiting, or evidence of systemic illness or sepsis; (4) pregnancy; (5) inability to tolerate or complete the outpatient regimen; or (6) lack of clinical response to outpatient therapy [6].

Hemodynamically stable patients with PID who do not meet criteria for admission may be treated as outpatients. The recommended regimen for outpatient PID treatment consists of ceftriaxone (250 mg IM in a single dose) plus doxycycline (100 mg PO every 12 h for 14 days) *with or without* metronidazole (500 mg PO every 12 h for 14 days) [6]. Third-generation cephalosporins, such as ceftizoxime or cefotaxime, are acceptable alternatives to ceftriaxone. An alternative regimen is cefoxitin (2 g IM in a single dose) with probenecid (1 g orally at the same time as the cefoxitin) plus doxycycline (100 mg PO every 12 h for 14 days) *with or without* metronidazole (500 mg PO every 12 h for 14 days) [6]. Patients treated for PID as an outpatient should be examined within 3 days to ensure improvement of their symptoms; lack of improvement may necessitate reassessment of the diagnosis and/or admission for intravenous antibiotics [7].

In patients meeting the criteria for admission, the recommended regimen includes intravenous antibiotics, continued until the patient is afebrile for at least 24 h. This regimen includes doxycycline (100 mg PO or IV every 12 h) plus either (1) cefoxitin (2 g IV every 6 h) or (2) cefotetan (2 g IV every 12 h) [6]. Alternative regimens include (1) clindamycin (900 mg IV every 8 h) plus gentamicin (2 mg/kg load, followed by 1.5 mg/kg every 8 h) or (2) ampicillin-sulbactam (3 g IV every 6 h) plus doxycycline (100 mg PO or IV every 12 h) [6].

The patient can be transitioned to oral medications once she is afebrile for at least 24 h while receiving parenteral antibiotics. Per CDC guidelines, a patient initially treated with parenteral cephalosporins can be transitioned to doxycycline (100 mg PO every 12 h) for 14 days. If clindamycin and

gentamicin were used, the patient can be transitioned to clindamycin (450 mg PO every 6 h) or doxycycline (100 mg every 12 h) for 14 days.

TOA

Patients with TOA must be admitted for inpatient management. In the past, management of tubo-ovarian abscesses was primarily surgical, which often required removal of the uterus and ovaries due to the extent of infection [7]. In current practice, TOAs are managed with intravenous antibiotics, with or without percutaneous drainage by interventional radiology.

The role of surgical management is far more limited in current practice, though women who are hemodynamically unstable with a diagnosis of TOA require emergent surgical exploration, often by laparotomy given the clinical acuity and need for abdominal visualization. Furthermore, women who remain persistently febrile or are not improving despite intravenous antibiotics and percutaneous drainage may require surgical exploration. Finally, up to half of postmenopausal women with TOA may have underlying malignancy, and some clinicians argue for more aggressive surgical management in these patients to allow for removal of adnexal masses and possible staging [19, 24].

Intravenous antibiotics should be administered until the patient has been afebrile for 24–48 h, followed by 14 days of oral antibiotics. Parenteral antibiotic regimens are the same as those for inpatient management of PID. Once a patient has improved clinically, including being afebrile for at least 24 h, oral antibiotics can be started. Recommended antibiotics include doxycycline (100 mg PO every 12 h) plus either clindamycin (450 mg PO every 6 h) or metronidazole (500 mg PO every 12 h); doxycycline should not be continued alone [6]. Twenty-four hours of inpatient observation of the patient's clinical status following transition to oral antibiotics is recommended.

In addition to parenteral antibiotics, TOAs are now commonly drained, often by interventional radiologists, as drainage has been shown to improve treatment success and shorten hospital stay [25]. The approach is most commonly percutaneous and less commonly transvaginal. Tubo-ovarian abscesses greater than 8 cm in diameter generally require drainage in addition to treatment with parenteral antibiotics, though wider availability of interventional radiology has led to earlier drainage of smaller abscesses [26]. Patients who remain febrile or with significant pain after 48 h of intravenous antibiotics alone, regardless of abscess size, may require drainage. The abscess contents should be sent for culture, to guide antibiotic therapy.

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Chapter 7
Vulvovaginal Dermatoses, Lesions, and Masses

Paula C. Brady and Natasha R. Johnson

Differential Diagnosis

Infectious

Herpes simplex virus (HSV)
Herpes zoster, also called shingles
Syphilis
Chancroid
Granuloma inguinale, also called donovanosis
Lymphogranuloma venereum (LGV)
Candida
Folliculitis/impetigo
Group A β-hemolytic streptococcus

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Scabies
Human Immunodeficiency Virus (HIV)
Tuberculosis

Noninfectious

Allergic or irritant contact dermatitis
Hidradenitis suppurativa
Lichen planus
Lichen sclerosis
Lichen simplex chronicus
Lipschutz ulcers
Post viral genital ulcers (aphthous ulcers)
Atrophic vaginitis
Inflammatory bowel disease
Pyoderma gangrenosum
Stevens-Johnson syndrome (SJS)
Toxic epidermal necrolysis (TEN)
Erythema multiforme
Bullous pemphigoid
Mucous membrane pemphigoid
Pemphigus vulgaris
Linear immunoglobulin A (IgA) dermatosis
Paraneoplastic pemphigus
Psoriasis
Eczema
Vulvar malignancy
Hematologic malignancy
Behçet's syndrome
Periodic fever, aphthous stomatitis, pharyngitis, and cervical adenitis (PFAPA)

Inguinal or Perineal Abscess

Chancroid
Lymphogranuloma venereum (LGV)
Hidradenitis suppurativa
Bartholin's gland or Skene's glands abscesses, urethral diverticulum

Bullae/Blisters/Desquamation

Stevens-Johnson syndrome (SJS)
Toxic epidermal necrolysis (TEN)
Erythema multiforme
Bullous pemphigoid
Mucous membrane pemphigoid
Pemphigus vulgaris
Linear IgA dermatosis
Paraneoplastic pemphigus
Allergic or irritant contact dermatitis

Ulcers/Erosions/Crusted Lesions

Herpes simplex virus (HSV)
Herpes zoster, also called shingles
Syphilis
Chancroid
Granuloma inguinale, also called donovanosis
Lymphogranuloma venereum (LGV)
Candida
Allergic or irritant contact dermatitis
Lichen planus
Lichen sclerosis
Lichen simplex chronicus

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Lipschutz ulcers
Post viral genital ulcers (aphthous ulcers)
Folliculitis/impetigo
Inflammatory bowel disease
Pyoderma gangrenosum
Stevens-Johnson syndrome (SJS)
Toxic epidermal necrolysis (TEN)
Erythema multiforme
Bullous pemphigoid
Mucous membrane pemphigoid
Pemphigus vulgaris
Linear IgA dermatosis
Paraneoplastic pemphigus
Psoriasis
Eczema
Vulvar malignancy
Hematologic malignancy
Behçet's syndrome
Periodic fever, aphthous stomatitis, pharyngitis, and cervical adenitis (PFAPA)
HIV
Tuberculosis

Fissures

Candida
Group A β-hemolytic streptococcus
Scabies
Allergic or irritant contact dermatitis
Hidradenitis suppurativa
Lichen planus
Lichen sclerosis

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Lichen simplex chronicus
Eczema
Desquamative inflammatory vaginitis (DIV)
Inflammatory bowel disease

Perineal Masses

Bartholin's gland cyst/abscess
Skene's gland cyst
Urethral diverticulum
Müllerian and Gartner (mesonephric) duct cyst
Canal of Nuck cyst
Epidermoid inclusion cyst
Condyloma acuminata
Acrochordons (skin tags)
Less common: lipomas, neurofibromas, vulvovaginal endometriosis, and vulvar leiomyomas

When You Get the Call Ensure the patient is in a private room on bed or stretcher equipped for gynecologic exams (i.e., with stirrups).

When You Arrive Review the patient's vital signs, making note of signs of systemic illness, including fever or tachycardia.

History

The history of the present illness is crucial when approaching perineal lesions, in order to determine exposures to sexually transmitted infections, irritants, or any other instigating factors, including trauma. Review the evolution of the current lesion, including whether onset was rapid or gradual, and whether an ulceration began as a blister or was preceded by tingling,

burning, pruritis, or pain. Ask patients to describe symptoms currently accompanying the chief complaint, including itching, pain, purulent drainage from a lesion, or vaginal discharge.

Review whether the patient has already tried any treatments, which may lend insight into the original etiology or suggest a secondary overlying contact dermatitis if topical treatments have been applied. Inquire regarding pubic hair removal practices, as hair removal may introduce contact irritants and infection. Review whether the patient uses scented soaps, douches, lubricants for intercourse, condoms, or spermicides. Review whether the patient has new sexual partners, partners who have had similar lesions, or recent travel.

A review of systems should include constitutional complaints such as fever, myalgias, malaise, preceding or concomitant infections, or complaints in any other organ systems (including pharyngitis or gastrointestinal complaints). Review whether the patient has, or has ever had, oral or eye ulcerations.

A full sexual history is vital, including the gender and number of sexual partners, types of sexual contact (oral, vaginal, anal), and any history of sexually transmitted infections. High-risk sexual behaviors or drug or alcohol use may indicate higher risk of exposure to sexually transmitted infections.

A full medical history should be obtained, including any current immunosuppression, HIV, or autoimmune or inflammatory bowel disease. A family history should also include inflammatory bowel disease, Behçet's syndrome, or other autoimmune diseases.

Physical Examination

As indicated, examine for patient's mouth for gingival inflammation and lesions of the buccal mucosa, and note any other skin findings on extensor or flexor surfaces, intertriginous regions, and the hands and feet.

A physical exam of the vulva and vagina should begin with observation, carefully noting the anatomic location of any

lesions and relation to other structures. The distribution of erythema or other skin changes should be noted, as well as the presence or absence of normal vulvar architecture (such as shortening or loss of labia minora and adhesion of the clitoral hood to the glans) and change in pigmentation (hypo- or hyperpigmentation). Lesions should be described in detail, including size, whether lesions (vesicles, ulcers) are single or multiple, and accompanying erythema and tenderness. Note whether masses, cysts, or abscesses are painful, erythematous, mobile, fluctuant, or firm and whether any purulent material can be expressed. Assess for lymphadenopathy, including painful fluctuant enlargement of lymph nodes called buboes, particularly in the inguinal region [1]. Of note, local and systemic infections, such as lower extremity infections, can also lead to inguinal lymphadenopathy. An adult with vulvar ulcerations should also have a speculum exam to assess whether the ulcerations are also present in the vagina, which often require additional, specific management.

Diagnosis

Diagnostic testing must be tailored to the specific cause. The symptoms of vaginal discharge and/or odor and the presence of abnormal discharge on examination warrant pH testing, preparation of a wet mount (microscopic evaluation of vaginal discharge prepared with normal saline and 10 % potassium hydroxide, separately), and vaginal culture. Elevated pH (greater than 4.5) may be seen in patients with bacterial vaginosis, trichomoniasis, and atrophic vaginitis [2]. Testing for suspected sexually transmitted infections—whether serologic or from the lesion—is dictated by presentation, prevalence of disease, and the patient's risk factors. Sexually transmitted infections resulting in genital lesions are detailed below.

For any ulcerations—suspected lichen planus, lichen sclerosis, malignancy, or other dermatologic conditions including blistering diseases or pyoderma gangrenosum—biopsy should be considered. Recurrent ulcerations require more

in-depth workup for autoimmune causes such as inflammatory bowel disease or Behçet's syndrome. Dermatology consultation should be considered for extensive ulcerations and desquamation.

Management

General symptom management applies to several pathologies. In general, erosions should be managed with sitz baths (sitting in warm water for 5–10 min, two to three times per day) with application of topical lidocaine 2 % jelly for analgesia and/or plain petrolatum as a barrier [3]. Patients should be counseled to avoid contact irritants, including scented soaps, and to wash the vulva gently with water, without soap. If patients report pruritis, they may use hydroxyzine or other sedating antihistamine as a sleep aid and to limit scratching.

Management approaches for specific etiologies—infectious and noninfectious—of vulvovaginal lesions are detailed below. Management of traumatic vulvovaginal injuries, including straddle injuries and vulvar hematomas, are discussed in Chap. 11, Vulvovaginitis and Vaginal Bleeding in Pediatric and Adolescent Patients.

Infectious

In general, when infectious causes of genital lesions are suspected, the World Health Organization offers guidelines for management of vulvovaginal ulcerations designed to avoid delays in treatment, particularly useful in low-resource settings lacking extensive diagnostic resources.

For patients with genital ulcers, the WHO recommends treatment for syphilis and chancroid, in addition to offering treatment for HSV-2 in areas in which prevalence is 30 % or more [1]. Depending on local disease prevalence, treatment for granuloma inguinale and/or lymphogranuloma venereum

is recommended as well. Any fluctuant lymph nodes should be aspirated. Patients' symptoms should be reassessed in 7 days or less. Partner treatment should be addressed, and HIV testing should be offered when relevant and available. Patients with genital buboes without ulcers should be treated for chancroid and lymphogranuloma venerum.

Treatment of sexual partners will be reviewed for each infection below. In general, if an infectious etiology of genital lesions is suspected, patients should avoid unprotected intercourse until all symptoms and lesions have resolved or 1 week after single-dose treatment [1].

Herpes Simplex Virus (HSV)

Herpes simplex virus is a chronic infection that cannot be cured, but can be managed with antiviral medications. Two serotypes are most clinically relevant: HSV-1 classically causes oral lesions, while HSV-2 is associated with anogenital lesions. Increasingly, HSV-1 is also associated with anogenital lesions [4]. Patients present with vesicles that progress to painful ulcerations, dysuria, dyspareunia, and bleeding and can have inguinal lymphadenopathy (Fig. 7.1).

Analysis of data from the National Health and Nutrition Examination Surveys (NHANES) from 2007 to 2010 reported a prevalence of HSV-2 among women aged 14–49 years in the United States of 20.4 %; the prevalence is 49.5 % among non-Hispanic black or African American women [6].

In patients presenting with ulcerations suspicious for HSV, cell culture and polymerase chain reaction (PCR) are preferred for diagnosis of HSV. Viral culture can be obtained by swabbing the base of an unroofed vesicle [7]. Culture, however, has low sensitivity, particularly in the diagnosis of recurrent lesions. PCR has much higher sensitivity than culture, with more rapid results and less sensitivity to collection and transport conditions [8]. PCR can also differentiate between HSV serotypes [4]. Direct fluorescent antibody (DFA) testing or enzyme-linked

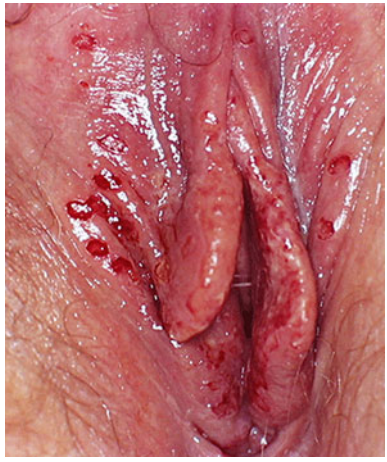

Fig. 7.1 Vulvar herpes simplex (Reprinted from Danby and Margesson [5], with permission of John Wiley & Sons, Inc.)

immunosorbent assays (ELISA) are also available, generating fast results, with moderate sensitivity [8]. Tzanck smears, in which the lesion base is scraped and examined for cytologic changes, lack sensitivity and specificity and cannot distinguish between HSV and varicella-zoster virus (VZV), which causes varicella (chickenpox) and herpes zoster (shingles) [9, 10].

Serologic testing is commonly performed to assess for HSV-specific glycoproteins, allowing for differentiation between HSV serotypes [4]. Serology, however, cannot reliably differentiate between past and present infections; IgM, which may be used as a marker of an acute infection for many other viruses, may be present even in recurrent HSV episodes [11]. Serologies may be clinically useful in symptomatic patients with negative HSV cultures or patients with recurrent lesions requiring diagnostic confirmation. HSV serologies can also be used to assess patients with HIV, at risk for acquiring HIV, or to assess the sexual partner of a patient with known herpes [4].

For primary (first-ever) HSV outbreaks, recommended treatment regimens are (1) acyclovir, 400 milligrams (mg) PO every 8 h for 7–10 days; (2) acyclovir 200 mg PO five times per day for 7–10 days; (3) famciclovir, 250 mg PO every 8 h for 7–10 days; or (4) valacyclovir 1 g PO every 12 h for 7–10 days [4].

For adults not on suppressive therapy with an episode of recurrence of genital herpes, the recommended regimen is (1) acyclovir 400 mg PO every 8 h for 5 days, (2) acyclovir 800 mg PO every 12 h for 5 days, (3) acyclovir 800 mg PO every 8 h for 2 days, (4) famciclovir 125 mg PO every 12 h for 5 days, (5) famciclovir 1000 mg PO every 12 h for 1 day, (6) famciclovir 500 mg once, followed by 250 mg every 12 h for 2 days, (7) valacyclovir 500 mg PO every 12 h for 3 days, or (8) valacyclovir 1000 mg PO once per day for 5 days.

Suppressive therapy reduces outbreaks by 80 % [12]. The regimen to prevent recurrent outbreaks in adults is (1) acyclovir 400 mg PO every 12 h, (2) famciclovir 250 mg PO every 12 h (3) valacyclovir 500 mg PO once daily, or (4) valacyclovir 1 g orally once daily [4].

Initial outbreaks in children should be treated with acyclovir, 40–80 mg per (kg) per day divided into 3–4 doses, administered for 5–10 days (maximum 1 g per day) [13]. In patients over 12 years of age, acyclovir is instead dosed as 1000–1200 mg/day divided into 3–5 doses for 7–10 days. Recurrent infections in patients over 12 years can also be treated with acyclovir: (1) 1000 mg divided into 5 doses for 5 days, (2) 1600 mg divided into 2 doses for 5 days, and (3) 2400 mg divided into 3 doses for 2 days [13].

IV acyclovir can be used for patients with severe outbreaks, particularly disseminated HSV. In adults, the recommended IV regimen is 5–10 mg/kg every 8 h until clinical improvement is obtained, followed by oral therapy for at least 10 days total [4]. For children over 12 years of age, IV acyclovir is dosed as 15 mg/kg per day divided into three doses for 5–7 days [13].

For symptomatic relief, patients may need to urinate into a warm water bath. Urinary retention may require temporary

Foley catheter placement. Topical, oral, and IV analgesics may be required for adequate pain control.

Counseling a patient diagnosed with HSV is crucial. Sexual transmission can occur during asymptomatic periods, though transmission is more common when patients have prodromal symptoms or lesions [12]. Prophylaxis and condom use may reduce, but not eliminate, the risk of transmission. Infection with HSV-2 may increase the risk of contracting HIV.

Pregnant women with partners known to have HSV should be counseled to avoid exposure to HSV in their third trimester (either intercourse with a patient with HSV-2 or genital HSV-1 or receptive oral sex with a partner with oral HSV-1). Suppressive therapy should be prescribed for pregnant women with genital HSV from 36 weeks of gestation onward [14]. The risk of neonatal infection should be explained.

Sex partners should be offered counseling and evaluation and can be offered HSV type-specific serologic testing.

Herpes Zoster

Zoster, also called shingles, represents a reactivation of the varicella-zoster virus, which causes a diffuse vesicular rash ("chickenpox") when a patient is first infected and remains latent in sensory ganglia roots, often reactivating in the context of immunosuppression or advancing age [15]. Zoster appears in a dermatomal distribution, rarely on the vulva, as vesicular lesions that break to form a crust (Fig. 7.2) [5]. Patients may report prodromal symptoms of pain or burning before lesions appear.

The diagnosis is usually clinically apparent; however, if necessary, PCR can be performed from lesion scrapings [16]. Direct fluorescent antibody (DFA) testing can also be performed from lesion scrapings, with rapid results but less sensitivity than PCR. Serology is less helpful, as IgM may represent a primary infection, reinfection, or reactivation [15].

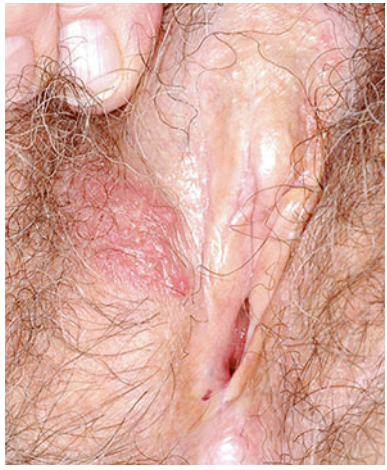

FIG. 7.2 Vulvar herpes zoster (Reprinted from Danby and Margesson [5], with permission of John Wiley & Sons, Inc.)

Recommended treatments, which should be initiated within 72 h of symptom onset, are (1) acyclovir 800 mg PO five times daily for 7–10 days, (2) famciclovir 500 mg PO three times daily for 7 days, or (3) valacyclovir 1000 mg three times daily for 7 days [15].

Patients with zoster, particularly those over age 50, are at risk of developing post-herpetic neuralgia. Antiviral medications reduce the risk of post-herpetic neuralgia, but additional medications may further mediate this risk and reduce pain [15]. Patients should be assessed for contraindications to any of these medications before they are started. Gabapentin 300 mg PO at bedtime or 100–300 mg PO every 8 h can be added and uptitrated to a total dose of 3600 mg per day; the major side effect is sedation. Tricyclic antidepressants such as nortriptyline can be initiated at a dose of 25 mg PO at bedtime and uptitrated by 25 mg every 2–3 days to a daily maximum of 150 mg. Tricyclic antidepressants are associated with sedation, constipation, dry mouth, and urinary retention; a starting dose of 10 mg can be considered in elderly patients. A course of oral prednisone may also

address pain; a recommended regimen is 60 mg PO daily for 7 days and then tapered.

Syphilis

Syphilis is a sexually transmitted infection caused by *Treponema pallidum*, a spirochete (spiral-shaped bacterium). The primary phase is usually characterized by a single painless ulcer (chancre) of the mouth, anus, cervix, or labia, accompanied by nontender lymphadenopathy [17]. The second stage of syphilis, which may overlap with the first, consists of a skin rash (often on the feet and hands), large raised lesions in the mouth, underarm, or groin called condyloma lata, fever, lymphadenopathy, pharyngitis, or myalgias [18]. Involvement of the central nervous system ("neurosyphilis") can occur at any stage. Syphilis is termed "latent" when a patient presents without symptoms but has positive serologic testing; early latent is defined as latency of less than 1 year. One-third of untreated cases will progress to involvement of the cardiovascular system and/or development of granulomatous lesions of any organ system, though the skin, skeletal system, and liver are the most common sites [17, 18].

Congenital syphilis is increasingly uncommon due to prenatal screening; however this should also be considered in infants presenting low birth weight, jaundice, anemia, and hepatosplenomegaly [19]. With regard to genital dermatologic findings, infants with congenital syphilis may present with papules and deep fissures in the perianal region. Infants may also have diffuse red papulo-squamous rashes, particular on the buttocks, palms, and soles, which may develop into bullae. The infant and mother should have serologic screening if congenital syphilis is suspected.

The definitive method of diagnosis for syphilis is darkfield examination and/or PCR of lesion material, which may not be available in all settings [18]. Serologic screening for syphilis typically begins with nontreponemal testing: rapid plasma reagin (RPR) or venereal disease research laboratory

(VDRL) [17]. These tests may result in false positives in patients with HIV, autoimmune disease, intravenous drug use, pregnancy, and older age [18].

Positive nontreponemal testing is confirmed with enzyme immunoassays or more specific treponemal testing with a fluorescent treponemal antibody–absorbed (FTA-ABS) test or the *T. pallidum* particle agglutination (TP-PA) test. Conversely, some centers have begun screening with treponemal tests, which, if positive, should be confirmed with a nontreponemal test. Of note, both treponemal and nontreponemal tests may not be reactive in early primary infection.

Examination of CSF is recommended in any patients with neurologic or ocular symptoms, for the diagnosis of neurosyphilis. Patients with confirmed syphilis should be tested for HIV.

Consider medicine or infectious disease consultation for management of syphilis treatment. Primary, secondary and early latent syphilis should be treated with one dose of benzathine penicillin G 2.4 million units intramuscularly (IM). Alternatives for penicillin allergies are (1) doxycycline 100 mg PO twice daily for 14 days, (2) tetracycline 500 mg PO four times daily for 14 days, and (3) ceftriaxone 1–2 g IM or IV daily for 10–14 days, though data is more limited for this last option [4]. Pregnant women must be treated with penicillin, even if desensitization is needed for penicillin allergy. Patients require serologic follow-up; nontreponemal titers are expected to fall fourfold in 6–12 months.

Infants and children diagnosed with syphilis should be managed by pediatric infectious disease specialists and should be evaluated for sexual abuse [4]. In children, primary, secondary, or early latent syphilis of less than 1 year is treated with benzathine penicillin 50,000 units/kg IM in a single dose (maximum 2.4 million units) [4]. In pediatric patients, latent syphilis of greater than 1 year or of unknown duration is treated with benzathine penicillin 50,000 units/kg IM for three doses at 1 week intervals (maximum total 7.2 million units). The management of more advanced syphilis—latent

and tertiary (neurosyphilis)—in children and adults will not be covered here.

Sexual partners are thought to be exposed only if the infected patient has mucocutaneous lesions, however partners exposed at any stage should be evaluated [4]. Sexual partners exposed within 3 months of the patient's diagnosis of primary, secondary, or early latent syphilis or late latent syphilis with high nontreponemal titers (>1:32) should be treated for presumed early syphilis even if serologies are negative. Partners exposed more than 90 days before the patient's diagnosis of primary, secondary, or early latent syphilis should be tested or simply treated if testing is not available. Long-term partners of patients with late latent syphilis should be tested and treated accordingly.

Chancroid

Chancroid is a sexually transmitted infection caused by *Haemophilus ducreyi*, a gram-negative bacterium [20]. It is more common in developing countries and in males. Patients may present with significant, painful lymphadenopathy, which become fluctuant, called buboes [1]. Sharply delineated painful ulcers develop, with little surrounding erythema; multiple small ulcers may coalesce into a single large ulcer. The annual incidence rate in the United States has been falling over time; only four cases were reported in the United States in 2013 [21].

An accurate diagnosis of chancroid relies on culture of *H. ducreyi* from the lesion. In addition, aspiration and culture of suppurative lymph nodes should be considered. Since the organism can be difficult to grow, the use of selective and supplemented media is necessary [20]. PCR can also be used and is more sensitive, but is not widely available [22]. For therapeutic purposes, large fluctuant buboes can be aspirated or incised and packed for symptomatic relief [23].

The Centers for Disease Control and Prevention (CDC) recommend four possible regimens: (1) azithromycin (1 g

PO in a single dose), (2) ceftriaxone (250 mg IM in one dose), (3) ciprofloxacin (500 mg PO every 12 h for 3 days), or (4) erythromycin base (500 mg PO every 8 h for 7 days) [4]. Ciprofloxacin should not be used in pregnancy. Children weighing less than 45 kg should be treated with (1) ceftriaxone (50 mg/kg IM up to 250 mg) in a single dose or (2) azithromycin (20 mg/kg PO up to 1 g) in a single dose [13]. Erythromycin is an alternative option; ciprofloxacin is not approved by the US Food and Drug Administration for people younger than 18 years of age.

Patients should be seen within a week to ensure symptom improvement, though complete healing of the ulcer may take longer. If symptoms have not improved, consider coinfection with another sexually transmitted infection or HIV, nonadherence with treatment, or bacterial resistance [4]. Sexual partners should be treated if they had contact with a patient infected with chancroid within the 10 days before the patient developed symptoms [4].

Granuloma Inguinale

Granuloma inguinale, also called donovanosis, is caused by the gram-negative bacterium *Klebsiella granulomatis* [4]. Occurring rarely in the United States, infections are most commonly identified in Papua New Guinea, parts of southern Africa, India, French Guyana, Brazil, and Australia [24].

Genital and perineal ulcers are slowly progressive, painless, and highly vascular, without associated lymphadenopathy ("pseudobuboes"); subcutaneous granulomas may be present. Extensive fibrosis can result in adhesions and sinus tracts [13]. The infection can extend into the pelvis, with dissemination to the intraabdominal organs, bones, or mouth.

K. granulomatis is difficult to culture [4]. The diagnosis can be made by visualization of dark-staining Donovan bodies on tissue crush preparation or histologic examination of biopsy specimens [4]. No FDA-cleared molecular tests for the detec-

tion of *K. granulomatis* DNA exist. *Haemophilus ducreyi* cultures should be obtained to exclude chancroid.

First-line treatment is azithromycin, 1 g orally once per week or 500 mg daily for at least 3 weeks and until all lesions have completely healed [1, 4]. Alternatives include the following, all for 3 weeks or until lesions have completely healed: (1) doxycycline (100 mg PO every 12 h), (2) ciprofloxacin (750 mg PO every 12 h), (3) erythromycin base (500 mg PO every 6 h), or (4) trimethoprim-sulfamethoxazole (one double-strength tablet (160/800 mg) PO every 12 h) [4]. Erythromycin and azithromycin are the first-line treatment in pregnancy. Children less than 45 kg can receive azithromycin (20 mg/kg PO in a single dose, maximum 1 g). Of note, doxycycline is not approved for children less than 8 years [13]. Gentamicin can be added to adult and pediatric regimens if improvements are not noted within the first few days of treatment.

The utility of empiric partner treatment in the absence of symptoms is unclear. Individuals who had sexual contact within 60 days of a patient's onset of symptoms should be examined [4].

Lymphogranuloma Venereum (LGV)

LGV is caused by *Chlamydia trachomatis* serotypes L1, L2, and L3 [25]. Once rare, LGV is becoming more common internationally and often coincides with HIV infection [26]. Patients most often present with an ulcer at the inoculation site. Patients subsequently develop tender lymphadenopathy, which may become fluctuant, called buboes [4]. Anal exposures, if untreated, can result in fistulas or strictures resembling inflammatory bowel disease [13].

Swabs of ulcerations or aspirates of inguinal buboes can be tested for *C. trachomatis*, using culture, direct immunofluorescence, or nucleic acid amplification testing. PCR, which is not widely available for this purpose, can differentiate LGV from non-LGV *C. trachomatis*. Serology can also be sent;

complement fixation titers above 1:64 are suggestive of infection with LGV [4].

Large and/or painful inguinal buboes might require aspiration through intact skin or incision and drainage. Aspiration or drainage may prevent the formation of inguinal/femoral ulcerations. Treatment with doxycycline (100 mg PO every 12 h for 21 days) is preferred. Alternatively, erythromycin base (500 mg PO every 6 h for 21 days) can be used [4]. Based on limited data, azithromycin (1 g orally once weekly for 3 weeks) is likely effective. Doxycycline should be avoided in pregnancy. Pediatric patients over 8 years of age should be treated with doxycycline (200 mg/day in two divided daily doses) for 21 days. As an alternative, erythromycin 50 mg/kg/day divided into four doses per day (up to 500 mg per dose) for 21 days can be used [13].

Individuals who had sexual contact within 60 days of a patient's onset of symptoms should be tested for chlamydia and presumptively treated with azithromycin (1 g PO in a single dose) or doxycycline (100 mg orally twice a day for 7 days) [4].

Candida

Vulvovaginal candidiasis, most commonly caused by *Candida albicans*, is associated with pruritis, dysuria, dyspareunia, and/or thick, white vaginal discharge. Patients may also present with swelling, erythema, vulvar fissures, and excoriations (Fig. 7.3) [5, 27]. Red plaques may be present within skin folds, with satellite lesions; pustules may form erosions [2].

Risk factors for vulvovaginal candidiasis include systemic antibiotic or steroid use, immunosuppression, and diabetes mellitus. A microscope slide of the patient's vaginal discharge prepared with saline and 10 % potassium hydroxide may reveal candida buds and hyphae and provide a rapid diagnosis; a vaginal culture can also be collected. Initial treatment of uncomplicated vulvovaginal candida entails fluconazole 150 mg PO in a single dose; patients may require another dose in 72 h if they continue to have symptoms.

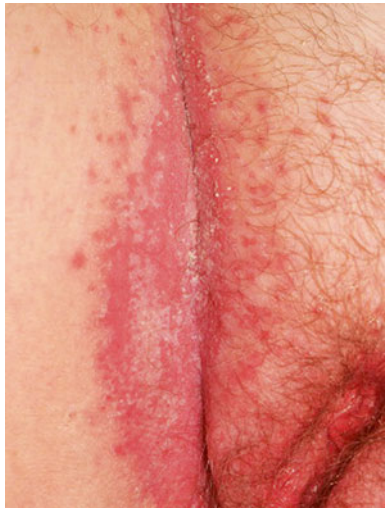

Fig. 7.3 Candida infection of the vulva (Reprinted from Pipkin [3], with permission from Elsevier)

Topical and intravaginal azoles are also acceptable and are available over the counter. Concomitant dermatitis may require short-term medium potency topical steroids. Combined topical antifungal and steroid preparations are available, such as a cream combining clotrimazole and betamethasone dipropionate (Lotrisone®, Merck, Whitehouse Station, NJ).

Folliculitis/Impetigo

Folliculitis can occur on the vulva or mons, particularly with hair removal techniques. These may be infected, developing into a superficial infection called impetigo, often caused by *Staphylococcus aureus* or *Streptococcus pyogenes* [3]. Yellow crusts and/or bullae may be present. Treatment is topical mupirocin 2 % ointment or an oral antibiotic with adequate skin flora coverage, such as cephalexin [3].

Group A β-Hemolytic Streptococcus

Group A β-hemolytic streptococcus vaginitis is more common in children than adults; it is associated with a red vaginal and/or perineal rash with or without fissures or purulent discharge. Vaginal culture is needed for diagnosis, and treatment is with penicillin VK (500 mg PO four times daily for 10–14 days) or clindamycin cream (2 % per vagina for 7–10 days) [5].

Scabies

Scabies are mites transmitted by skin-to-skin contact. Lesions are most often present on the hands, particularly between the fingers, and at the elbow but can also be present on the vulva or buttocks [28]. Classic scabies lesions are raised tracts in which the parasites burrow [29]. Patients can also present with blisters, nodules, or excoriations, rarely with lymphadenopathy. Diagnosis is most commonly made by biopsy or scraping, to assess for eggs. Treatment is permethrin cream (5 %) applied once from the neck down and removed 8 h later. Close contacts are generally counseled for treatment, and bedding and clothing should be washed in hot water [29].

Noninfectious

Allergic or Irritant Contact Dermatitis

Contact dermatitis can result in severe vulvar pruritis; fissures and lichenification can result from scratching. More severe reactions may present with vesicles and bullae, which may result in erosions (Fig. 7.4) [3]. Irritant contact dermatitis develops with exposure, while allergic contact dermatitis can occur at an interval after exposure [30]. Common irritants are related to hygiene, including sweat, urine, soaps and detergents, excessive bathing including douches, hair removal

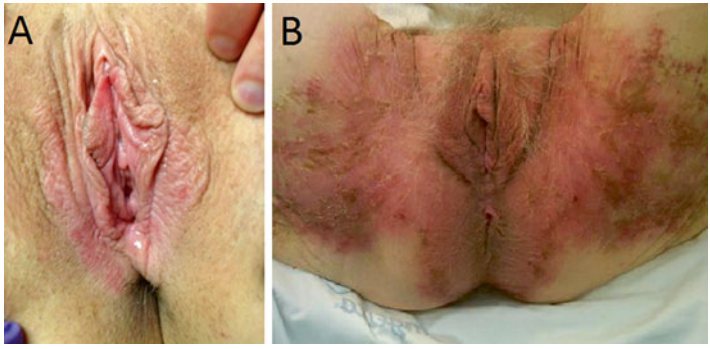

Fig. 7.4 Irritant dermatitis. (**a**) Irritant dermatitis from Dial soap. (**b**) Irritant dermatitis from urinary incontinence with candidal superinfection (Photos courtesy of Natasha R. Johnson, MD)

(shaving, waxing, chemicals), baby wipes, and sanitary pads. Condoms (latex), spermicide, and sperm are also contact irritants [30].

A full history may reveal a possible contact irritant. On physical exam, the dermatitis will be in the distribution of the exposure, though contact dermatitis may coincide with other dermatoses or infections. Excoriations may be seen. Patients should also be assessed for concomitant bacterial or fungal infections. Genital culture for yeast should be performed. Biopsy should be considered for ulcerative lesions to rule out dermatoses. The goal of therapy is to identify the contact irritant and eliminate it. If the contact irritant is difficult to identify, the patient can be referred for patch testing.

Patients should be educated to wear loose-fitting, cotton clothing, avoid use of soap on the vulva, and eliminate douching. Assess hygienic practices and inquire about incontinence of urine and feces, which are irritants. Petrolatum can be applied as a barrier over particularly irritated or ulcerated skin [32]. Patients with erosions or ulcerations should perform sitz baths (sitting in warm water for 5–10 min), twice per day until lesions improve. Patients can use antihistamines to alleviate itching, including loratadine during the day and/or hydroxyzine, a sedating antihistamine, in the evening.

Depending on the severity of the lesions, patients may require topical corticosteroids [32]. For mild irritation, hydrocortisone 2.5 % ointment applied twice each day may be sufficient. Moderate irritation can be treated with triamcinolone acetonide 0.1 % ointment, while high-potency topical steroids may be required for severe dermatitis (clobetasol propionate ointment 0.05 %). Topical steroids should be used twice daily until lesions have resolved. Patients may require oral steroids for severe dermatitis.

Atrophic Vaginitis

In postmenopausal women, the vaginal mucosa becomes thin and dry and increasingly sensitive to irritants, trauma, and bacterial overgrowth. In severely atrophic vaginitis, purulent discharge and fissures of the vulva and vestibule may develop. Vaginal estrogen creams, tablets, and an estradiol vaginal ring are equally effective in treating vulvovaginal atrophy [34].

Lichen Planus

Lichen planus is an uncommon inflammatory condition of the skin, nails, and genitals [35]. The classic mucosal involvement is Wickham striae—reticulate white striations—most often found on the buccal mucosa [35]. Erosive lesions can also appear in the mouth [36]. Up to one-quarter of patients with lichen planus have genital involvement. Lichen planus is characterized by pruritic purple papules of the vulva; erosive lichen planus is associated with deep painful, friable erosions leading to burning, dyspareunia, and vaginal discharge (Fig. 7.5) [37]. Cases involving the vulva and vagina are most commonly erosive, leading to painful desquamation and ulceration, frequently resulting in scarring and destruction of architecture [38].

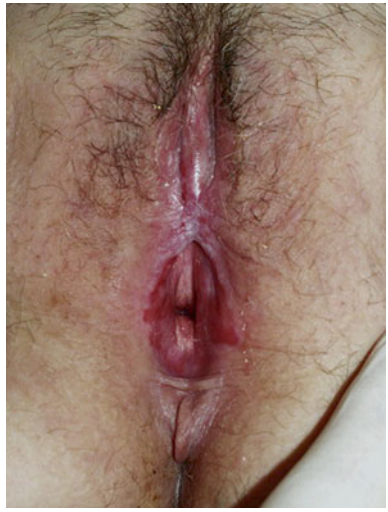

FIG. 7.5 Vulvovaginal lichen planus (Reprinted from Pipkin [3], with permission from Elsevier)

Nonerosive lichen planus is likely to be controlled with high-potency topical corticosteroids and emollients, such as Vaseline® (Unilever, London, England). Treatment can be started with betamethasone valerate 0.1 % ointment twice per day for 6 weeks and then as needed [39]. Erosive vulvar lichen planus is more resistant to treatment; clobetasol propionate 0.05 % ointment can be used daily for 3 months, after which steroid strength and frequency are decreased. Topical steroids are first-line treatment, after which topical tacrolimus, systemic steroids, tacrolimus, cyclosporine, or other immunosuppressants may be considered [38, 39].

When vaginal disease is present, steroid suppositories, such as hydrocortisone acetate 25 mg suppositories twice per day for 2 months, can be used [40]. As with vulvar disease, steroid frequency can be tapered to maintenance usage (once or twice weekly) once improvement has be achieved. Patients with vaginal erosions are at risk for synechiae and vaginal narrowing; use of vaginal dilators with steroid therapy can be considered to maintain vaginal patency [40].

Women with erosive vulvovaginal lichen planus are at increased risk of vulvar squamous cell carcinoma (estimated at 2.4 %) and warrant regular clinical exams [41].

Lichen Sclerosis

Lichen sclerosis is a chronic inflammatory destructive condition of the perineal and perianal skin. The incidence of lichen sclerosis is bimodal, occurring most commonly in prepubertal girls or postmenopausal women [42]. The most common presenting complaint in vulvar pruritis; patients may also report dyspareunia or dysuria. The vagina is spared—unlike in lichen planus—though women may have narrowing of the vaginal introitus. Exam will often reveal vulvar skin that is thin and whitened (white crinkling or "cigarette paper"), often in a "figure of eight" shape around the vaginal introitus and anus, with loss of architecture of the labia minora and phimosis of the clitoral hood to the glans (Fig. 7.6) [38, 43].

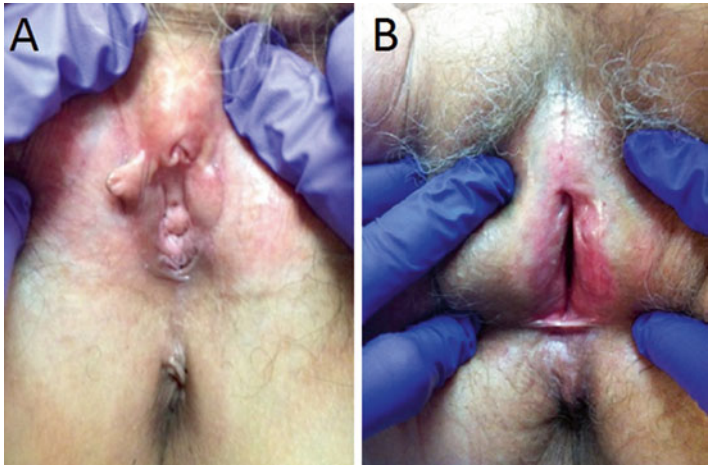

FIG. 7.6 Lichen sclerosis. (**a**) Mild to moderate lichen sclerosis, associated with loss of architecture of the labia minora. (**b**) Severe lichen sclerosis, with loss of labia minora and phimosis of the clitoral hood (Photos courtesy of Natasha R. Johnson, MD)

Patients may also have vulvar fissures or erosions, particularly due to scratching.

Biopsy is recommended in postpubertal women to rule out other causes of pruritis and erosions. Otherwise, diagnosis is clinical. Lichen sclerosis is most often managed with high-potency topical corticosteroids, such as clobetasol propionate 0.05 % ointment one to two times per day for 4–6 weeks, after which frequency can be weaned to maintenance (once or twice weekly) [39, 42]. Patients may require increased frequency of clobetasol for flares.

Approximately 2–5 % of women with lichen sclerosis develop vulvar squamous cell carcinoma and warrant regular clinical exams [39].

Desquamative Inflammatory Vaginitis (DIV)

DIV is a painful vaginitis not associated with infection. Patients report burning, discharge, and dyspareunia. On physical examination, primarily the vagina is involved, though the vestibule can be affected, with erythema and fissures [5]. Microscopic examination of the vaginal discharge reveals parabasal cells (round cells not usually present on microscopy) and increased white blood cells (>10 per high-power field). Treatment is with hydrocortisone acetate suppositories (3–5 g at night for 14 days then tapered) or intravaginal clindamycin (2 % cream vaginally for 2–4 weeks).

Postviral and Lipschutz Ulcers

Genital ulcerations have been noted after infections with cytomegalovirus, influenza A, and Epstein-Barr Virus [44, 45]. These ulcerations are likely often classified as idiopathic, when patients are not tested for viral triggers. EBV is most commonly associated with genital ulcerations, likely through direct cytotoxicity in vulvar epithelium as well as triggering an immunologic response that manifests as vulvar ulcers [44]. CMV and EBV-related ulcers often have more

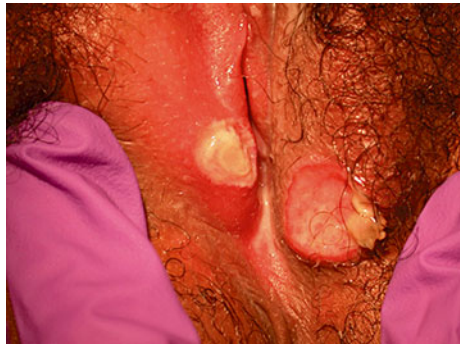

Fig. 7.7 Lipschutz ulcers (Reprinted from Huppert [46], with permission of John Wiley & Sons, Inc.)

marked prodromal symptoms than Lipschutz (idiopathic) ulcers.

Lipschutz ulcers, also called ulcus vulvae acutum or reactive nonsexually related acute genital ulcers, are vulvar ulcerations without other identifiable etiology, often occurring in young, virginal patients (Fig. 7.7) [47]. The lesions are well demarcated, with raised edges, often with a gray or white base. These lesions can sometimes be red-black and develop eschars [44]. Lesions vary in size. They are usually, though not exclusively, located on the interior labia minora, often on opposing surfaces (called "kissing ulcers") [44]. These are often preceded by prodromal symptoms of fever and malaise.

In general, biopsies are not helpful. A targeted infectious workup can be conducted; serologic testing for EBV is indicated if postviral genital ulcers are suspected. CMV is less strongly associated with genital ulcers. EBV can be tested by viral culture or PCR from the ulcer base or by EBV serology [48]. Testing for influenza can also be performed, depending on a clinician's index of suspicion. Depending on patient age and sexual activity (or concern for sexual abuse in a pediatric patient), testing an ulcer for HSV is reasonable.

Consider a Foley catheter for urinary diversion, and 2 % lidocaine jelly for topical analgesia. The utility of steroids is

unclear, though some expert opinions recommend a trial of topical corticosteroids, such as clobetasol 0.05 % ointment 0.05 % every 12 h for 7–10 days [46, 49]. Oral corticosteroids are reserved for refractory cases. Up to 30 % of women may have superinfection of their vulvar ulcers; assess for purulence or overlying erythema and treat with a broad-spectrum antibiotic such as a cephalosporin or sulfonamide to address skin flora [46].

Hidradenitis Suppurativa

Hidradenitis suppurativa is a chronic inflammatory skin disorder of the skin in the axillary, inguinal, and genital regions, characterized by recurrent tender nodules and abscesses that progress to draining sinuses, resulting in raised, firm, and discolored scars [50, 51]. Lesions may also involve the breasts and buttocks. Highest incidence appears to be in women in their 20s, though it has been described in prepubertal and postmenopausal women; in women, lesions often occur premenstrually [31, 51]. Risk factors include family history, smoking, and obesity [50, 51].

Diagnosis is usually made based on a history of recurrent abscesses in the axilla and/or groin with scarring [51]. Biopsies and bacterial cultures are reserved for severe and refractory cases. Localized lesions can be treated with topical clindamycin (10 mg per milliliter (mL) two times per day for 3 months) or triamcinolone (2–5 mg injected into lesions) [51]. For more advanced disease, systemic tetracycline (500 mg PO every 12 h for 3 months), erythromycin (500 mg PO every 12 h), doxycycline (100 mg PO every 12 h), or minocycline (100 mg PO every 12 h), clindamycin, and rifampin (300 mg PO every 12 h, each, for 10 weeks) have also been used [33, 52, 53]. Small series of patients treated with medications with antiandrogenic properties have reported success, including management with combined oral contraceptive pills containing ethinyl estradiol 50 micrograms (μg)/norgestrel 500 μg [54]. In severe cases, isotretinoin or systemic immunosuppression or surgical excision of sinus tracts may

be required; laser therapy has also been used. All patients should be counseled for weight loss and smoking cessation.

Inflammatory Bowel Disease

Inflammatory bowel disease (IBD)—Crohn's disease in particular—is associated with vulvar manifestations. Crohn's disease is a chronic inflammatory disease that primarily affects the gastrointestinal tract, and many involve any section along its length [47]. The perianal region may be directly affected, with sinus or fistulous tracts or ulcerations; mucocutaneous lesions (often resembling aphthous ulcers) occur in up to 75 % of patients [55]. Crohn's disease is also associated with vertical linear fissures (called "knife-cut" ulcers) which may precede diagnosis of the IBD (Fig. 7.8) [5, 56]. The etiology of these ulcerations is unclear; proposed mechanisms include deposits of antigens or immune complexes in the skin or immune system cross-reactivity.

If the lesions are determined to be part of a syndrome of IBD, treatment should be targeted at the underlying illness, usually through immunosuppressive medications. Consultation with gastrointestinal specialists (or the patient's own specialist) is advisable. Topical steroids and

Fig. 7.8 Fissure of the gluteal cleft associated with Crohn's disease (Reprinted from Leu et al. [49], Figure 7.2, with kind permission from Springer Science and Business Media)

tacrolimus have been noted to be helpful in treating perineal disease. Oral metronidazole has also been shown to be helpful as well [5].

Pyoderma Gangrenosum

A destructive sterile inflammatory skin condition, pyoderma gangrenosum (PG) can present with bullae, erosions, and ulcerations with discharge (Fig. 7.9) [57, 58]. Lesions can appear anywhere on the body; vulvar PG is more common in pediatric patients. The ulcers are rapidly progressive and raised with necrotic bases, with up to 2 cm of surrounding erythema; the lesions are often instigated by trauma [47]. Ulcers may coalesce into a larger erosion. These lesions have been described in all age groups.

PG is associated with underlying illness in 50 % of patients, including inflammatory bowel disease, primary biliary cirrhosis, hematologic or other malignancies, Wegener's granulomatosis, and systemic lupus erythematosus [59].

Biopsy is usually required for diagnosis. Proposed diagnostic criteria include rapid progression of a painful ulcer

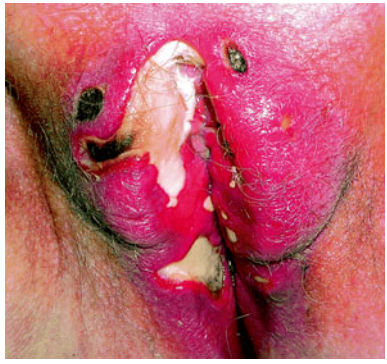

Fig. 7.9 Vulvar pyoderma gangrenosum (Reprinted from Sau and Hill [57], with permission of John Wiley & Sons, Inc., and the Royal College of Obstetricians and Gynaecologists)

with an irregular, violaceous border, for which other causes of ulceration have been ruled out. In addition, two minor criteria are required: (1) pathergy, meaning the lesion was instigated by trauma, or cribriform scarring, (2) a systemic disease associated with PG, (3) specific histopathologic changes, and (4) rapid response to steroid treatment [60]. Patients should have a full workup for underlying conditions, including but not limited to a complete blood count, complete metabolic panel, hepatitis testing, serologic assessment for autoimmune disease and hypercoagulability, and serum and urine immunoelectrophoresis; consider assessment by gastroenterology for IBD if no other source is identified [47, 59].

Once other causes of ulceration have been ruled out, limited disease can be managed with topical steroids, such as clobetasol 0.05 % ointment or cream [61]. Full lesion healing can take 1–2 months. Application of topical tacrolimus—a calcineurin inhibitor that is immunosuppressive—as a 0.1 % ointment applied twice daily over several months, has also been described for limited, local disease [62]. Severe disease may necessitate systemic immunosuppression; consider dermatology consultation in these cases; more aggressive treatment modalities include systemic corticosteroids, dapsone, tumor necrosis factor (TNF) inhibitors, and cyclosporine [47]. Small case series also suggest that gentle sharp debridement and wound reconstruction may encourage healing [57, 63].

Blistering Diseases

A variety of rare blistering diseases can involve the vulvovaginal region, including but not limited to Stevens-Johnson syndrome, toxic epidermal necrolysis, mucous membrane pemphigoid, and pemphigus vulgaris [64]. These patients require multidisciplinary management, and gynecology is usually involved after the diagnosis is made, often by biopsy, for assessment of the vulvovaginal region. These patients often receive systemic immunomodulatory therapies, which will not be covered here, and the role of the gynecologist is to recommend any therapies specific to the vulvovaginal region.

Stevens-Johnson syndrome (SJS) and **toxic epidermal necrolysis (TEN)** are severe necrotizing mucocutaneous reactions, most often occurring in response to medications, though infections such as *Mycoplasma pneumoniae* can be triggers [65]. SJS and TEN are on a continuum with one another, in which TEN affects more body surface area (>30 %).

Erythema multiforme is an immune-mediated condition involving target-like skin lesions, with or without central disruption (vesicles, blistering, or ulceration), with mucosal involvement typically only with the more severe versions [66]. Onset is usually between ages 20 and 40 years. The majority of cases are triggered by infections, namely, HSV; other identified causes include but are not limited to medications, autoimmune disease, and malignancy [67]. Patients with vulvovaginal involvement of erythema multiforme may have pigment changes, but scarring and stenosis may be less common than in SJS and TEN [68].

Mucous membrane pemphigoid (also called cicatricial pemphigoid) is an autoimmune condition characterized by subepithelial blisters leading to painful erosive lesions in mucosal membranes; age of onset is commonly after age 60 years, though it may also appear in children [69]. Lesions occur most often in the mouth, though the nose, upper respiratory tract and esophagus, vagina, and anus can also be involved.

Bullous pemphigoid is the most common autoimmune subepidermal blistering disease; most cases are sporadic, but some have been associated with UV light, radiation, and medications such as furosemide and various antibiotics [3, 70]. Tense bullous lesions form, often preceded by eczematous or urticarial skin. Mean age of onset is over 60 years. Vulvar involvement is more common in children and can occur in isolation [71].

Linear IgA disease is a rare autoimmune disease in which IgA is deposited along the cutaneous basement membrane; it affects adults over 60 years and children under 5 years [3, 72]. Genital involvement is more common in children. Oral

ulcers are often also present. Lesions may present as pruritic vesicles and bullae in groups or as an urticarial plaque with vesicles at the periphery [3].

Pemphigus vulgaris is an autoimmune intraepidermal blistering disease that usually presents after age 60 years, though it may appear in children [72]. Lesions are classically large flaccid blisters of the mucosal surfaces and skin, usually first appearing in the oral cavity and quickly progressing to painful ulcerations. The Nikolsky's sign should be present, in which epidermal detachment occurs when pressure is applied. Vulvovaginal lesions are reported in up to one-half of cases, most commonly involving the distal one-third of the vagina; cervical involvement has also been reported, which may be mistaken for cervical dysplasia on Papanicolaou smears [73–75]. Genital lesions are thought to occur after involvement of other sites, and patients diagnosed with this condition should have genital exams as genital lesions may be unrecognized [76].

Paraneoplastic pemphigus is an autoimmune syndrome similar to these other blistering diseases, occurring in response to a systemic neoplasm, such as lymphoma or leukemia [3].

Vulvovaginal lesions in patients with these blistering diseases are likely manifestations of the disease, though superinfection in the setting of immunosuppression or malignancy should be considered. Any blistering diseases involving the vaginal mucosa may result in vaginal stenosis or agglutination, putting patients at risk for developing chronic pain, sexual dysfunction, dyspareunia, and obstruction of urinary or menstrual flow [77]. Patients with a history of vulvovaginal SJS and TEN are also at risk for developing vulvovaginal adenosis—the presence of ectopic endometrial or cervical glandular epithelium—which has been associated with cellular atypia, squamous cell carcinoma, and adenocarcinoma [78, 79].

A useful set of management guidelines have been outlined for vulvovaginal SJS and TEN, but are applicable to these other conditions. Prevention of adhesion formation and agglutination after desquamating lesions broadly involves

intravaginal glucocorticoids and menstrual suppression [80]. Specifically for SJS and TEN, a regimen of betamethasone valerate 0.1 % cream applied every 12 h to the vulva externally and betamethasone valerate 0.1 % ointment every 12 h to the internal vaginal mucosa via dilators is advisable, to maintain vaginal patency, if appropriate given the patient's age and history of sexual activity [77]. If the patient is not on systemic antifungal therapy, topical antifungal creams can be considered because intravaginal steroids can predispose to fungal infections.

Less Common Causes of Vulvar Lesions

Vulvar malignancy: The most common vulvar malignancy is squamous cell carcinoma, which is most often related to human papilloma virus infections in women younger than 55 years. Rates of vulvar cancer are also increased in women with immunosuppression and lichen sclerosis [81]. Vulvar malignancies usually present with pruritis, though ulcerations and pain can also occur. Any suspicious lesions should be biopsied; vulvar colposcopy can also be considered to guide biopsies. While squamous cell cancers are the most common, vulvar intraepithelial neoplasia (a premalignant condition), basal cell carcinoma, sarcoma, melanoma, and extramammary Paget's disease should also be considered [81]. These diagnoses can be clarified by biopsy. Patients with vulvar dysplasia or malignancy should be referred to a gynecologic oncologist.

Behçet's syndrome: Behçet's syndrome is a vasculitis causing relapsing oral and genital ulcers and uveitis; other symptoms include skin lesions such as erythema nodosum and thrombophlebitis [82]. The prevalence of Behçet's syndrome ranges from 1:10,000 in Japan to 1:500,000 in North America and Europe. It rarely presents before puberty or after age 50. Genital lesions are commonly round and well demarcated. Approximately 60 % of genital ulcers from Behçet's syndrome result in scarring, which may be visible on physical exam [83].

Periodic fever, aphthous stomatitis, pharyngitis, and cervical adenitis (PFAPA) syndrome: PFAPA appears in children, before age 5, and consists of recurrent fevers lasting less than a week, aphthous ulcers, pharyngitis, and cervical adenitis without concomitant signs of infection [84]. This is a diagnosis of exclusion [84].

Tuberculosis is a very rare cause of vulvar lesions or ulcers, but which may be suspected based on a patient's travel and exposures. Cutaneous tuberculosis ulcers may begin as papules and develop into painful ulcers, with a pseudomembrane [47, 85]. Biopsy or PCR can be performed for diagnosis.

For the diagnosis and management of vulvar psoriasis, please see Chap. 11, Vulvovaginitis and Vaginal Bleeding in Pediatric and Adolescent Patients.

Perineal Masses

Bartholin's gland cysts are collections in the Bartholin's glands or ducts, which exit the vestibule at 4:00 and 8:00. These glands are most likely to become obstructed in reproductive age women, and patients present with enlarged, fluctuant masses under the gland exits (Fig. 7.10). Asymptomatic gland cysts do not require intervention. Painful and erythematous gland enlargements may be superinfected, which are usually polymicrobial infections; gland abscesses should be drained.

Patients with symptomatic Bartholin's gland cysts or suspected abscesses can be managed with incision and drainage *inside* the vaginal introitus—not through the labia—preferably with insertion of a Word catheter (a small latex catheter with a terminal balloon holding a few milliliters.) The catheters allow continued drainage and should be in place for 4–6 weeks, with the protruding end tucked into the vagina [86]. Patients do not need antibiotics unless the physical exam suggests overlying cellulitis or systemic infection (i.e., leukocytosis and/or fever). Patients with recurrent symptomatic gland cyst or abscess may undergo marsupialization, in which

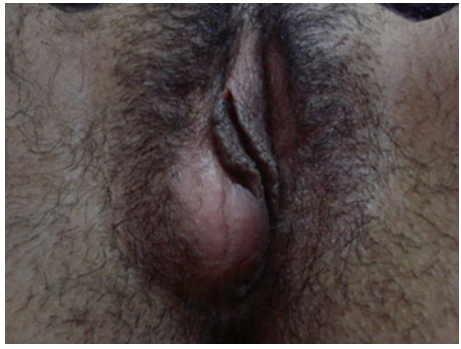

Fig. 7.10 Right Bartholin's gland cyst (Reprinted from Maldonado [86], with permission of Elsevier)

the cyst wall is incised and sutured to the overlying mucosa. In postmenopausal women, Bartholin's gland cysts should be biopsied due to risk of adenocarcinoma.

Skene's glands, also called paraurethral glands, emerge at either side of the urethral meatus and may also become enlarged. A **urethral diverticulum**, which communicates with the urethral lumen, presents in a similar way, though these may be located more proximally than Skene's gland cysts. Ultrasonography, urethrocystoscopy, or MRI can be used to differentiate the two lesions. Skene's gland abscesses can be incised and drained, while urethral diverticula should not be incised and can initially be managed with sitz baths and antibiotics [52]. Persistent, symptomatic urethral diverticula may need to be excised by specialists in female pelvic floor surgery.

Embryologic remnants in the vagina—**müllerian and Gartner (mesonephric) ducts**—can also become cystically enlarged; clinically, the differentiation between the two is unimportant. Symptomatic, enlarged ducts should be imaged with MRI to exclude urethral diverticula and can then be excised [87]. Gartner duct cysts may also be associated with congenital urinary and renal system anomalies.

A **canal of Nuck cyst** is a hernia through the inguinal canal into the labia majora; one-third of these contain bowel [86].

For large symptomatic labial enlargements suspected to be canal of Nuck cyst, an MRI should be obtained to clarify the anatomy; these cysts should be excised by general surgeons. Epidermoid inclusion cysts, which are usually less than 5 mm, occurring on the labia majora at any age, do not usually require intervention [86]. Lipomas, neurofibromas, vulvovaginal endometriosis, and vulvar leiomyomas are less common possibilities as well.

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Chapter 8
Spontaneous Abortions

Paula C. Brady and Katherine D. Pocius

Definitions

Spontaneous Abortion Also known as a miscarriage, or early pregnancy loss, it occurs in pregnancies less than 20 weeks of gestational age. Up to 20 % of clinically recognized pregnancies will end in miscarriage [1]. Approximately 50 % of spontaneous pregnancy losses are due to chromosomal abnormalities [2]. Risk factors for spontaneous abortion include, but are not limited to, maternal age greater than 35 years, antiphospholipid antibody syndrome, congenital uterine anomalies, uncontrolled diabetes or thyroid disease, low body mass index, obesity, smoking, and prior miscarriages [3–6]. In women with three or more prior miscarriages, the risk of miscarriage is greater than 40 % [7].

Early Pregnancy Failure The failure of a pregnancy to continue to develop normally. This term is often used interchangeably

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with the term "missed abortion," which technically means a pregnancy that has been demised and retained for weeks [8]. Given the early and accurate diagnosis of most pregnancy failures, the term "missed abortion" seldom applies anymore. Most early pregnancy criteria are diagnosed by ultrasound findings; see the "Diagnosis" section below.

Threatened Abortion Vaginal bleeding, often light to moderate and without passage of tissue, in a pregnancy prior to 20 weeks of gestation, in a patient with a closed cervix.

Inevitable Abortion Bleeding and cramping in pregnancy prior to 20 weeks of gestation without passage of any products of conception, with an open cervix.

Incomplete Abortion Some but not all products of conception have passed spontaneously, but retained products—usually fragments of the placenta—remain.

Complete Abortion The patient has completely passed all products of conception without any interventions; the cervix is closed.

Septic Abortion An infection of the upper genital tract following any type of abortion [9]. Patients may present with pain, fever, vaginal discharge or bleeding, and uterine tenderness on physical examination. Broad-spectrum antibiotic coverage and expeditious surgical evacuation are crucial, as patients can quickly become severely septic [10].

Molar Pregnancy Nonviable pregnancies occurring in less than 0.1 % of gestations, resulting from abnormal fertilization [11]. Also called hydatidiform moles, molar pregnancies are classified as complete (with no fetal parts) or partial (with fetal parts) [12, 13]. Approximately 20 % of molar pregnancies are complicated by persistent trophoblastic tissue; most cases are nonmetastatic proliferations, though invasive moles and metastases can develop [14, 15]. The risk for persistent trophoblastic disease after a molar pregnancy is significantly higher following a complete molar pregnancy (20 %) as compared to partial molar pregnancy (5 %); risk

factors also include age greater than 40 years, an enlarged uterus, presence of theca lutein cysts, and elevated serum beta-human chorionic gonadotropin (hCG) (over 50,000 milli-international units per milliliter, mIU/mL) [15–17].

When You Get the Call Ask for a full set of vital signs, and request a pelvic ultrasound if one has not already been performed, if the patient is sufficiently stable.

When You Arrive Review the patient's vital signs in detail to assess for evidence of septic physiology or anemia, including tachycardia and hypotension. For immediate management of sepsis, please see Chap. 1, Acute Pelvic Pain, and, for hemorrhage, see Chap. 2, Vaginal Hemorrhage. If possible, review the medical record to verify whether an intrauterine pregnancy has been confirmed in this patient prior to her presentation.

History

Ask the patient for the date of her last menstrual period and whether she has had any bleeding or complications during this pregnancy prior to her current presentation. Review whether an intrauterine pregnancy had been confirmed prior to her presentation. Ask the patient to describe the onset and severity of her symptoms; if she is bleeding, inquire how often she is changing her pads. A patient report of soaking two maxi pads per hour for 2 h is a rough estimate of excessive bleeding. Ask about associated symptoms, including fever. If the patient had already been diagnosed with a spontaneous abortion prior to her current presentation, review when and how the diagnosis was made and whether she received any treatment or interventions.

Review the patient's obstetrical history in detail, including prior deliveries, ectopic pregnancies, or miscarriages. The patient's medical history should be reviewed, including hypertension and asthma (both of which limit the use of some uterotonic medications), bleeding diathesis and use of anticoagulant medications, as well as her surgical history.

Physical Examination

An abdominal examination should be performed to assess the patient's tenderness, noting the presence of peritoneal signs, including rebound (pain with abdominal pressure is quickly withdrawn) or involuntary guarding. While women having a miscarriage may have uterine cramping, acute abdominal tenderness may indicate another process, such as infection or blood in the peritoneal cavity.

A speculum exam should be performed to assess the amount of vaginal bleeding; wall suction, available in most emergency room examination areas, may be helpful in patients with copious bleeding. Any products of conception visualized at the cervical os should be removed with a ring forceps and sent to pathology for confirmation. Of note, if the tissue cannot be easily extracted, abort efforts to remove it; this tissue could represent a cervical implantation or abnormally adherent placental tissue, and extraction could lead to severe hemorrhage. A bimanual exam should be performed to assess whether the cervix is open (indicating spontaneous or inevitable abortion).

Diagnosis

The diagnosis of a spontaneous abortion is made using a combination of the patient's history, physical examination, and imaging. All pregnant patients with vaginal bleeding and pain should have a blood type, antibody screen, and complete blood count checked; in patients known or suspected to be in the first trimester, a serum hCG should also be obtained.

Transvaginal ultrasound is crucial to the assessment of patients with possible spontaneous abortion. The diagnosis of a spontaneous abortion should begin with confirmation of an intrauterine pregnancy, either by an earlier ultrasound this pregnancy or during a patient's current presentation, by visualization of a yolk sac or fetal pole on imaging [18]. Without either of these, the patient has a pregnancy of

unknown location. Please see Chap. 3, Pregnancy of Unknown Location and Ectopic Pregnancy, Fig. 3.1, for a flowchart of the diagnosis of patients with positive serum hCG and pain and/or bleeding.

Absence of a Confirmed Intrauterine Pregnancy

Patients with spontaneous abortions and ectopic pregnancies may present similarly with bleeding and pain. A patient with a positive pregnancy test without documentation of an intrauterine pregnancy, particularly those presenting with bleeding and/or pain, should be considered at risk of an ectopic pregnancy. In hemodynamically stable patients, a repeat hCG is checked in 2 days to establish the hCG trajectory. Please refer to Chap. 3, Pregnancy of Unknown Location and Ectopic Pregnancy, for a discussion of hCG trends and diagnosing pregnancy location. Of note, the proposed hCG trends for differentiating intrauterine, ectopic and failing pregnancies are guidelines only, and deviations are often observed; hCG trends should be correlated with the patient's clinical findings.

Septic Abortion

A septic abortion is diagnosed in any pregnant patient at less than 20 weeks of gestational age, with a fever over 38 °C (100.4 °F) not attributable to any source other than intrauterine contents. Patients may also have abdominal pain, particularly fundal tenderness. Of note, in patients undergoing medical management of an early pregnancy failure, fevers in the first 24 h may be related to administration of prostaglandin analogs such as misoprostol, but infection must be ruled out regardless [19].

Diagnostic criteria of sepsis are shown in Table 8.1 [20, 21]. In patients with fever or otherwise concerning for infection, a complete blood count should be obtained to assess for

Table 8.1 Clinical criteria of sepsis and severe sepsis

Sepsis	Severe sepsis
Suspected source plus 2 or more: 1. Temperature >38.3 °C (101 °F) or <36 °C (96.8 °F) 2. Heart rate >90 beats per minute 3. Tachypnea (>20 breaths/min) 4. WBC >12,000 μ/L or <4000 μ/L or normal with >10 % immature (band) forms	Sepsis plus one or more: 1. Systolic blood pressure <90 mmHg or decrease from baseline by 40 mmHg 2. Elevated lactate (>1 mmol/L; >4 particularly concerning, sign of organ hypoperfusion) 3. Acute lung injury: PaO_2/FiO_2 <250 (in the absence of pneumonia) or <200 (with pneumonia) 4. Acute oliguria <0.5 mL/kg/h despite fluid resuscitation 5. Creatinine >2 mg/dL 6. INR >1.5 7. Platelets <100,000/uL 8. Bilirubin >2 mg/dL

Adapted from Fischerova [20]; Dellinger et al. [21]

leukocytosis and bandemia, which are indicative of infection. In patients with temperatures over 101 °F, blood and urine cultures should be obtained. In patients with signs of sepsis, electrolytes, creatinine, liver function tests, a blood type and antibody screen, coagulation studies (prothrombin time (PT), activated partial thromboplastin time (aPTT) and fibrinogen), and a lactate level should be ordered. Consider an arterial blood gas if the patient is in distress. Nucleic acid amplification testing (NAAT) of a cervical swab for *Neisseria gonorrhoeae* and *Chlamydia trachomatis* can also be helpful. A pelvic ultrasound can help clarify whether a patient has any possible retained intrauterine products of conception, which require evacuation if septic abortion is suspected.

Hemorrhage

Recognition of severe hemorrhage is crucial, and resuscitation should begin alongside diagnosis. Diagnostic criteria of hemorrhagic shock are shown in Table 8.2 [22]. Patients with hemorrhage must have a complete blood count, blood type and antibody screen, coagulation studies and a fibrinogen level ordered. Coagulation factors and fibrinogen may become abnormal due to excessive blood loss.

Table 8.2 Stages of hemorrhagic shock

Class I: blood volume lost <15 %	**Class II**: blood volume lost 15–30 %
Heart rate <100 beats per minute	Heart rate >100 beats per minute
Blood pressure normal	Blood pressure normal
Respiratory rate 14–20 breaths per minute	Respiratory rate 20–30 breaths per minute
Urine output >30 mL/h	Urine output 20–30 mL/h
Mental status normal	Mental status mildly anxious
Class III: blood volume lost 30–40 %	**Class IV**: blood volume lost >40 %
Heart rate >120 beats per minute	Heart rate >140 beats per minute
Blood pressure decreased	Blood pressure decreased
Respiratory rate 30–40 breaths per minute	Respiratory rate >35 breaths per minute
Urine output 5–15 mL/h	Urine output negligible
Mental status anxious/ confused	Mental status confused/ lethargic
Often marks the onset of decompensated hypovolemic shock	

Committee on Trauma [22]

Early Pregnancy Failure

Early pregnancy failure can be diagnosed according to strict ultrasonographic guidelines. Ultrasound criteria of early pregnancy failure include (1) gestational sac at least 25 millimeters (mm) in diameter without an embryo (also called an anembryonic pregnancy), (2) an embryo with a crown rump length of 7 mm or more without fetal heart activity, (3) no fetal heart activity 11 days or more after an ultrasound showing a gestational sac with a yolk sac, and (4) no fetal heart activity 14 days or more after an ultrasound showing a gestational sac without a yolk sac [23].

Threatened Abortion

In patients presenting with a threatened abortion and ultrasound evidence of an intrauterine pregnancy, certain ultrasound findings can increase a clinician's concern for impending spontaneous abortion. A slow fetal heart rate in the first trimester confers an increased risk of spontaneous abortion. A fetal heart rate of less than 100 beats per minute up to 6.2 weeks of gestation and a fetal heart rate below 120 beats per minute from 6.3 to 7 weeks of gestation are associated with an increased risk of demise [24]. Subchorionic hematoma, which appears as a hypoechoic area behind the gestational sac, is associated with double the risk of spontaneous abortion; subchorionic hematomas are also associated with an increased risk of preterm premature rupture of membranes, placental abruption, and stillbirth [25].

Incomplete and Complete Abortion

The diagnosis of an incomplete or complete abortion is reserved for patients with a confirmed intrauterine pregnancy; otherwise, the patient technically has a pregnancy of unknown location. The differentiation between incomplete and complete abortion can be challenging. Patients who have

undergone complete abortion usually report cramping and heavy bleeding with passage of tissue, followed by vast improvement or resolution of their vaginal bleeding by the time of assessment.

The use of ultrasound to differentiate complete from incomplete abortion, by assessing for retained products of conception, is controversial, as ultrasounds have a false-positive rate of 34 % for retained products of conception, and Doppler flow may be present in the endometrial linings of patients who do not ultimately have retained products of conception [26, 27]. The endometrial lining may not be significantly thicker in patients with incomplete versus complete abortions, though the presence of hyperechoic material in the endometrial lining is suggestive of retained products of conception [28].

Given the limitations of ultrasound, management should be guided by the patient's symptoms. Patients with prolonged and heavy bleeding are more likely to have retained products of conception; no strict guidelines exist, but bleeding that soaks two or more maxi pads per hour or that lasts more than 3 weeks may be indicative of retained products of conception. Abdominal pain is not correlated with retained products of conception [28].

Molar Pregnancy

Molar pregnancy commonly presents with vaginal bleeding and elevated hCG [14]. As diagnosis is increasingly made in the first trimester, more extreme symptoms of enlarged uterine size, hyperthyroidism, hyperemesis, and respiratory distress are less common [16].

In patients with the diagnosis of molar pregnancy suggested by imaging or clinical presentation, a complete blood count, blood type and antibody screen, clotting studies, liver and renal function testing, and chest radiograph should be obtained [15]. Less than 50 % of molar pregnancies are detected by ultrasound prior to evacuation, and the remainder is only diagnosed by pathologic analysis of uterine contents

following uterine evacuation for a presumed early pregnancy failure or incomplete abortion [30]. Rates of detection by ultrasound are higher for complete molar pregnancies than partial molar pregnancies [30]. The classic ultrasound appearance of a complete mole is the "cluster of grapes" or "snowstorm" finding (Fig. 8.1) [12]. By ultrasound, a partial mole may have less cystic degeneration of the placenta, and a gestational sac or embryo may be visible (Fig. 8.2) [12].

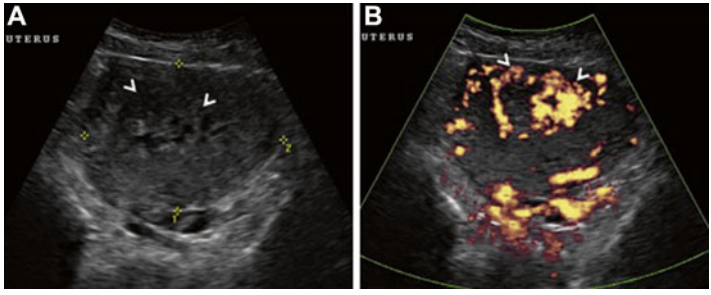

FIG. 8.1 Complete hydatidiform mole. Grayscale (**a**) and power Doppler (**b**) sonographic images demonstrate cystic spaces within the endometrial cavity with increased vascularity (*arrowheads*). No fetus or gestational sac is seen (Reprinted from Shanbhogue et al. [12], with permission from Elsevier)

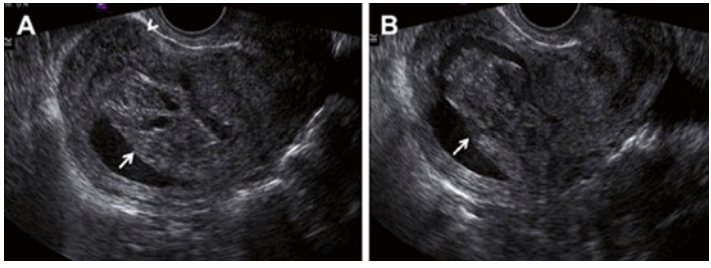

FIG. 8.2 Partial hydatidiform mole. Grayscale sonographic images of the uterus demonstrate cystic changes within the placenta (*arrowhead* in **a**) and an abnormal nonviable fetus (*arrows* in **a** and **b**) (Reprinted from Shanbhogue et al. [12], with permission from Elsevier)

Management

All pregnant patients with vaginal bleeding and rhesus (Rh)-negative blood type should receive Rho(D) immune globulin to avoid isoimmunization.

Any patient without a confirmed intrauterine pregnancy should be assessed and closely followed for a possible ectopic pregnancy. Please see Chap. 3, Pregnancy of Unknown Location and Ectopic Pregnancy, for more information.

Antibiotic prophylaxis is generally recommended for patients requiring dilation and curettage in early pregnancy. Many antibiotics protocols exist, largely extrapolated from the surgical abortion literature, and there is insufficient evidence to support one over another. Ideally, antibiotic prophylaxis should be initiated preoperatively and used in the shortest possible course. Options for antibiotic prophylaxis include: (1) doxycycline 200 mg PO or IV preoperatively, or (2) azithromycin 1 g PO or IV and metronidazole 500 mg PO or IV preoperatively [29, 31, 32].

Hemorrhage

Particularly in patients with hemodynamic changes or estimated blood loss of 500 mL or more, resuscitation efforts should begin immediately with crystalloid and packed red blood cells as necessary, in parallel with operative planning. Please see Chap. 13, Preparing for Urgent or Emergent Surgery, for further information on resuscitation and blood products.

Patients with clinically significant hemorrhage, particularly unstable vital signs, should be managed with urgent **dilation and curettage**. **Uterotonics** can be administered to limit blood loss, shown in Table 8.3 [33–37]. Furthermore, while preparing to proceed to the operating room, **uterine tamponade** can be established by gently introducing a Foley catheter or Bakri® balloon (Cook Medical, Bloomington, IN) into the uterus using a ring forceps [34, 38, 39]. A 30 mL Foley catheter can be

Table 8.3 Uterotonic medications

Medication	Comment
Misoprostol 800–1000 μg PO, SL, PV, or PR	Peak serum concentration of misoprostol is lower following rectal administration
Oxytocin 10 units IM or 10–40 units IV in 1 L of normal saline or lactated Ringer's	Not helpful in the first trimester
Methylergonovine maleate (Methergine®, Novartis, East Hanover, New Jersey) 0.2 mg IM every 2–4 h	Contraindicated in patients with hypertension
Carboprost tromethamine (Hemabate®, Pfizer, New York, NY) 0.25 mg IM every 15–90 min, maximum 8 doses	Contraindicated in patients with asthma or suspected amniotic fluid embolism

From O'Connell et al. [33]; American College of Obstetricians and Gynecologists [34]; Nygaard et al. [35]
PO oral, *SL* sublingual, *PV* vaginally, *PR* rectally, *IM* intramuscular

inflated with up to 60 mL of normal saline, while a Bakri balloon can hold 500 mL, which is often too large for the uterine cavity following a first trimester spontaneous abortion [40]. Uterine tamponade can also be applied postoperatively in patients with persistent bleeding. If tamponade is curative, the balloon can stay in place for 12–24 h, with or without uterotonics and antibiotics [40].

If bleeding continues despite dilation and curettage and uterine tamponade, patients may require additional interventions, including **uterine artery embolization** (UAE), laparoscopy, laparotomy, or rarely hysterectomy. UAE, performed by interventional radiology, has been used with great success to treat postabortion complications including atony and abnormal placentation [42]. UAE involves the cannulation of the femoral artery followed by catheter-guided delivery of embolic particles to the uterine arteries. UAE is a relatively

low-risk and well-tolerated procedure, though it can result in significant cramping and fevers; complications include groin puncture site infection or hematoma, contrast allergy, arterial trauma, or accidental embolization of nontarget vessels [41]. If interventional radiology is not available, surgical intervention may rarely be required, including hypogastric artery ligation and/or hysterectomy [43, 44].

Please see Chap. 2, Vaginal Hemorrhage, for more information on the diagnosis and management of vaginal hemorrhage.

Septic Abortion

In pregnant patients with signs of sepsis and the history, physical exam, labs and imaging reveal no source of infection other than the uterus, resuscitation must begin quickly while mobilizing resources to proceed to the operating room for uterine evacuation. Please refer to Chap. 1, Acute Pelvic Pain, for more information on the management of sepsis. If a patient is septic and hemodynamically unstable, with the uterus being the most likely source of infection, patients may rarely have to go to the operating room for evacuation and potentially other exploratory procedures following an abbreviated assessment and without imaging. Delayed uterine evacuation places patients at risk of worsening sepsis and death [45]. Patients may require further surgery, including hysterectomy, for failure to respond to antibiotics, abscess, or necrotizing pelvic infections. Please see Chap. 16, Complications of Minimally Invasive Gynecologic Surgery, for more information on necrotizing infections.

The patient should receive crystalloid resuscitation, with goals of a central venous pressure of 8–12 mmHg; mean arterial pressure of at least 65 mm of mercury (Hg); urine output of greater than 0.5 mL/kg/h; normalized lactate level; and hemoglobin level of 7–9 g per deciliter (dL) [21]. Repeat a lactate and any other lab values as indicated (such as CBC and coagulation studies in a patient with DIC) during resuscitation to assess progress.

Intravenous broad-spectrum antibiotics should be started within an hour of presentation. A common regimen is ampicillin (2–3 g IV every 6 h), clindamycin (900 mg IV every 8 h), and gentamicin (2 mg/kg IV one time, followed by 1.5 mg/kg IV every 8 h). Another option is ampicillin-sulbactam, 3 g IV every 6 h [46]. Tissue obtained from any uterine evacuation should be sent for culture to direct antibiotic selection.

In patients who present with fever after complete abortion or prior surgical evacuation, with neither significant symptoms (vaginal hemorrhage or pain) nor pelvic ultrasound findings concerning for retained products of conception, treatment for mild endometritis can be initiated. Options include amoxicillin-clavulanic acid (875 mg PO every 12 h) alone or amoxicillin (500 mg PO every 8 h) plus metronidazole (500 mg PO every 8 h) [47]. Clindamycin can also be given orally (600 mg every 6 h), and gentamicin can be given intramuscularly (4.5 g every 24 h), which is less convenient but feasible if no other options are available. Of note, chlamydia and gonorrhea are not addressed by this regimen, and testing for these bacteria should be sent [48].

Molar Pregnancy

Patients with molar pregnancies require surgical evacuation by uterine curettage; hysterectomy is an alternative for patients who are done with childbearing [15]. In patients who undergo uterine curettage, contraception is vital to prevent a new pregnancy during the post-procedural monitoring period.

Following uterine evacuation or hysterectomy, serial serum hCG measurements are vital to monitoring for persistent trophoblastic disease. Serum hCG levels should be obtained each week until levels are negative for 3 weeks, followed by monthly testing for 6 months [14]. An abnormal hCG trend requiring further assessment is defined as a plateau—four sequential hCG levels within 10 % of one another—an increase of 10 % or more of three sequential values, or detectable serum hCG more than 6 months after evacuation [49].

Complete Abortion

In patients with prior confirmed intrauterine pregnancies and without signs of infection following their complete abortions, no further management is commonly necessary. Patients with suspected complete abortions without documentation of intrauterine pregnancies should be carefully counseled and followed for pregnancies of unknown location. Please see Chap. 3, Pregnancy of Unknown Location and Ectopic Pregnancy, for more information. Patients should be counseled that they may have bleeding for several weeks following a complete abortion and to follow up with their continuity providers.

Incomplete Abortion and Early Pregnancy Failure

Patients with a retained failed early pregnancy or an incomplete abortion, and without evidence of infection or hemorrhage may elect for expectant, medical, or surgical management. The relative success rates of these options are shown in Table 8.4 [50, 51]. The rate of infection is low (2–3 %) and similar among all three methods. The rate of unplanned hospital admission and dilation and curettage is higher in patients pursuing expectant or medical management.

Table 8.4 Management of early pregnancy failure

Treatment	Success
Expectant	Incomplete abortion: 84 % in 2 weeks and 91 % in 6–7 weeks Embryonic: 59 % in 2 weeks and 76 % in 6–7 weeks Anembryonic: 52 % in 2 weeks and 66 % in 6–7 weeks
Medical	Incomplete abortion: 93 % in 8 days Embryonic: 88 % in 8 days Anembryonic: 81 % in 8 days
Surgical	97 %

Luise et al. [50]; Zhang et al. [51]

Expectant Management Expectant management can be considered in women without signs of infection at less than 14 weeks of gestational age [52]. Expectant management can be attempted for 4 weeks, after which intervention is generally recommended. Failed expectant management is suspected in patients who do not report heavy menses; ultrasound may provide additional supporting evidence (particularly if an intrauterine gestational sac is still identified). Patients who successfully pass a failed pregnancy should be counseled that light bleeding may persist for over 2 weeks; bleeding is a few days shorter in duration in patients electing for medical or surgical interventions [53].

Medical Management Medical management is performed with misoprostol, a prostaglandin analog, which leads to uterine contractions that expel the gestational tissue. Medical management of an incomplete abortion or early pregnancy failure without hospital admission is generally recommended in women at less than 10 weeks of gestational age, largely extrapolated from the elective abortion literature [54]. Contraindications include high clinical suspicion for ectopic pregnancy, current use of an intrauterine device (IUD), long-term corticosteroid use, adrenal insufficiency, coagulopathy or anticoagulant therapy, significant anemia (usually defined as a hemoglobin of less than 9.5 or 10 g/dL), misoprostol allergy, and inability to follow up [55]. Patients should be counseled that misoprostol leads to painful cramping and heavy vaginal bleeding and can also result in nausea and vomiting, diarrhea, and headache [56]. Misoprostol can be associated with fevers of greater than 38 °C (100.4 °F) in 40 % of women without other signs of infection, particularly in the first 24 h, though patients should be assessed for infection regardless [19].

Several misoprostol regimens are used; the World Health Organization recommends misoprostol 800 μg vaginally or 600 μg sublingually for missed abortions and 600 μg orally for incomplete abortions [56, 57–59]. Patients should be counseled to call their providers if significant vaginal bleeding and passage of tissue have not occurred in

24–48 h. The addition of mifepristone confers no advantage in the medical management of early pregnancy failure [60].

Surgical Management For patients with signs of infection or clinically significant hemorrhage, or who prefer surgical management, dilation and curettage is performed. Suction curettage is preferable to sharp curettage [61]. Antibiotic prophylaxis is recommended for patients undergoing dilation and curettage for spontaneous abortion, though there is insufficient evidence to recommend any one of the proposed regimens. Prophylaxis should be initiated preoperatively and used in the shortest possible course. Options include: (1) doxycycline 200 mg PO or IV preoperatively or (2) azithromycin 1 g PO or IV and metronidazole 500 mg PO or IV preoperatively [29, 31, 32].

Follow-Up

Following any type of spontaneous abortion, patients should be counseled to observe pelvic rest—meaning no intercourse, douching, or use of tampons—for 2 weeks, in order to avoid infection. Patients should be counseled to follow up with their continuity providers within 2–4 weeks, to monitor their postabortion symptoms, and to discuss contraception and future pregnancy planning. No clear guidelines exist regarding a recommended interval to attempting conception. The common advice to wait 3 months before attempting conception may be excessive, as recent research does not show an increase in adverse outcomes in patients conceiving within 3 months of a spontaneous loss [62].

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Chapter 9
Sexual Assault

Oluwatosin O. Onibokun

Definitions

Sexual Assault A broad term defined as any sexual act performed by an assailant or assailants on another person without the victim's consent. These acts include genital, anal and/or oral contact, contact through clothes, and contact by a part of another's body or by an object, including forced kissing, or groping. Acute assault is defined as an assault occurring within 5 days or 120 h of presentation.

Rape Any assault by a person involving vaginal, anal or oral penetration of another person without that person's consent.

According to the Centers for Disease Control and Prevention (CDC) close to one in five women (19.3 %) in the United States have been victims of rape at some time in their lives, which encompasses completed forced penetration, attempted forced penetration, or completed penetration facilitated by alcohol or drugs [1]. Of these, 45.4 % of the female

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victims endorsed being raped by an intimate partner and 46.7 % by an acquaintance. Most female victims of completed rape were first raped before 25 years of age (78.7 %), while 40.4 % were first raped before 18 years of age [1].

Sexual Assault Nurse Examiner (SANE) Given the need to standardize and optimize care of victims of sexual assault, gynecologists are often not first responders for the acute evaluation of a sexual assault survivor in most parts of the United States [2]. Acute evaluation of a stable patient in the emergency room may be performed by the sexual assault nurse examiner (SANE), a specially trained forensic nurse. The first SANE programs were initiated in the late 1970s and today have expanded to up to 700 programs across the United States [2, 3].

These nurses document forensic evidence of the sexual assault, provide medical care, assure that prophylaxis against sexually transmitted infections and emergency contraception are ordered, facilitate psychological support for survivors, and participate in the prosecution of sexual assault through expert testimony [4]. A gynecologist may be asked to examine a patient who has been sexually assaulted without a SANE if the patient declines SANE involvement or no SANE is available. Given the high incidence of sexual assault, gynecologists should have an understanding of the acute evaluation of sexual assault victims, including its complexity and challenges.

When You Arrive Review a full set of vital signs and quickly assess for injuries. Ensure that pain is addressed. Of note, in institutions where a SANE program is present, the SANE is paged right away and is expected to present within 1 h. If the SANE is not available, it is the responsibility of the emergency department team to conduct the medical forensic examination.

Assessment of Safety Consider the safety and anonymity of the patient. Evaluate for the need to protect the patient's identity, for example, by making the patient's hospital admission status not available to outside callers.

Registration A patient should be asked if her insurance can be billed for the visit and should be aware that an explanation of

benefits will be sent to the holder of the insurance policy. In the event the patient does not wish to have her insurance billed, hospital registration can provide options.

History

In situations in which a SANE is involved, the history and physical and forensic evaluation are performed with the SANE in conjunction with members of the health care team, in order to (1) minimize the number of times a patient must recount her experiences, (2) obviate repetitive physical exams, and (3) ensure that evidence collection is not compromised.

If the attack occurred less than 120 h prior, the documentation provided in the evidence collection kit should be used. After 120 h since the attack, the following is the suggested documentation:

Obtain a detailed history of the assault, including the date, time, and location of the assault and record the patient's exact words whenever possible, using quotation marks. Record the number of assailants and their physical descriptions if known. Clarify the nature of the assault, including oral, vaginal, and/or anorectal contact or penetration, the use of force or coercion and the use of alcohol or illicit drugs before the assault. Finally, ask the patient whether she showered, bathed, otherwise cleaned herself, ate, or brushed her teeth following the assault. In summary, address the following questions: (1) what happened, (2) when did this happen, (3) where did this happen, (4) who did this to you, (5) what hurts, and (6) what are your concerns? Facilitating a supportive and comfortable environment for the survivor is important, and survivors should not be pressured into providing details that they do not feel comfortable discussing.

Beyond the assault, a complete medical, obstetric, and gynecologic history should be obtained. The survivor's last consensual sexual intercourse before the assault should be recorded, which is particularly crucial in analyzing collected

specimens for DNA evidence [5]. The patient's vaccination history should be reviewed, including hepatitis B and tetanus.

Consent

Obtain verbal and written consent for the physical exam and evidence collection, as dictated by the medical institution and jurisdiction; providers should be aware of complexities in obtaining consent from minors or patients with intellectual disability [6]. Evidence should not be collected unless a patient is able to consent.

Consent should be obtained for medical care, including general care, pregnancy and sexually transmitted infection (STI) testing, human immunodeficiency virus (HIV) and STI prophylaxis, photographic documentation, and permission to contact the patient later regarding her medical care.

Regarding evidence collection, in addition to the forensic exam, consent is also required for notification of law enforcement and toxicology screening [6]. Law enforcement can subpoena the patient's medical record without consent.

Physical Examination

The physical examination can understandably be a very difficult part of the evaluation for the patient in the setting of an acute or prior assault. It is essential that patients feel empowered during their examination process, which should proceed at a comfortable pace for the patient, and every step should be clearly explained [5].

The provider should document the demeanor of the patient, avoiding adjectives and instead describing the patient's affect and behaviors, such as "The patient is squeezing a pillow, rocking in her chair." This description can be used as evidence in legal proceedings. Assess the patient for signs of drug or alcohol effects, including but not limited to memory loss, slurring, drowsiness, and/or compromised motor

function [5]. If the patient is impaired, consent cannot be obtained until the patient is deemed to be of sound mind. During the physical exam, consider ways to ensure evidence preservation, such as asking the patient to undress for the examination with a sheet underneath her, to collect any debris as evidence, after which the sheet would be folded and submitted as evidence.

A full head-to-toe exam is important in order to assess for concurrent injuries, including genital and extragenital findings and trauma. A light source such as a Wood's lamp can be used to identify debris and semen on the skin. In women, evaluation of the skin, breasts, external genitalia, vagina, anus, and rectum should be performed, keeping in mind that a patient can decline any part of the exam. In cases of oral assault, inspection of the palate, frenulum, and dental condition is required. Careful documentation of trauma can strengthen a patient's legal case and corroborate her account of events; extragenital trauma such as bruises, abrasions, erythema, and edema is seen more often than anogenital trauma [7]. If genital trauma occurs, it is found most commonly in the posterior fourchette and is more common in postmenopausal women and minors [5].

A SANE will sometimes perform colposcopic evaluation in order to detect subtler genital trauma, more often in children. Colposcopes and Wood's lamps are not routinely used by gynecologists for acute evaluation of sexual assault survivors, and there is limited data on the use of these tools by gynecologists in sexual assault evaluation.

Forensic Evaluation

Assault survivors have the right to decline forensic evaluation. Forensic evidence is most helpful when collected within 72 h of the assault [5]. Of note, forensic evidence of oral or anal assault is only collected if the assault occurred within 24 h prior to the patient's presentation.

The forensic exam includes collection of the victim's clothing, swabs, or smears as dictated by the history of the assault—including external genitalia, vagina, cervix, anus, mouth, or any other area that the assailant's bodily fluids may have been deposited—scalp and pubic hair, fingernails, and photographic documentation [5]. Reference samples should be collected, including blood and pulled scalp and pubic hair. The evidence should be collected and stored carefully and securely, assuring a robust chain of evidence and in accordance with local and national protocols to maintain credibility in the court of law.

Management

The patient's physical injuries should be addressed. In addition, her psychological and emotional health requires attention, and patients may benefit from consultation with social work, referral to support or advocacy groups, and education of family members or support people, as appropriate.

Sexually Transmitted Infections

The CDC recommends that decisions regarding testing for STIs be made on an individual basis [1]. The decision of whether to test for STIs may be influenced by low likelihood of post-assault follow-up, which limits the utility of a test-and-treat approach, determination of chronology of infection (i.e., the infection may have predated the assault), and potential legal ramifications of test results [8].

Chlamydia, Gonorrhea, and Trichomoniasis

In the initial examination, testing adult victims of sexual assault for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* can be performed using nucleic acid amplification tests (NAATs) at the site of penetration or attempted penetration.

In children, cultures are preferred, given the serious ramifications of a false-positive result [8]. In adults, examination of a vaginal swab spread on a slide with application of normal saline or potassium hydroxide—also called a wet mount—can also be considered, particularly in the presence of abnormal vaginal discharge, for the evaluation of *Trichomonas vaginalis*, in addition to bacterial vaginosis and candidiasis. The presence of sperm can also be noted.

Ultimately, however, the CDC recommends presumptive treatment of STIs, given the difficulty patients may have in attending follow-up visits after sexual assault. If a patient elects to take prophylaxis against common STIs, the antibiotic regimen should address *C. trachomatis, N. gonorrhoeae* and *T. vaginalis*. For this purpose, the CDC recommends ceftriaxone (250 mg IM once) plus azithromycin (1 g PO once) plus metronidazole (2 g PO once) or tinidazole (2 g PO once) [8].

Hepatitis B

While there is little data specifically addressing the risk of hepatitis B transmission during a sexual assault, immunization should be considered for sexual assault survivors at the time of the initial examination if they have not been previously vaccinated [9]. Baseline testing for immunity (HBsAb) should be sent when the first dose is given. Additional doses are given 1 month and 2–6 months after the first dose, for a total of 3 doses. If the assailant is known to be infected with hepatitis B, immunoglobulin can be considered.

HIV

HIV testing should be performed after sexual assault. Rapid antibody testing should be used when possible, which, if positive, can be confirmed with an enzyme-linked immunosorbent assay (ELISA). Positive results within 3 weeks of an assault indicate that infection predated the assault [5].

In HIV-negative women, HIV post-exposure prophylaxis (PEP) is crucial in areas with high prevalence of HIV but is controversial in low-prevalence areas. The risk of transmission depends on the likelihood of the assailant carrying HIV, the number of assailants, the occurrence of anal penetration (which carries a higher risk of transmission) and/or ejaculation, and whether genital lesions are present or other genital injury [5].

PEP should be started within 72 h and should be managed by an infectious disease specialist, as several treatment regimens exist and recommendations may vary by region [8]. Common regimens include (1) stavudine 40 mg and lamivudine 150 mg, each twice daily, or (2) zidovudine 300 mg and lamivudine 150 mg, each twice daily, or (3) tenofovir 300 mg and emtricitabine 200 mg, each once daily; a protease inhibitor may be added to any of these regimens, largely determined by specialist recommendations for an individual patient [5]. The recommended course is 28 days. Patients should be clearly counseled regarding the importance of medication adherence, the side effects (particularly nausea), and that PEP reduces but does not eliminate the risk of HIV transmission [5]. Alternatively, the CDC advises that a limited course of 3–7 days of PEP can be provided to patients who wish to return for HIV testing and/or counseling [8]. Following sexual assault, HIV-negative women should return for testing in 6 weeks and 3 months, and patients should use condoms during sexual activity until 3 months have passed [5].

Tetanus

In patients with open wounds and who have not been vaccinated within 10 years, booster shots of anti-tetanus toxoid should be given [5].

Human Papillomavirus (HPV)

HPV vaccination is recommended for female survivors of sexual assault from the age of 9 years to 26 years. The first dose should be given at the time of the assault, with additional doses 1–2 months and 6 months later, for a total of 3 doses [7].

Pregnancy

Reproductive-age women should have a baseline pregnancy test even if they are using contraception. A positive test within 5 days of assault indicates that the pregnancy predated the assault [10].

Although risk of pregnancy from assault is thought to be low, emergency contraception (EC) is recommended if assault could result in pregnancy in the survivor. EC should be initiated as soon as possible, and can be administered up to 5 days (120 h) after assault, depending on the method (Table 9.1). Emergency contraceptive regimens include (1) levonorgestrel (a progesterone-only pill) in a single oral dose of 1.5 mg, up to 120 h after assault; (2) ulipristal acetate (an antiprogestin) in a single 30 mg oral dose, up to 120 h after assault; (3) multiple combined estrogen-progesterone pills in 2 doses, with the number of pills depending on the formulation used, with administration of the first dose up to 72 h after assault; and (4) a copper intrauterine device (IUD), which may be inserted up to 120 h after assault and remain in situ for up to 10 years [11]. Success rates of levonorgestrel and ulipristal may be lower in obese women, though both regimens are acceptable to prescribe to obese women [12].

When considering any contraceptive intervention, consult the CDC recommendations for medical eligibility of contraceptive use [13].

TABLE 9.1 Summary of options for emergency contraception (EC) in the United States

Method	Mechanism of action	Considerations	Dose	Efficacy	Contraindications
Ulipristal acetate	Delays or prevents ovulation		30 mg PO once, within 120 h of exposure	Failure rate <2 %	Confirmed pregnancy
Levonorgestrel (progesterone-only pill)	Delays or prevents ovulation	Provide antiemetics for side effects of nausea and vomiting Retake dose if vomiting within 2–3 h of administration	1.5 mg PO once, within 120 h of exposure Alternatively, 0.75 mg PO every 12 h for 2 doses, associated with more nausea	Failure rate <2.5 %	Confirmed pregnancy Contraindications to progesterone contraception likely do not apply given short treatment duration. See CDC Medical Eligibility Criteria for Contraceptive Use, Appendix D
Combined estrogen-progesterone	Delays or prevents ovulation	Provide antiemetics for side effects of nausea and vomiting Retake dose if vomiting within 2–3 h of administration	Each dose should contain 100 mg of ethinyl estradiol and 0.5 mg levonorgestrel, given 12 h apart for 2 doses. The first dose is given within 72 h of exposure	Failure rate of 3.2 % Less effective than levonorgestrel, and should be considered only if other options are unavailable	Confirmed pregnancy Contraindications to estrogen-containing contraception likely do not apply given short treatment duration. See CDC Medical Eligibility Criteria for Contraceptive Use, Appendix D

Copper intrauterine device (IUD)	Oocyte toxicity, inhibition of sperm function, endometrial inflammation	Ideal for women also seeking long-term contraception Recommend testing for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* at time of insertion Significantly higher cost compared to other forms of EC	Intrauterine device, within 120 h of exposure. Efficacious for up to 10 years	Most effective form of emergency contraception, with failure rate of 0.09 %	Confirmed pregnancy Cancer of genital tract Uterine malformation Copper allergy Mucopurulent cervicitis

From Li et al. [11], Glasier et al. [12], Centers for Disease Control and Prevention (CDC) [13]

Aftercare

As part of discharge planning, the safety of the patient's home should be assessed; referral to a shelter should be provided as needed. Follow-up should be established for repeat STI testing as indicated [7]. Management of HIV post-exposure prophylaxis with a specialist should also be established. Routine gynecologic care should be established or continued.

Routine aftercare is important, as survivors are at risk of difficulty with sexual function, tolerating pelvic examinations, posttraumatic stress disorder (PTSD), anxiety and depression, among other complications [14]. Patients may benefit from emotional support through advocacy groups in the community or from referral to counselors specializing in treating victims of trauma.

Legal Considerations

Laws regarding sexual assault reporting vary by state. In general, the patient has the right to decide whether to report the crime, and the district attorney's office decides whether to press charges. Sexual assault or suspected sexual assault of minors and the elderly requires mandatory reporting by the provider in all states. Health-care providers involved in the acute evaluation of survivors can be called to testify in court.

In order to preserve forensic evidence for legal proceedings, a strict chain of custody must be maintained. The forensic evidence kit should be secured and sealed in a locked refrigerator with a completed log book; organization and state protocols should be followed in the transfer of evidence to law enforcement agents if applicable. A kit may be collected while a patient is still undecided regarding whether to involve law enforcement; the timing for submission of an evidence kit to law enforcement varies by jurisdiction and can extend to 10 years [5].

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Chapter 10
Acute Pelvic Pain in Pediatric and Adolescent Patients

Paula C. Brady

Definitions

Adnexal Torsion Twisting of the ovary and/or fallopian tube leading to occlusion of vascular flow, resulting in pain and eventual necrosis. Adnexal torsion constitutes 3 % of gynecologic emergencies [1]. Risk factors for adnexal torsion include ovarian cysts greater than 5 cm and prior adnexal torsion. In children, 50 % of torsions occur in the absence of any other ovarian pathology (such as a mass) [2]. This is attributed to laxity of the utero-ovarian ligament, leading to ovarian hypermobility. Rarely, isolated tubal torsion may occur (often in association with hydrosalpinx or other adnexal pathology), which presents with symptoms indistinguishable from ovarian torsion.

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Differential Diagnosis

Ovarian mass/cyst (with or without rupture)
Adnexal torsion
Uterine outflow obstruction

- Imperforate hymen
- Transverse vaginal septum
- Cervical agenesis
- Vaginal atresia
- Obstructed uterine horn
- Obstructed hemivagina with ipsilateral renal agenesis (OHVIRA)

Dysmenorrhea
Endometriosis
Mittelschmerz (ovulation pain)
Urologic (nephrolithiasis, cystitis, pyelonephritis, acute urinary retention), gastrointestinal (appendicitis, gastroenteritis, bowel obstruction), musculoskeletal, hematologic (sickle cell crisis, porphyria), and psychiatric
Postoperative complications (Chap. 16)
Sexual abuse (Chap. 9)

In sexually active patients: ectopic pregnancy (Chap. 3); sexually transmitted infections, pelvic inflammatory disease, and tubo-ovarian abscess (Chap. 6); and spontaneous abortion (Chap. 8).

Please see Chap. 1 for a full discussion of this differential diagnosis, including dysmenorrhea, endometriosis, and mittelschmerz, which are not discussed here.

When You Get the Call Ask for a full set of vital signs, and request an ultrasound (transabdominal in virginal patients) if one has not already been performed. Request that the patient not receive further pain medications prior to a physical

examination by gynecology, if possible, to allow for an accurate assessment.

When You Arrive Review the full vital signs flow sheet and whether the patient has received any pain medications, which may affect the patient's physical exam findings. Assess the patient's discomfort and distress.

History

Review the time course of the patient's symptoms, including whether the pain began acutely or developed over weeks to months, and whether she has associated symptoms, including fever, nausea, or emesis. Review the location and quality of her pain, including aching, sharp, continuous, or episodic. Review whether she has ever had this pain before or suffers from chronic pain. Ask whether the patient's abdomen feels or appears distended.

Review the patient's full medical and surgical history, including whether she recently had surgery. Inquire whether the patient has begun menstruating; in adolescents, review whether the patient has ever been sexually active, which broadens the differential diagnosis. Review whether she has a history of polycystic ovarian syndrome, ovarian cysts, or ovarian torsion.

Physical Examination

An abdominal exam should be performed, which may reveal distention or a pelvic mass, focal right lower quadrant pain due to appendicitis or adnexal torsion, flank pain due to nephrolithiasis or pyelonephritis, or suprapubic pain potentially due to cystitis. Peritoneal signs—including rebound (pain on the abrupt release of abdominal palpation), involuntary abdominal guarding, or shake tenderness (pain with shaking the patient's abdomen or bed)—indicate intra-abdominal infection, inflammation or hemorrhage, from such processes as appendicitis, adnexal torsion and ovarian cyst rupture, respectively.

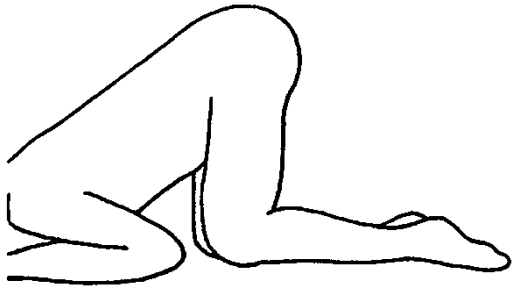

Fig. 10.1 Knee-chest position for pediatric gynecologic examination

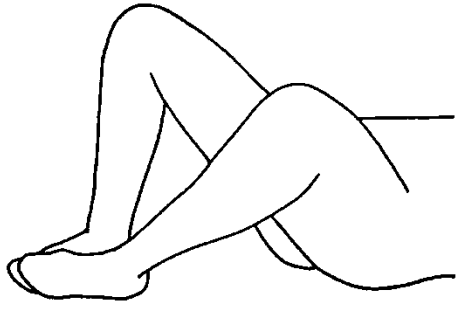

Fig. 10.2 Frog-leg position for pediatric gynecologic examination

Pelvic exams are not required for complaints of pelvic pain, particularly if the source is identified by history or imaging. If necessary, genital exams in children can be performed in the knee-chest (Fig. 10.1) or frog-leg positions (Fig. 10.2). The external genitalia can be inspected for evidence of hematocolpos (vaginal distension with menstrual blood). In children, a rectal exam may reveal hematocolpos or a pelvic mass [3]. In sexually active adolescents, a bimanual exam may reveal evidence of pelvic inflammatory disease, an adnexal mass concerning for an ovarian cyst or neoplasm, ectopic pregnancy or tubo-ovarian abscess, or an immobile uterus in patients with significant endometriosis or other pelvic adhesions.

Diagnosis

Tachycardia, tachypnea, and fever suggest systemic infection; any evidence of sepsis and/or hemodynamic instability requires urgent assessment and resuscitation by a pediatrician or pediatric emergency physician. A low-grade fever is nonspecific and can be associated with infection, ovarian torsion, ovarian cyst rupture, or genital outflow tract obstruction.

A complete blood count and urinalysis should be collected in children and adolescents with acute pelvic pain; leukocytosis may be present in patients with adnexal torsion, ovarian cyst rupture, outflow tract obstruction, or infection. Electrolytes can be checked in patients with nausea and emesis. A beta-human chorionic gonadotropin (hCG) should be checked in postmenarchal patients.

In patients with suspected gynecologic outflow tract obstructions, transperineal or transabdominal ultrasounds are a helpful first step to diagnosis. Magnetic resonance imaging (MRI) can be used to further clarify the patient's anatomy and identify any associated renal anomalies [4].

In patients with presentations suspicious for ovarian cysts or torsion, ultrasound is the first-line modality for diagnosis. Though usually not necessary, computed tomography or MRI may clarify cystic or complex components initially seen on ultrasound and evaluate for metastasis [6]. Please see Chap. 4, Adnexal Masses and Ovarian Cyst Rupture, for more information on the diagnosis of ovarian masses. Please refer to Chap. 5, Adnexal torsion, for more information on ovarian and tubal torsion.

Among patients found to have pelvic masses, tumor markers can be sent for complex ovarian masses concerning for malignancy. Endodermal sinus tumors, embryonal cell carcinomas, immature teratomas, and mixed germ cell tumors are associated with elevated levels of alpha-fetoprotein (AFP), while hCG is associated with choriocarcinoma, embryonal cell carcinoma, and mixed germ cell tumors [5, 6]. Lactate dehydrogenase (LDH) is associated with dysgerminomas [6].

Estradiol and inhibins are markers of granulosa cell tumors; estradiol produced by a granulosa cell tumor in a pediatric patient may result in signs of precocious puberty. Cancer antigen 125 (CA-125) is a marker of epithelial ovarian cancer, which is very uncommon in children and adolescents, and can also be elevated in benign gynecologic neoplasms or conditions (such as endometriosis), and systemic illness.

Management

Outflow Tract Obstruction

Imperforate Hymen

The hymen, which is the result in utero cannulation of the vaginal plate, can have varying degrees of obstruction, including imperforate (no opening), microperforate (very small opening), cribriform (multiple small openings), and septate (largely cannulated, though with a septation). Imperforate hymen is the most common congenital anomaly of the female reproductive tract, estimated to occur in 1 in 1,000–2,000 women [7]. These are sometimes diagnosed soon after birth, when vaginal mucous distends the membrane, though many others present after menarche [8]. An imperforate hymen is ideally repaired when the tissues are exposed to estrogen, in infancy or after puberty [8, 9].

After menarche, patients may present with pain, particularly cyclical pelvic pain and back pain, or urinary and bowel dysfunction due to pain or mass effect. Patients with completely imperforate hymens will have primary amenorrhea; patients with microperforate or cribriform hymens may have some menstrual bleeding, but may still present with symptoms of vaginal obstruction. Patients may present with vaginal distention with menstrual blood (hematocolpos) and uterine distension with blood (hematometra) or blood in the fallopian tubes (hematosalpinx); patients may also have hydronephrosis due to mass effect [8]. On exam, patients will

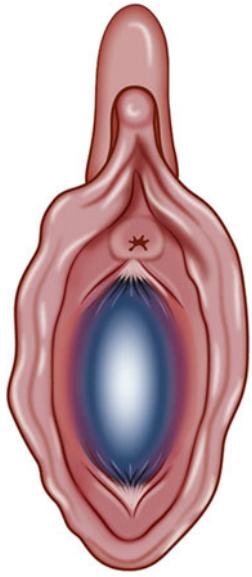

FIG. 10.3 Bulging imperforate hymen (Reprinted from Dietrich et al. [10], with permission from Elsevier and the North American Society for Pediatric and Adolescent Gynecology)

have a bulging membrane at the distal vagina, often blue tinged, and vaginal distension on rectal exam (Fig. 10.3) [10].

An imperforate hymen should be repaired definitively, and not just incised and drained, as the hymen may heal closed and symptoms may recur [8]. For the repair (performed under anesthesia), an elliptical incision should be made in the membrane and excess tissue excised, after which the hymeneal tissue is sutured to the hymeneal ring with a small diameter Vicryl or Chromic suture [11].

Transverse Vaginal Septum

Transverse vaginal septa are attributed to failure of the müllerian ducts and/or urogenital sinus to canalize normally; 46 % occur in the upper vagina, while 35 % occur

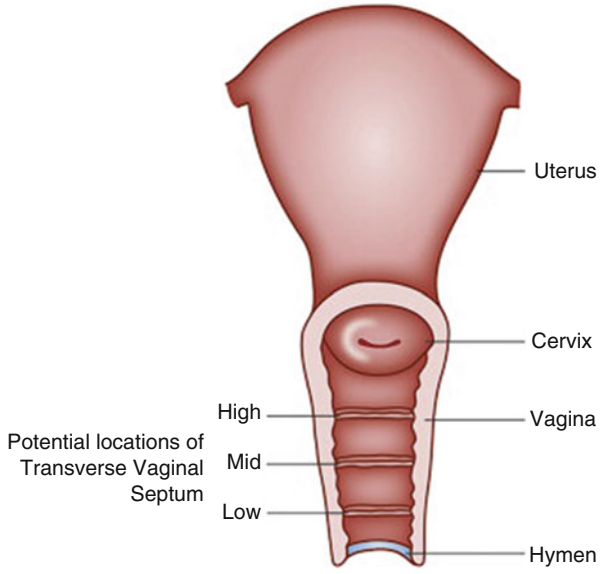

FIG. 10.4 Transverse vaginal septum (Reprinted from Dietrich et al. [10], with permission from Elsevier and the North American Society for Pediatric and Adolescent Gynecology)

in the midvagina (Fig. 10.4) [8, 12]. Patients present with symptoms similar to those with imperforate hymen. Patients with incomplete septa may have some menstrual bleeding, but may still present with symptoms of outflow tract obstruction. The vagina may appear shortened, or like a "blind pouch"; the proximal obstruction may be palpated by rectal exam [9]. The transverse vaginal septum should be visualized with MRI, to clarify the location and thickness—usually less than 1 centimeter (cm)—and to confirm the presence of a cervix [4].

Surgical repair is preferable at the time of distention of the septum by the hematocolpos, which acts as a tissue expander. Small septa can be resected and repaired in an end-to-end anastomosis of the vaginal mucosa. A Z-plasty, using vaginal mucosal flaps, may be performed to reduce the risk of vaginal stenosis (Fig. 10.5) [13, 14]. Thick septa require repair by a

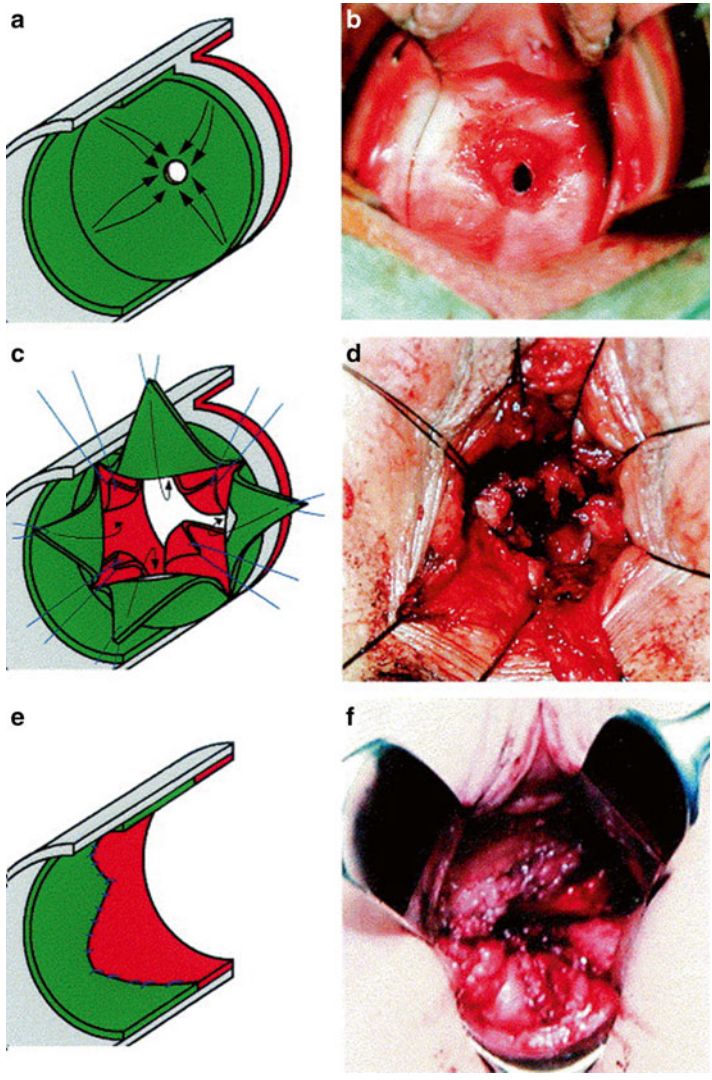

FIG. 10.5 Z-plasty for resection of a transverse vaginal septum. (**a**, **c**, and **e**) Show the basic principle of the operation. The mucosa of the vaginal vault (anterior portion of the barrier) is colored green. The mucosa of the upper pocket (where the cervix is located, posterior portion of the barrier) is colored red. There is a gray-colored midseptum. Stay sutures are blue. The corresponding intraoperative situation is demonstrated by photographs **b**, **d**, and **f** (Reprinted from Wierrani et al. [13], with permission from Elsevier and the American Society for Reproductive Medicine)

specialist and may require a skin graft [8]. Postoperative use of dilators is recommended to maintain vaginal patency [9].

Cervical Agenesis

Cervical agenesis, or the congenital absence of the cervix, is rare and presents similarly to a transverse vaginal septum (Fig. 10.6(I)). This diagnosis is confirmed by MRI. Hysterectomy is often recommended, as surgically created fistulous tracts between the uterus and vagina expose the patient to ascending infection that can result in sepsis and death [8, 15]. Alternatively, some patients are treated with menstrual suppression, with oral contraceptive pills or gonadotropin-releasing hormone agonists, to allow patients to participate in later decisions regarding their reproductive potential [16].

Vaginal Atresia

Vaginal atresia is the congenital absence of the lower vagina; the incidence is estimated at 1 in 5,000 women (Fig. 10.6(I)) [17]. Vaginal atresia results from failure of the urogenital sinus to contribute to the lower vagina; a normal upper vagina, cervix and uterus are present above the obstruction. Patients will present with primary amenorrhea and cyclical pelvic and back pain. The uterus, cervix and upper vagina (particularly if distended with menstrual blood) may be palpable by rectoabdominal exam. Physical exam reveals a dimple in the position of the vaginal introitus [18]. MRI should be obtained to clarify the thickness of the anomaly and assess for renal anomalies.

Like thick vaginal septa, surgical repair requires a specialist, at the time of vaginal distension with menstrual blood. Careful dissection is performed to the point of the upper vagina, after which the vaginal mucosa is pulled through, though a skin graft may be required [8]. Postoperative vaginal dilation is recommended to maintain vaginal patency.

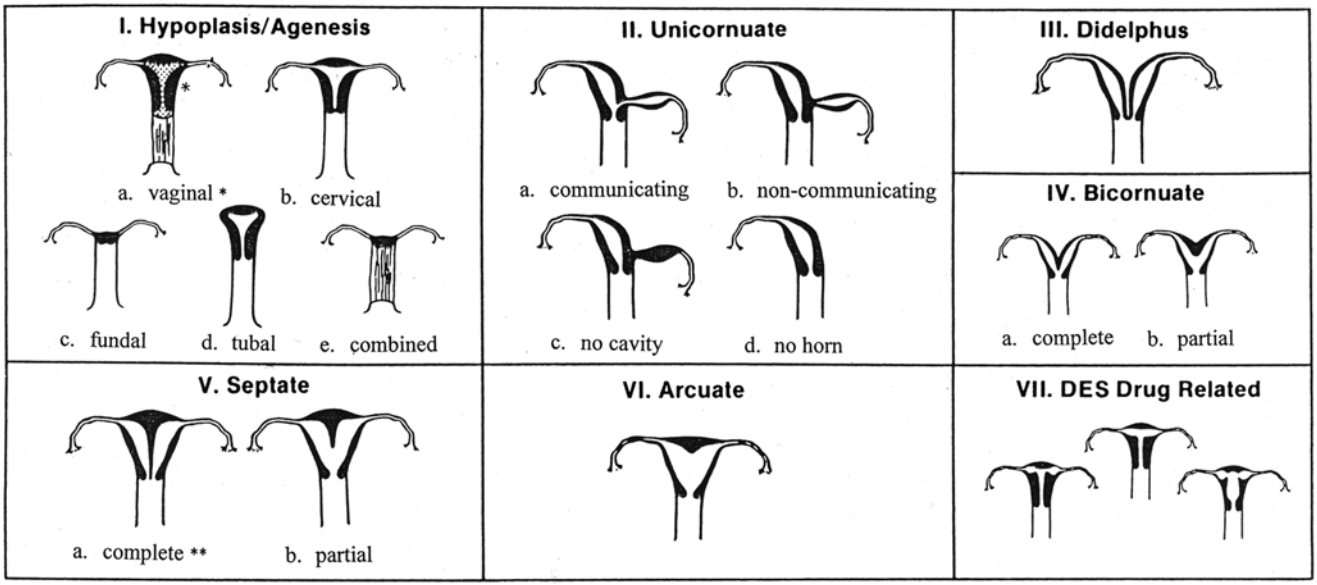

FIG. 10.6 Müllerian anomalies. * Uterus may be normal or take a variety of abnormal forms. ** May have two distinct cervices (Reprinted by permission from the American Society for Reproductive Medicine. (*Fertil Steril* [20])

Obstructed Hemivagina with Ipsilateral Renal Agenesis (OHVIRA)

Patients may also present with symptoms of gynecologic outflow tract obstruction due to a rare syndrome of an obstructed hemivagina with ipsilateral renal agenesis, called OHVIRA [19]. Patients with OHVIRA have uterus didelphys (2 uteri, each with a cervix) and a longitudinal vaginal septum, with one side obstructed (Fig. 10.7). These patients will have menstrual flow from one uterine cavity through the unobstructed hemivagina, but may eventually present with progressively worsening cyclical pelvic pain due to the second obstructed uterine cavity. On physical examination, patients will have a bulge in the vagina [18]. The diagnosis can be confirmed by MRI. Surgical repair entails excision of the vaginal wall of the obstructed hemivagina, to create a unified vaginal vault and allow for unobstructed menstrual flow [8, 11].

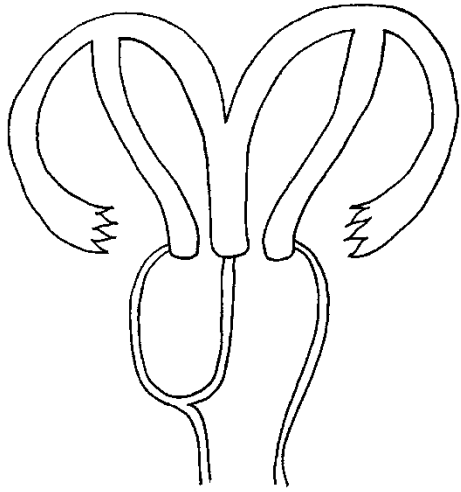

Fig. 10.7 Obstructed hemivagina with ipsilateral renal agenesis (OHVIRA). The ipsilateral renal agenesis is not shown in this image

Obstructed Uterine Horn

Most uterine anomalies—including arcuate, septate, unicornuate, bicornuate, or didelphys uteri—are asymptomatic and may only be diagnosed due to infertility, miscarriage, or obstetrical complications [8, 20]. A patient may, however, have a rudimentary uterine horn that does not communicate with the vagina or contralateral lower uterine segment, leading to obstruction (Fig. 10.6(IIb)). Like OHIVRA, patients may have menstrual bleeding from an unobstructed hemiuterus, but may complain of progressive dysmenorrhea. This diagnosis can be confirmed with ultrasound or MRI, and management is usually by hemihysterectomy [8].

Other uterine anomalies that do not usually present emergently, including nonobstructive longitudinal vaginal septa or müllerian agenesis (Mayer-Rokitansky-Küster-Hauser syndrome), which is the congenital absence of the upper vagina with absence or hypoplasia of the uterus, cervix and fallopian tubes, will not be covered here.

Adnexal Cysts and Masses

Ovarian cysts may be detected antenatally or within the first few weeks of life. Ovarian cysts in neonates are usually the result of hormonal stimulation in utero and generally regress in the first year of life, particularly those less than 5 cm in diameter [21–23]. Serial ultrasound, every 4-6 weeks, is recommended. Aspiration of simple cysts may be indicated for fetal or neonatal cysts greater than 4–5 cm [24]. Torsion may occur at any age; intestinal obstruction may also result from large ovarian cysts in neonates, due to mass effect and inflammation. Either of these is an indication for surgical management.

Simple cysts, representing functional cysts in the vast majority of patients, are the most common adnexal masses in pediatric and adolescent patients [6]. In patients without

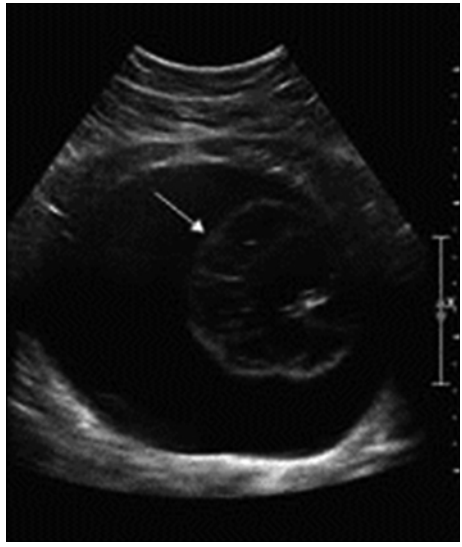

FIG. 10.8 Ovarian teratoma. The ultrasound shows a 14 cm cystic mass and 7 cm solid component (*arrow*), referred to as a Rokitansky nodule (Reprinted from Kelleher and Goldstein [6], with permission)

symptoms concerning for torsion, simple cysts can be followed with serial ultrasound and can take up to 3 months to resolve [6]. In postpubertal patients, hormonal suppression with oral contraceptive pills is often prescribed to prevent recurrence of simple cysts, though the efficacy of this intervention has not been confirmed [25].

Mature teratomas, also called dermoids, are benign germ cell tumors that represent up to 70 % of ovarian neoplasms in children [26]. These are bilateral in 10 % of patients [25]. On imaging, fat fluid levels, linear echogenic bands (hair fibers, also called dermoid mesh), and a "Rokitansky nodule" or "dermoid plug"—a central echogenic area—are suggestive of mature teratomas (Fig. 10.8) [27].

Ovarian cystectomy is recommended for the management of ovarian teratomas, and ovarian preservation is a priority

in this age group. Emergent intervention is only required in cases of suspected ovarian torsion, which can be performed by laparotomy or laparoscopy. Laparoscopy is associated with less pain, shorter hospital stay, and a lower complication rate than laparotomy [28]. Laparotomy may be chosen to reduce the risk of dermoid rupture, which is thought to result in adhesive disease and may rarely result in chemical peritonitis; laparoscopic technique can be adjusted (including use of a tissue recovery bag to remove the cyst from the abdomen) to limit spillage of cyst contents [29,30]. Intraoperatively, pelvic washings should be collected prior to the removal of a dermoid (or any ovarian mass with complex or otherwise concerning features) for staging purposes, in the rare event that malignant transformation is diagnosed [31]. If rupture of a dermoid occurs, copious irrigation is recommended to minimize the risk of chemical peritonitis [6]. Annual ultrasounds have been suggested postoperatively to assess for recurrence [32].

Epithelial neoplasms represent less than 20 % of ovarian neoplasms in children; these include serous and mucinous cystadenomas, and the vast majority are benign. Please refer to Chap. 4 for information on the ultrasound features of cystadenomas. [33]. Management is surgical, by either laparoscopy or laparotomy. Approximately 10 % of cystadenomas recur after cystectomy [34]. Following removal of a cystadenoma, follow-up every 6 months with physical exam and/or imaging has been recommended, though no formal guidelines have been published [28].

Malignant ovarian tumors account for only 1 % of pediatric and adolescent ovarian neoplasms; ovarian malignancies in this age group are usually germ cell or sex cord-stromal tumors, which are generally associated with a positive prognosis [35–37]. Please refer to Chap. 4 for information on the ultrasound features of ovarian malignancy. Tumor markers, discussed in "Diagnosis," should be collected in patients with suspicious ovarian masses, prior to surgical removal. Surgical management is indicated for ovarian masses suspicious for malignancy; laparotomy is usually performed to allow for full

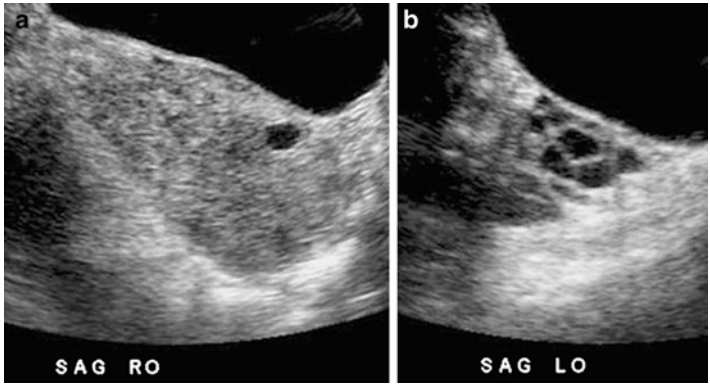

FIG. 10.9 Ovarian torsion by ultrasound in an prepubertal girl (**a**) The torsed ovary is enlarged and heterogeneous and measures $7.9 \times 3.8 \times 6.3$ cm corresponding to a volume of 361.6 cm^3. (**b**) The contralateral normal ovary measures $2.8 \times 1.4 \times 1.9$ cm corresponding to a volume of 14.2 cm^3 (Reprinted from Servaes et al. [41], Fig. 10.1, with kind permission from Springer Science and Business Media)

exploration of the abdomen and to limit risk of rupture of the mass, which is thought to worsen prognosis [38, 39]. Any patient with malignancy should be managed by a surgical or gynecologic oncologist.

Adnexal Torsion

Children with torsion of the ovary and/or fallopian tube usually present with abdominal pain, nausea, and vomiting and may have low-grade fever or leukocytosis [40]. By ultrasound, half of pediatric patients with torsion will have an adnexal mass [2]. Even in the absence of a mass, a torsed ovary will appear more heterogeneous and significantly larger than the contralateral normal ovary (Fig. 10.9) Please refer to Chap. 5, Adnexal Torsion, for an in-depth discussion of ultrasound findings in patients with ovarian and tubal torsion. [41].

Management of suspected adnexal torsion is surgical, usually by laparoscopy. Every effort should be made to preserve the ovary, as over 94 % of discolored or hemorrhagic ovaries

will regain normal ovarian function and appearance by ultrasound [42, 43].

Oophoropexy, or surgical fixation of the ovary, can be considered to prevent recurrent torsion, though the practice is somewhat controversial [44]. Oophoropexy may be considered in a patient with only one ovary, torsion in the absence of risk factors or an ovarian mass, or recurrent torsion. Given the high rate of recurrence of ovarian torsion in children (>15 % in some series), some providers advocate for oophoropexy in all pediatric patients with ovarian torsion [45]. There are no randomized studies comparing recurrence rates or long-term effects on fertility following oophoropexy. Techniques include truncation of the utero-ovarian ligament and fixation of the ovary to the ipsilateral round ligament, pelvic sidewall, uterosacral ligament, or posterior uterus, using absorbable or permanent suture [46, 47].

Please see Chap. 5 for more information on the diagnosis and management of ovarian and tubal torsion.

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Chapter 11
Vulvovaginitis and Vaginal Bleeding in Pediatric and Adolescent Patients

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Differential Diagnosis

Vaginal Bleeding or Bloody Vaginal Discharge

Trauma
Foreign body
Shigella species
Yersinia species
Neonatal withdrawal bleeding
Menses:
- Menarche
- Precocious puberty
- Hypothyroidism

Hemangioma
Malignancy

(continued)

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Infectious Vulvovaginitis

Streptococcus pyogenes (Group A streptococcus)
Haemophilus influenzae
Streptococcus pneumoniae
Staphylococcus aureus
Shigella species
Yersinia species
Neisseria gonorrhoeae
Chlamydia trachomatis
Trichomonas vaginalis
Herpes simplex virus (HSV)
Herpes zoster
Syphilis
Chancroid
Granuloma inguinale, also called donovanosis
Lymphogranuloma venereum (LGV)
Molluscum contagiosum
Condyloma acuminata
Pinworm
Scabies
Candida species
Tinea cruris
Post viral or idiopathic genital ulcers
Human immunodeficiency virus (HIV)
Tuberculosis

Noninfectious Vulvovaginitis

Inflammatory and/or immune-mediated:
- Allergic or irritant contact dermatitis
- Atopic dermatitis
- Foreign body

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Inflammatory and/or immune-mediated continued:
- Lichen sclerosis
- Behçet syndrome
- Inflammatory bowel disease
- Pyoderma gangrenosum
- Stevens-Johnson syndrome (SJS)
- Toxic epidermal necrolysis (TEN)
- Erythema multiforme
- Bullous pemphigoid
- Mucous membrane pemphigoid
- Pemphigus vulgaris
- Linear immunoglobulin A (IgA) dermatosis
- Paraneoplastic pemphigus
- Hidradenitis suppurativa
- Psoriasis
- Periodic fever, aphthous stomatitis, pharyngitis, and cervical adenitis (PFAPA)

Hormonal
- Labial adhesions

Urologic
- Urethral prolapse
- Ectopic ureter

Other
- Zinc deficiency
- Hemangioma
- Hematologic malignancy
- Vaginal malignancy
- Langerhans cell histiocytosis

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Vesicles/Ulcers

Herpes simplex virus
Herpes zoster, caused by varicella-zoster virus
Molluscum contagiosum
Post viral or idiopathic genital ulcers
Allergic or irritant contact dermatitis
Ulcerated hemangioma
Impetigo
Syphilis
Chancroid
Granuloma inguinale, also called donovanosis
Lymphogranuloma venereum (LGV)
Periodic fever, aphthous stomatitis, pharyngitis, and cervical adenitis (PFAPA)
Behçet syndrome
Langerhans cell histiocytosis
Pyoderma gangrenosum
Stevens-Johnson syndrome (SJS)
Toxic epidermal necrolysis (TEN)
Erythema multiforme
Bullous pemphigoid
Mucous membrane pemphigoid
Pemphigus vulgaris
Linear IgA dermatosis
Paraneoplastic pemphigus
Hidradenitis suppurativa
Hematologic malignancy
Human immunodeficiency virus (HIV)
Tuberculosis

Please refer to Chap. 7, Vulvovaginal Dermatoses, Lesions and Masses

(continued)

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Vulvovaginal masses

- Acrochordons (skin tags)
- Vaginal polyp
- Redundant hymeneal tissue (often mistaken for polyp)
- Epidermoid inclusion cyst (sebaceous cyst)
- Urethral prolapse
- Hemangioma
- Condyloma acuminata
- Bartholin's gland cyst/abscess
- Uncommon cases: Vaginal malignancy, lipomas, neurofibromas

Please refer to Chap. 7, Vulvovaginal Dermatoses, Lesions and Masses for full list

When You Get the Call Ask for a full set of vital signs. Ensure the patient is in a private room to allow for an exam.

When You Arrive Review the patient's vital signs, making note of signs of symptomatic anemia (tachycardia, hypotension) in a patient with bleeding or evidence of infection (fever, tachycardia); of note, pediatric vital sign ranges differ from adult ranges. Determine who is accompanying the patient (parent, legal guardian) for purposes of consent and reviewing the patient's history.

History

The patient history should be tailored to the chief complaint. Obtain a complete history of the present illness including onset, duration, and severity of bleeding, associated symptoms of vulvovaginitis including discharge or itching, and any vulvovaginal trauma. A review of systems can include dysuria, pain with defecation and fevers.

Obtain a full medical history including any recent infections in the patient or family members—including respiratory and gastrointestinal infections, scabies, pinworm—known hematologic or autoimmune disorders, or a history of epistaxis, bleeding gums or petechiae. If the complaint is vaginal discharge or bleeding, ask whether she has had prior presentations for retained foreign bodies. When caring for an adolescent patient, review whether she has reached menarche and whether menses are regular. Inquire whether she is sexually active and using contraception.

Review recent antibiotic use, exogenous estrogen exposure (either through oral contraceptive use in adolescents, inappropriate access to hormonal medications in children, or use of herbal medications), or use of any new soaps, detergents, lotions, or other possible contact irritants. Consider, based on the patient's prior presentations, medical history, social history, and current presentation—and an account of her current presentation in her own words—whether the patient is vulnerable to sexual or physical abuse. Symptoms such as headaches, abdominal pain, or nightmares may indicate abuse [1].

Physical Examination

Note secondary sexual characteristics, including breast development and pubic and axillary hair development. As indicated, check for oral ulcers and plaques, scales, or bullae on extensor or flexor surfaces. Check for abscesses or scars in the axilla (suggestive of hidradenitis suppurativa). Assess for any other skin findings including café-au-lait spots and hemangiomas. Make note of bruises and abrasions elsewhere on the patient's body, which may lend insight into the mechanism of injury or may indicate physical or sexual abuse.

Perform an abdominal exam, specifically looking for pelvic masses. A pelvic mass may be most easily palpated by rectal exam. In order to perform vulvar exams in children, the knee-chest (Fig. 11.1) or frog-leg position (Fig. 11.2) is recom-

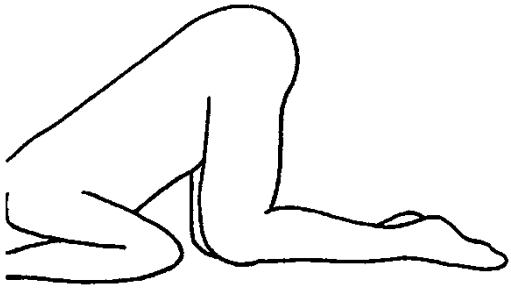

Fig. 11.1 Knee-chest position for pediatric gynecologic examination

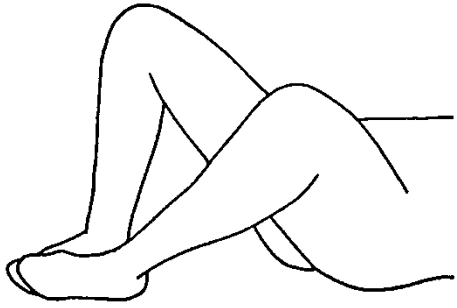

Fig. 11.2 Frog-leg position for pediatric gynecologic examination

mended. An anxious child can be accompanied onto the exam table by a parent, and the patient can be positioned in the frog-leg position while sitting between the parent's legs in the same position. During the examination, ensuring the patient's comfort and sense of control is a priority.

Depending on the patient's age, anxiety, and level of discomfort, conscious sedation may be required with the aid of anesthesiologists or emergency physicians. Exam under general anesthesia is indicated for vaginal hemorrhage, rapidly expanding vulvar hematoma, complex injuries, any injury not adequately visualized at the bedside, or if the patient is unable to tolerate the exam [2]. With or without sedation, in patients with perineal trauma or possible foreign bodies in the vagina, the perineum should be

irrigated with warm saline to optimize visualization. Topical application of 2 % lidocaine jelly to the vulva may improve patient comfort and visualization [1].

In patients with perineal trauma, if the traumatic injury is clearly external, internal exams are not commonly required in female children and adolescents. Assess for vaginal bleeding occurring separately from any visible perineal injury, which may indicate injury in the proximal vagina, likely necessitating anesthesia (conscious sedation or general anesthesia) to allow for complete examination and possible vaginoscopy using a hysteroscope or cystoscope [2]. In patients with blunt perineal injuries due to mechanisms other than straddle injuries, or penetrating injuries, cystoscopy and proctoscopy may also be required [3]. Observe for a vulvar hematoma.

Rarely, patients may be noted to have perineal burns, which warrant consultation by a burn specialist [4]. Of note, uniform and well-demarcated burns are concerning for inflicted injuries (i.e., abuse); purposeful chemical burns can involve batteries or other chemicals such as trichloroacetic acid. Accidental burns tend to be irregular and more superficial.

In patients complaining of discharge or itching, make note of erythema and/or excoriations, which may indicate the presence of contact irritant or infectious vulvovaginitis, and labial adhesions that may be obstructing urine outflow, leading to vaginitis. Note signs of *Candida*—thick white vaginal discharge or white or erythematous plaques.

Enterobius vermicularis (pinworm) may be suspected if the patient has itching, particularly at night, and perianal excoriations. Pinworm eggs may be detected by the "scotch tape test," by applying scotch tape to the perianal skin then briefly to a slide.

The physical exam may reveal stigmata of lichen sclerosis, including white, atrophic skin over the vulva and loss of vulvar architecture (labia minora), associated with itching [5]. Assess for vulvovaginal skin lesions, including condyloma, café-au-lait spots, or hemangiomas. Vaginal masses or tumors may also be found, including urethral polyps, vulvovaginal

polyps, or very rare vaginal malignancies. Upon retraction of the labia minora, the urethral prolapse will appear as a red ring of tissue protruding from the urethral orifice.

Diagnosis

The physical exam of a child with vaginal bleeding or vulvovaginitis will often suggest the diagnosis.

For **vulvovaginitis or vaginal discharge**, consider obtaining bacterial and/or fungal cultures. A swab of vaginal discharge can also be collected for a wet prep (microscopic examination of vaginal discharge prepared with normal saline and potassium hydroxide, separately) for detection of *T. vaginalis*, bacterial vaginosis, *Candida,* or dermatophytes, which cause tinea cruris. As indicated by the patient's presentation, consider sending nucleic acid amplification testing (NAAT) for *N. gonorrhoeae*, *C. trachomatis* and *T. vaginalis* from a vaginal swab (preferred) or urine sample (see "Bacterial and Protozoan Infections" below).

Of note, the diagnosis of chlamydia, gonorrhea, trichomoniasis, syphilis and HIV in children beyond the neonatal period is highly concerning for sexual abuse. Anogenital warts and genital HSV may also (though not always) be associated with abuse. Patients diagnosed with one sexually transmitted infection should be fully screened for others, and assessed for abuse with a multidisciplinary team.

If a foreign body in the vagina is suspected, pelvic radiograph or transabdominal or transperineal ultrasound may be helpful in establishing the diagnosis. If imaging and physical exam are nondiagnostic or poorly tolerated by the patient, exam under anesthesia may be required.

For **ulcerations**, viral culture and polymerase chain reaction (PCR) performed on swabs of the ulcer base are preferred for the diagnosis of HSV in patients with active lesions. Serum testing for syphilis and Epstein-Barr virus may also be helpful.

Identifying the etiology of **vaginal bleeding** is largely dependent on the physical exam; vulvar or vaginal lesions, polyps, lacerations or masses, or the presence of a foreign body should be visible at that time. If suspicion, based on the

history or initial physical exam, is for pelvic trauma, vaginal masses, or retained foreign bodies, the patient may require an exam under anesthesia and vaginoscopy.

In patients with complaints of abnormal vaginal bleeding who are postmenarchal, check a pregnancy test. Please see Chapter 2, Vaginal Hemorrhage, for more information on the assessment of abnormal vaginal bleeding in reproductive age women.

Management

Management of each condition is detailed below. Any patients with vulvovaginitis should be counseled regarding vulvar hygiene, namely, wiping after voiding or defecating from the vagina in the direction of the anus, avoiding possible contact irritants such as bubble baths or scented soaps, avoiding excessively washing or scrubbing the vagina or vulva, wearing loose-fitting clothes, and sleeping without underwear [6, 7].

Perineal Trauma

If the perineal trauma is a mild abrasion with slow oozing, consider applying ice packs. If this is insufficient, consider hemostatic agents such as gelatin foams [1]. If the perineal laceration is not hemostatic or appears deep, suturing may be required. Depending on the patient's age, anxiety, and pain, conscious sedation may be required before suturing; general anesthesia may be required for extensive or intravaginal lacerations. Local anesthesia should be administered, followed by interrupted sutures using a small diameter Chromic or Vicryl suture [1]. A Foley catheter should be placed prior to repairing a periurethral laceration.

Vulvar hematomas may form, associated with edema, fluctuance and/or ecchymosis. If a **vulvar hematoma** is forming, apply ice packs (Fig. 11.3). Consider placing a Foley catheter in the bladder if the hematoma is distorting perineal anatomy, potentially leading to urinary retention. Surgical intervention

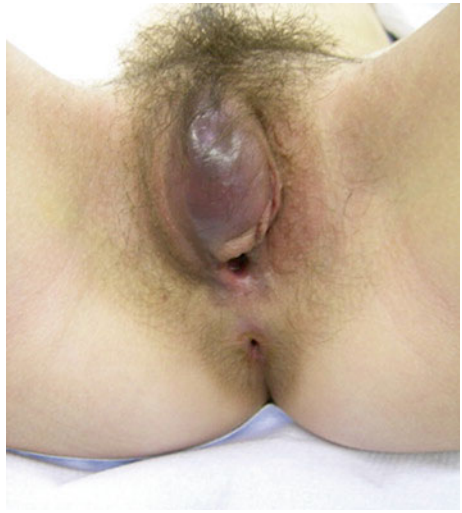

Fig. 11.3 Right labial hematoma (Reprinted from Mok-Lin and Laufer [8], with permission from Elsevier)

is generally avoided for vulvar hematomas as most are self-limited; drainage may also introduce infection. Large or expanding hematomas should be incised to limit expansion and prevent skin necrosis; clot should be evacuated and any visible sources of bleeding should be controlled. Translabial ultrasound can be useful in differentiating edema (which should not be incised) from a hematoma if drainage is being considered. Insertion of a Word catheter has been described to prevent vulvar hematoma reaccumulation [8]. During the resolution of a vulvar hematoma, ecchymosis may be visible for weeks [9]. Patients should observe restricted activity during healing, for comfort and to avoid further trauma.

Burns beyond the most limited, shallow burns should be managed in conjunction with a burn specialist. Chemical burns should be extensively irrigated to prevent further injury. Any burns to the vaginal epithelium should be treated with estrogen to prevent scarring. Silver sulfadiazine 1 % may be applied to vulvar burns during the healing process, followed by an occlusive dressing [4].

Noninfectious Vulvovaginitis

Foreign Body

Among girls presenting with vulvovaginal complaints, 4 % have foreign bodies in the vagina, including toilet paper, tissue paper or paper towel, cloth, parts of toys, crayons, coins, and batteries [10]. Intravaginal batteries may result in alkaline burns [11]. Dermatitis may result from inflammation related to the foreign body (Fig. 11.4). Compared to girls with infectious or nonspecific vaginitis, those with foreign bodies are more likely to present with vaginal bleeding than vaginal discharge. Malodorous discharge is not routinely present with an intravaginal foreign body.

In order to extract a foreign body from the vagina, consider numbing the perineum with a topical analgesic, such as 2 % lidocaine jelly. The vagina should be irrigated with warm water to remove the foreign body. Consider conscious sedation

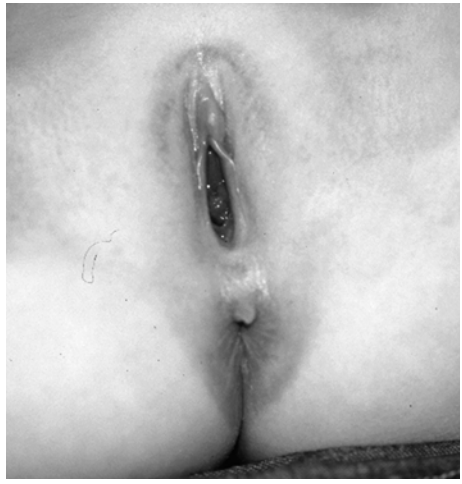

Fig. 11.4 Vaginal foreign body producing chronic irritation discharge (Reprinted from Fischer [15], with permission from John Wiley & Sons, Inc)

depending on the patient's age, anxiety, and pain and for objects that cannot be removed with simple irrigation.

The possibility of sexual abuse should be considered, particularly if the patient cannot provide a history of the object.

Nonspecific Vulvovaginitis

Vulvovaginitis is the most common cause of vaginal bleeding in prepubertal girls. Most vulvovaginitis is noninfectious, often due to hygiene issues. The absence of labial fat pads and pubic hair exposes thin, hypoestrogenized vulvovaginal skin to irritants and trauma. Other causes of vulvovaginitis, including sexually transmitted infections, must be excluded before initiating the treatments below.

Patients and their caregivers should be counseled regarding vulvar hygiene. Sitz baths—sitting in warm water for 5–10 min, two to three times per day—followed by gently patting the vulva dry are usually helpful as well.

Patients with persistent vaginal discharge following lifestyle changes and a negative assessment may be treated with a limited course of antibiotics such as amoxicillin or a cephalosporin [1]. If a patient has recurrent infections, a two-week course of vaginal estrogen cream, such as Premarin® (Wyeth Pharmaceuticals, Philadelphia, PA) or Estrace® (Actavis, Parsippany, NJ), may be initiated to reduce susceptibility to infection.

Conversely, persistent vaginal pruritus or irritation that does not resolve following lifestyle changes and sitz baths may be managed with a two-week course of daily or twice daily hydrocortisone 1 % cream. Lidocaine jelly or an antihistamine such as hydroxyzine (50 milligrams (mg) per day PO in children under 6 years and 50–100 mg/day PO in patients over 6 years, divided into 4 doses), or diphenhydramine (5 mg/kg per day PO divided into 4 doses, maximum 300 mg/day), may also be helpful [23]. The antihistamines may be sedating.

Please see "Allergic or irritant contact dermatitis" in Chap. 7, Vulvovaginal Dermatoses, Lesions and Masses.

Atopic Dermatitis

Atopic dermatitis, also called eczema, is often associated with a strong family history of eczema and a personal history of atopy, which describes a collection of conditions including asthma and seasonal allergies [6]. On physical exam, vulvar atopic dermatitis can appear similar to allergic or irritant contact dermatitis. The vulvar skin is erythematous, potentially lichenified (thickened), sometimes with a peripheral scale (Fig. 11.5).

Atopic dermatitis is managed with behavioral changes as detailed under "Management." Sitz baths may be helpful. Patients can also be treated with a short course of hydrocortisone 1 % cream or ointment twice per day for up to 2 weeks, in addition to emollients such as plain petrolatum.

Lichen Sclerosis

Lichen sclerosis is a chronic inflammation of the perineal and perianal skin; approximately 7–15 % of all cases occur in prepubertal females [12]. Patients report pruritis, pain, dysuria, and/or bleeding. On exam, the vulvar skin is thin, white, and/or atrophic with ulcerations; over time, vulvar architecture will be lost, with scarring of the labia minora, posterior

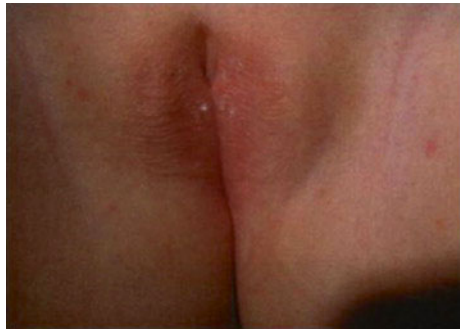

FIG. 11.5 Atopic vulvitis (Reprinted from Simpson and Murphy [6], with permission from Elsevier)

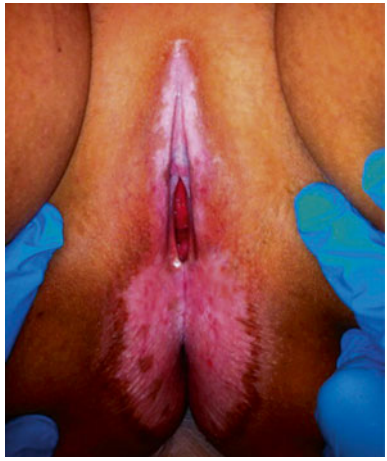

Fig. 11.6 Lichen sclerosis (Reprinted from Bercaw-Pratt et al. [5], with permission from Elsevier and the North American Society for Pediatric and Adolescent Gynecology)

fourchette, and clitoral hood (Fig. 11.6) [1]. The associated risk of malignancy, chiefly squamous cell carcinoma, in postmenopausal women is not observed in children.

In pediatric patients, treatment can usually be initiated without biopsy, as the risk of underlying malignancy is lower than in adults. Biopsy may be indicated for persistent disease despite corticosteroid treatment [5].

In pediatric patients, treatment of lichen sclerosis usually requires high-potency steroid ointment or cream, including clobetasol propionate 0.05 % daily or twice per day for 2 weeks, which is then tapered in frequency or potency if adequate response is noted [5]. The high potency steroid can be spaced to daily, then to every other day, then replaced with a taper of hydrocortisone 2.5 %, followed by the 1 % preparation [1]. Topical steroids may need to be restarted for flares. Other options include mometasone, or immunomodulators such as calcineurin inhibitors [13, 14].

For symptoms of itching, patients may take sedating antihistamines, including hydroxyzine (50 mg/day in children under 6 years and 50–100 mg/day in patients over 6 years, divided into 4 doses) or diphenhydramine (5 mg/kg/day PO divided into 4 doses, maximum 300 mg/day, and consider lower doses in children under 12 years). Further irritation can be managed with topical emollients such as plain petrolatum jelly or A + D® ointment (Bayer, Leverkusen, Germany) [5].

Zinc Deficiency

Zinc deficiency may result from inadequate dietary intake, chronic malabsorptive disease, or acrodermatitis enteropathica (a rare congenital defect of zinc absorption) [15]. Zinc deficiency may present as well-demarcated erosions on the vulva (Fig. 11.7). It usually presents at birth or at weaning in infants with acrodermatitis enteropathica, or after 6–9 months of exclusive breastfeeding, from mothers with low zinc content in their breast milk [15]. Treatment is zinc supplementation.

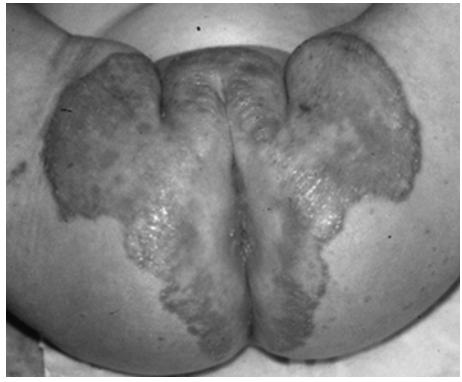

Fig. 11.7 Zinc deficiency (Reprinted from Fischer [15], with permission from John Wiley & Sons, Inc)

Psoriasis

Psoriasis is an inflammatory disease with a strong genetic predisposition; the most common form is chronic plaque psoriasis, in which patients have red or silver scaly plaques on extensor surfaces of the extremities, scalp, and genital regions, sometimes with nail changes, ocular complaints, or arthritis. Vulvar presentations are more common in children and may be misdiagnosed as eczema or fungal infections initially [15, 16]. Vulvar lesions are pruritic, erythematous, and well demarcated, though not often scaly like other psoriatic skin plaques (Fig. 11.8). The vagina is spared, though the inguinal regions and gluteal clefts may be involved; satellite lesions may also be present [6].

Treatment of psoriasis in children and adults is similar. Vulvar psoriasis is often first managed with topical corticosteroids, as other topical treatments (vitamin D analogues, tazarotene, calcineurin inhibitors) may cause irritation [17]. Mild-strength corticosteroids, such as 1 % hydrocortisone, or moderate-strength corticosteroids should be applied once or twice daily for a maximum of 2 weeks; high-potency steroids should be avoided as these regions are susceptible to steroid atrophy [6, 18]. Patients with severe, systemic dis-

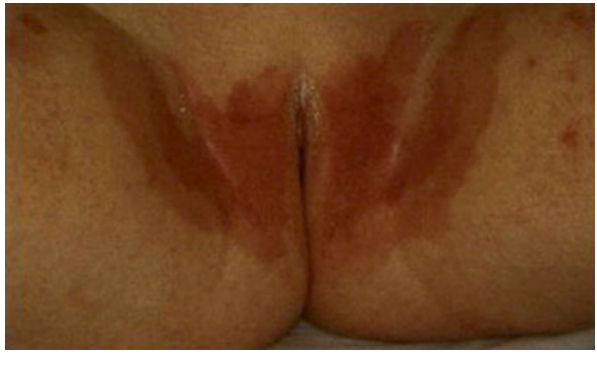

Fig. 11.8 Vulvar psoriasis (Reprinted from Simpson and Murphy [6], with permission from Elsevier)

ease require management by a multidisciplinary team and may require treatment with systemic immunomodulators like infliximab [19].

Infectious Vulvovaginitis or Ulcers

Treatment for common pathogens is shown in Table 11.1.

Bacterial and Protozoan Infections

Respiratory, gastrointestinal, or sexually transmitted infections may lead to pediatric vulvovaginitis. **Streptococcus pyogenes** (Group A streptococcus) is the most common respiratory pathogen leading to vaginitis; it is isolated in up to 20 % of girls with vulvovaginitis [1]. A history of recent streptococcal pharyngitis may raise suspicion for streptococcal vaginitis. Vulvovaginitis resulting from *S. pyogenes* is characterized by vaginal discharge and perineal skin erythema and edema [22]. Treatment of *S. pyogenes* in children consists of amoxicillin (40 mg/kg PO divided into 3 doses daily for 10 days) [23]. Less commonly occurring respiratory pathogens implicated in vaginitis include *Haemophilus influenzae*, *Streptococcus pneumoniae*, and *Staphylococcus aureus* [23].

Shigella most commonly causes diarrhea illness but has also been associated with mucopurulent sanguineous vaginal discharge in girls. Diarrheal illness may only be reported in one-quarter of patients with *Shigella*-related vaginitis, most cases of which are caused by *S. flexneri* [24, 25]. Azithromycin is generally successful in treatment of *Shigella* infections in patients under 18 years of age; fluoroquinolones, commonly used in adults, are not administered to children given concerns for adverse musculoskeletal effects [26]. Though resistance has been reported, trimethoprim-sulfamethoxazole can also be used if a vaginal culture confirms susceptibility. The potential utility of cefixime has also been reported [24]. *Yersinia* is another enteric pathogen associated with vaginitis.

Table 11.1 Common pathogens

Pathogen	Treatment in adolescents, children over 45 kg	Children weighing less than 45 kg
Neisseria gonorrhoeae	Ceftriaxone: 250 mg IM once	Ceftriaxone: 25–50 mg/kg IV or IM once (up to 125 mg IM)
Chlamydia trachomatis	Azithromycin: 1 g PO once Alternative for children over 8 years: Doxycycline 100 mg PO every 12 h for 7 days	Erythromycin base or ethylsuccinate: 50 mg/kg/day PO in four divided doses, maximum 2 g/day, for 14 days
Trichomonas vaginalis	Metronidazole: 2 g PO in a single dose	Metronidazole: 15 mg/kg/day PO, maximum 2 g/day, in three divided doses for 7 days
Initial outbreak of genital HSV ulcers	(1) Acyclovir: 400 mg PO every 8 h for 7–10 days (2) Acyclovir: 200 mg PO five times per day for 7–10 days (3) Famciclovir: 250 mg PO every 8 h for 7–10 days (4) Valacyclovir: 1 g PO every 12 h for 7–10 days	Acyclovir: 80 mg/kg per day PO, maximum 1.2 g per day, divided into 3–4 doses *See text for management of neonatal HSV*

(continued)

Table 11.1 (continued)

Pinworm	(1) Albendazole: 400 mg (in children 20 kg or more) or 200 mg (in children < 20 kg) PO one time, repeated in 2 weeks
	(2) Pyrantel pamoate: 11 mg/kg PO, maximum 1 g, one time, repeated in 2 weeks
Tinea	Econazole, naftifine, oxiconazole, sulconazole 1 % preparations once per day, or clotrimazole, miconazole (not in children under 2 years) or tolnaftate 1 % preparations twice per day for 4–6 weeks
	Children over 12 years can also receive terbinafine 1 % cream twice per day or butenafine or ketoconazole 1 % cream once per day
Candida	Clotrimazole, econazole, miconazole (not for children under 2 years) 1 % preparations applied to the vulva twice per day for 10–14 days
	Adolescent patients with significant intravaginal involvement can use these over-the-counter formulations:
	(1) Miconazole 2 % cream 5 g intravaginally daily for 7 days
	(2) Miconazole, 100 mg vaginal suppository daily for 7 days
	(3) Miconazole, 200 mg vaginal suppository daily for 3 days
	(4) Clotrimazole 2 % cream, 5 g intravaginally daily for 3 days

From Committee on Infectious Diseases [20]; Centers for Disease Control and Prevention [21]

Sexually transmitted bacterial infections that may cause vulvovaginitis in pediatric and adolescent patients include **Neisseria gonorrhoeae** and **Chlamydia trachomatis. N. gonorrhoeae** infection in a prepubertal child is highly concerning for sexual abuse, and a multidisciplinary approach is needed; admission to the hospital should be considered, in order to coordinate resources [27]. Treatment is shown in Table 11.1. Co-treatment of chlamydia is recommended in all age groups. Chlamydia may be contracted either at birth or by sexual contact. If patients did acquire chlamydia at birth, however, persistence is thought to be unlikely past age 2–3 years given exposures to antibiotics for other reasons [1]. Sexual abuse should be considered in children who test positive for chlamydia; the index of suspicion is highest for children over 2 years [28]. Recommended treatment is shown in Table 11.1.

Trichomonas vaginalis, a flagellated protozoan, is also a sexually transmitted infection; it is rare in children whose poorly estrogenized vaginal epithelium is inherently less susceptible to trichomoniasis. Like chlamydia, it can be vertically transmitted from mother to infant at the time of vaginal birth, or by sexual contact [29]. As the effects of maternal estrogen wane and the vaginal pH of an infant changes, it has been theorized that a *T. vaginalis* infection may resolve. Treatment is indicated in a symptomatic child, and is shown in Table 11.1. When trichomoniasis occurs in postpubertal adolescents, it has most often been contracted through sexual contact.

For other sexually transmitted infections, namely, lymphogranuloma venereum (LGV), syphilis, chancroid, and granuloma inguinale, please see Chap. 7, Vulvovaginal Dermatoses, Lesions and Masses.

Herpes Simplex Virus

Herpes simplex virus (HSV) is a chronic viral infection that can be managed with antiviral medications. Two serotypes are most clinically relevant: HSV-1 classically causes oral lesions, while HSV-2 is associated with anogenital lesions. Increasingly,

HSV-1 is also associated with anogenital lesions and may be the cause of up to 50 % of herpes-related genital ulcers [20].

Neonates can be exposed to HSV during delivery. Symptoms manifest between birth and 6 weeks of life, in three iterations: (1) skin, eye, and mouth lesions, (2) central nervous system infection resulting in seizures and hypotonia, and (3) disseminated disease affecting several organ systems including the liver and lungs [20]. The incidence is estimated at 1 in 3,000–20,000 live births. Care of patients with suspected neonatal HSV requires consultation with pediatric infectious disease specialists. The recommended regimen for treatment of known or suspected neonatal herpes is acyclovir, at a dose of 60 mg/kg IV divided into 3 doses for 14 days for disease limited to the skin and mucous membranes, while treatment is continued for 21 days for disease that is disseminated or involving the central nervous system, followed by oral suppressive therapy for 6 months [21].

HSV presenting after the neonatal period is more likely to present with either oral or genital ulcers. Analysis of data from the National Health and Nutrition Examination Surveys (NHANES) from 1999 to 2002 reported a seroprevalence of HSV-1 of 31.9 % among girls aged 6–13 years [30]. From 2005 to 2010, the seroprevalence of HSV-1 among adolescents aged 14–19 years was 30.1 % [31]. From 2007 to 2010, the reported prevalence of HSV-2 among women aged 14–19 years was 1.5 % [32]. About 50 % of genital HSV diagnosed in children is related to sexual contact, more common over age 5 [33]. Other methods of transmission include nonsexual contact with children's genitalia by adults during child care or autoinoculation from an oral lesion.

Please see Chap. 7, Vulvovaginal Dermatoses, Lesions and Masses, for diagnostic modalities.

Treatment of an initial outbreak of HSV genital ulcers is discussed in Table 11.1. Parenteral therapy may be indicated in patients with immunosuppression, severe multisystem disease or encephalitis.

Chronic suppressive therapy is indicated in immunocompetent pediatric patients over 12 years of age experiencing six

or more recurrences per year. Acyclovir is recommended for chronic suppressive therapy (800 mg/day PO in two divided doses) for up to 12 months [20].

For **Zoster** please see "Vulvovaginal Dermatoses, Lesions and Masses"

Molluscum Contagiosum

Molluscum contagiosum is viral infection of the skin and mucous membranes causing painless flesh-colored umbilicated lesions, ranging from 1 mm to 1 cm in diameter, appearing on the vulva, thighs, and buttocks, which may become inflamed; lesions are rarely isolated to the vulva in children, as they may be in adults [15]. Molluscum is a common infection in children, though it may also occur in immunocompromised adults. Presentation with bleeding is not common, unless the patient has been scratching the lesions. Biopsy is not necessary for diagnosis, which is usually made based on clinical exam. Adults with molluscum contagiosum should be tested for other sexually transmitted infections and HIV; children presenting with molluscum are most often healthy [34].

As treatment can be uncomfortable, expectant management is acceptable in healthy pediatric patients with few lesions; spontaneous resolution is expected [15, 35]. Other options include, but are not limited to, application of topical anesthetic followed by curettage, which may result in scarring, application of liquid nitrogen, which is painful, and imiquimod 5 % cream applied overnight for three to five nights per week for up to 16 weeks, though imiquimod is not approved by the Food and Drug Administration for this purpose [15].

Condyloma Acuminata

Between 10 and 20 % of children will have warts, most commonly on the extremities, body, and face, with the peak incidence occurring between 12 and 16 years [36]. Spontaneous

resolution is common among all warts; for anogenital warts, spontaneous resolution occurs in up to 20 % of patients within 4 months and up to 75 % within 5 years [37].

Warts are caused by the human papillomavirus. Ninety percent of anogenital warts are caused by HPV strains 6 and 11 [38]. Anogenital warts are multiple, flesh-colored papules, which may form large exophytic masses. These may be asymptomatic or present with pain, itching, or bleeding [36].

A provider should consider sexual abuse in pediatric patients with anogenital warts; however, the mode of transmission of anogenital warts can also be nonsexual, such as on a caregiver's hands, or vertical, at the time of delivery [36]. If the patient's history or physical exam raises concern for sexual abuse, consider checking for sexually transmitted infections, including gonorrhea, chlamydia, HIV, hepatitis B and C, and syphilis [39].

Data regarding treatment of anogenital warts in children are limited, and treatment is often limited by children's pain tolerance. Expectant management initially is acceptable. For symptomatic patients, imiquimod 5 % cream, applied 3 nights per week for up to 16 weeks, or podophyllotoxin 0.5 % solution, applied 3 nights per week for up to 4 weeks, are acceptable [40]. For large or persistent lesions, surgical excision and laser therapy are options [36].

Pinworm

Enterobius vermicularis (pinworm) is most common in children in preschool or grade school and their families or caregivers. It should be suspected in patients with exposure to pinworm and/or who report perianal itching that is worse at night. Transmission is by the fecal-to-oral route, directly or via fomites [20]. Serology is not helpful; diagnosis is made by applying scotch tape to the perineum, then to a slide for identification of eggs. Treatment is indicated in a symptomatic child, and is shown in Table 11.1. The rate of reinfection is high.

For **scabies**, please see Chap. 7, Vulvovaginal Dermatoses, Lesions and Masses.

Candida

Candidiasis is a less common cause of vulvovaginitis in children, unless a patient has recent exposure to antibiotics or is immunosuppressed or diabetic [6]. Candidiasis may also occur in younger children wearing diapers. Newborn infants may have been inoculated during a vaginal delivery.

Candida vulvovaginitis may appear as well-demarcated erythematous plaques, sometimes accompanied by satellite lesions. Erythema, edema and excoriations may be visible. Diagnosis can be made clinically or using a vaginal fungal culture and/or microscopic examination of a vaginal swab or vulvar scraping prepared on a slide with 10 % potassium hydroxide, revealing buds and hyphae.

Treatment is primarily in the form of topical azoles, discussed in Table 11.1. Creams may address vulvar symptoms more completely than vaginal suppositories. For patients with an extensive *Candida* rash over the perineum and buttocks, antifungal creams can be used over these areas as well. Oral fluconazole is an option but interacts with several other medications including but not limited to phenytoin, tacrolimus, warfarin, cyclosporin A, and protease inhibitors.

Tinea

Tinea cruris is an uncommon cause of pediatric genital eruptions. Tinea infections produce erythematous and scaly plaques in the groin, sometimes extending onto the mons [15]. Lesions are extremely pruritic. Diagnosis is made by scraping the lesion onto a slide and preparing with a potassium hydroxide solution to visualize segmented hyphae and arthrospores. The lesions should also appear red when illuminated with a Wood's lamp [20].

Treatment is with topical antifungal creams. for 4–6 weeks, shown in Table 11.1. Oral griseofulvin can be used in refractory cases.

Post Viral or Idiopathic Genital Ulcers

Genital ulcerations have been diagnosed in the setting of systemic cytomegalovirus, influenza A, and Epstein-Barr virus (EBV) infections [41, 42]. EBV is most commonly associated with genital ulcerations; patients commonly report prodromal constitutional symptoms such as fever, sore throat, and myalgias. Cases in which no cause is discovered are called "Lipschutz" ulcers, also called ulcus vulvae acutum or reactive nonsexually related acute genital ulcers [43, 44]. The lesions vary in size and color, from white/gray to red or black and are often present on opposing labia, called "kissing ulcers" (Fig. 11.9) [41].

In general, biopsies are unhelpful. Serum testing for EBV infection may be highest yield. Influenza testing can be sent as deemed appropriate, and lesions can easily be swabbed for HSV.

Lidocaine jelly 2 % can be used for topical analgesia, and urine may need to be diverted with a Foley catheter in patients with very painful ulcers. The utility of topical steroids is unclear, though some recommend clobetasol 0.05 % cream or ointment twice per day for 7–10 days [45, 46]. Thirty per-

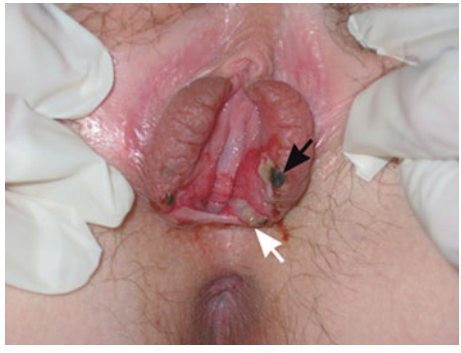

FIG. 11.9 Lipschutz ulcers. Pseudomembrane designated by *white arrow*; eschar designated by *black arrow* (Reprinted from Rosman et al. [44], with permission from John Wiley & Sons, Inc)

cent of vulvar lesions are superinfected; any evidence of purulence, erythema, or other signs of infection should be treated with broad-spectrum antibiotics, such as cephalosporins or sulfonamides [45].

Hormonal Causes of Vulvovaginal Complaints

Labial Adhesions

Labial adhesions are the fusion of the labia minora over the midline, attributed to the hypoestrogenic state of prepubertal girls. Usually, these will resolve spontaneously at puberty, when systemic estrogen rises [47]. When patients are symptomatic, usually this is because the flow of urine has been obstructed, resulting in an irritant dermatitis [48]. Topical estrogen cream, such as Premarin® (Wyeth Pharmaceuticals, Philadelphia, PA) or Estrace® (Actavis, Parsippany, NJ), administered twice daily for 10–14 days, is the primary therapy [49]. In most patients, topical estrogen treatment is sufficient to resolve adhesions. Second-line or adjunctive treatment with topical betamethasone 0.05% twice daily for 4-6 weeks may be required [48]. Long-standing or scarred labial adhesions may be more difficult to resolve; after failed or incomplete treatment with topical estrogen and steroids, persistent adhesions may rarely need to be separated after application of topical analgesics. Patients with significant adhesions may require sedation and separation in the operating room [47]. After separation, applications of topical estrogen cream should continue for two weeks; sitz baths and topical emollients such as plain petrolatum jelly or A + D® ointment are also helpful [1].

Neonatal Withdrawal Bleeding

In response to waning effects of maternal estrogen postnatally, neonates may have blood-tinged vaginal discharge or light vaginal bleeding in the first few weeks of life, which requires no further workup [50].

Precocious Puberty

Precocious puberty has commonly been defined as the onset of secondary sexual development before the age of 8 years in girls and 9 years in boys. More recently, this definition has been revised, and precocious puberty can be considered in the setting of development of breasts or pubic hair before age 7 years in Caucasian girls and age 6 years in African American girls [51]. The incidence of precocious puberty among children in the United States is estimated at 0.01–0.05 % per year; it is more common in girls and African Americans [52]. Causes of precocious puberty are either central, meaning the premature activation of the hypothalamic-pituitary-ovarian axis, or peripheral, due to excess hormone production, such as by estrogen-secreting ovarian cysts [23, 52].

Menarche generally occurs 2–3 years after the first sign of puberty, which is usually breast development and can be detected by physical examination [51]. Isolated premature menarche, defined as menarche in the absence of the secondary sexual characteristics, is very rare, and the cause is unknown. In a series of 17 patients with isolated premature menarche, most had a few menstrual cycles followed by amenorrhea until puberty, with no reported detrimental effects on final adult height or fertility [53].

The diagnosis of precocious puberty or isolated menarche does not constitute an emergency. These patients should be referred to pediatric or reproductive endocrinologists for further assessment and management, which is dictated by the underlying etiology.

Menarche

Patients may present with hemorrhage during their first menses, as certain hematologic disorders may be revealed at menarche, including thrombocytopenia and bleeding disor-

ders such as von Willebrand disease [54]. Please see Chap. 2, Vaginal Hemorrhage, for information on the diagnosis and management of vaginal hemorrhage and bleeding diathesis. Of note, adolescents' menses may also be irregular for the first 3 years post-menarche due to anovulation [55].

Hypothyroidism

Hypothyroidism can produce premature menstruation, in a syndrome of premature thelarche, growth delay, galactorrhea, and ovarian cysts—which can be massive—in varying combinations, called Van Wyk-Grumbach syndrome [56, 57]. Hypothyroidism can also cause menorrhagia [54]. Premature menstruation and thelarche will regress with thyroid replacement therapy.

Urologic Causes of Vulvovaginal Complaints

Urethral Prolapse

Urethral prolapse, which is the protrusion of the distal urethra, may be mistaken for a vaginal mass (Fig. 11.10). Urethral prolapse is most common in African American girls, presenting most often around 4 years of age [58]. Urethral prolapse is often nontender, though patients many complain of dysuria; hematuria is rare.

Urethral prolapse should be managed with sitz baths (sitting in warm water for 5–10 min) twice per day until symptoms improve and topical estrogen therapy, such as Premarin® cream (Wyeth Pharmaceuticals, Philadelphia, PA) or Estrace® cream (Actavis, Parsippany, NJ), applied daily with a fingertip or cotton-tipped applicator, for at least 2 weeks. In patients with suspected urethral prolapse, the differential diagnosis includes paraurethral cysts, prolapsed urethroceles, or urethral polyps [1].

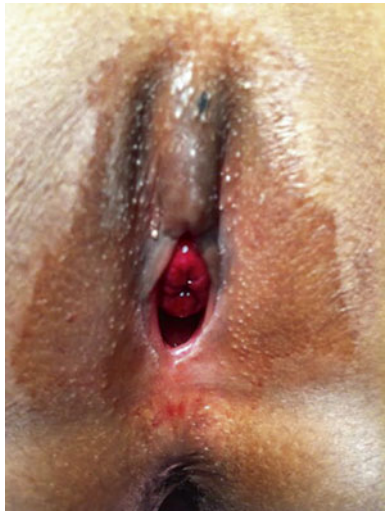

Fig. 11.10 Urethral prolapse in a prepubertal female (Reprinted from Kondamudi et al. [57], with permission from Elsevier and the American Academy of Emergency Medicine)

Ectopic Ureter

An ectopic ureter draining into the gynecologic organs or directly onto the perineum may constitute a significant contact irritant. Ultrasonography or computed tomography and voiding urethrocystography can be used to diagnose an ectopic ureter; cysto-vaginoscopy may also be required [59]. Given case reports of vaginal clear cell cancers in patients whose ectopic ureter drained into the vagina, experts suggest vaginal exams in alternating years, with Pap smears at those exams in children, and annual Pap smears in adolescents [1].

Less Common Vulvovaginal Pathology

Several rare etiologies of vulvar ulcerations or masses are described in Chap. 7, Vulvovaginal Dermatoses, Lesions and Masses. These include hematologic malignancy, Behçet's syn-

drome, inflammatory bowel disease, pyoderma gangrenosum, Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), erythema multiforme, bullous pemphigoid, mucous membrane pemphigoid, pemphigus vulgaris, linear IgA dermatosis, paraneoplastic pemphigus, and hidradenitis suppurativa.

Hemangiomas

Hemangiomas are benign blood vessel proliferations occurring in 2 % of all newborns. Twenty percent of these children will have multiple hemangiomas [60]. Most hemangiomas will involute spontaneously, though skin changes may persist. In the genital region, hemangiomas are most often complicated by ulceration [61]. Occasionally, ulceration may precede the diagnosis of hemangioma, and biopsies may be nonspecific. An ulcerated hemangioma should be kept clean with bathing and dressed with a topical antibiotic, such as mupirocin 2 % ointment, or silver sulfadiazine cream. Lesions can be treated with pulsed dye laser, which leads to more rapid resolution [62].

Lobular capillary hemangiomas, also called pyogenic granulomas, have been reported in the vagina, though they are more often found on the oral mucosal membranes and the skin; these hemangiomas can bleed heavily and repeatedly [63, 64]. Cauterization with silver nitrate is first-line therapy; lesions that bleed recurrently may require excision.

Malignancy of the Lower Genital Tract

Vaginal and pelvic malignancies are very rare causes of vaginal bleeding in children but can present with bleeding due to friability of the mass or abnormal hormone production.

Endodermal sinus tumors and rhabdomyosarcomas are rare malignancies in children that can present with vaginal bleeding or bloody discharge. These are usually diagnosed by age 3 years [48, 65]. In children under 3 years with rhabdomyosarcoma of the genital tract, the mass is usually in the

lower vagina, while in children over 10 years, the mass is more likely to be situated in the upper vagina or cervix [66]. The tumor may appear protruding from the vagina as a grapelike, vascular mass. Early stage treatment can involve chemotherapy, conservative surgery, and radiation therapy for some, with an overall 5-year survival of 87 % [67]. Similar to rhabdomyosarcomas, endodermal sinus tumors present with bloody discharge or a mass protruding from the vagina. These tumors secrete alpha fetoprotein (AFP), which can be detected in the serum.

Langerhans Cell Histiocytosis

Langerhans cell histiocytosis is a rare syndrome of abnormal proliferation of immune cells, with peak incidence at 1 year of age [61]. This condition can involve multiple organ systems, including bone and the central nervous system. Patients commonly present with yellow-brown papules at the hairline, over the trunk, and in the axilla or groin. Vesicles, pustules, ulcerations or eczematous rashes can also be present [68]. Perianal petechiae and purpura may be identified. If Langerhans cell histiocytosis is suspected, lesions should be biopsied.

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Chapter 12
Obstetrics in the Emergency Room

Rachel A. Pilliod

Normal Labor

Definitions

Pregnancy Dating Pregnancy can be divided into three trimesters, with the first trimester classically defined as 2–13 6/7 weeks gestational age (GA), the second trimester as 14–27 6/7 weeks GA, and the third trimester as after 28 weeks GA. Between 37 and 42 weeks, a pregnancy is considered to be at term, while before 37 weeks, a pregnancy is considered preterm, with higher risks of neonatal morbidity including respiratory distress and jaundice [1].

Pregnancies are dated by the first day of the last menstrual period (LMP), with the estimated due date (EDD) 40 weeks after the LMP. Many electronic applications can be used to calculate the current gestational age and EDD based on the LMP [2]. If a pregnant patient with unsure dating presents for emergency care, a rough estimate of GA is the fundal height.

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Measured in centimeters from the pubic bone to the most cephalad aspect of the uterus (called the fundus), the fundal height in centimeters is roughly equivalent to the GA in weeks. When ultrasound is available, first trimester dating can be obtained by measuring a fetal crown-rump length (CRL). In fetuses thought to be 14 weeks GA or more, the biparietal diameter (BPD) is used for dating the pregnancy. The head circumference, abdominal circumference, and femur length can also be used in various regression formulas to estimate gestational age [2]. If this estimate differs by more than 2 weeks from the LMP or the LMP is unknown, ultrasound measurements may be used to make management decisions; however, the possibility of fetal growth restriction should be considered (as may be the case in a patient presenting with hypertension) [2].

Viability The survival of a fetus outside the uterus. The estimated survival rate of extremely preterm infants is 9% at 22 weeks, 33 % at 23 weeks, 65 % at 24 weeks and 81 % at 25 weeks, though surviving fetuses may suffer significant morbidity including necrotizing enterocolitis, sepsis, retinopathy, bronchopulmonary dysplasia and intracranial hemorrhage, and long-term neurodevelopmental impairment [3]. The gestational age threshold for resuscitation may vary by institution, but is generally 23–24 weeks.

Gravidity (G) The number of times a woman has been pregnant.

Parity (P) The number of deliveries a woman has had at or beyond 20 weeks GA. Parity is frequently further described in a series of numbers representing term deliveries, preterm deliveries, abortions, and living children, in that order; abortion accounts for all pregnancies that did not extend beyond 20 weeks, including therapeutic and spontaneous abortions. For instance, a woman who has had three pregnancies total—an early spontaneous abortion, a term delivery of a healthy baby, and a set of living twins delivered prematurely (counted as a single pregnancy but with two living children)—is represented as G3P1113. The prefixes nulli- and multi- are also used to describe parity, referring to women with zero or at least one delivery, respectively.

Labor Cervical dilation secondary to forceful contractions, diagnosed by physical exam. The first stage of labor entails cervical dilation to 10 centimeters (cm), at which point a patient is "fully dilated." Labor progresses more quickly in multiparous women as compared to nulliparous women; early labor (up to 5–6 cm of dilation) can last for several hours, while dilation at a rate of 1 cm per hour is generally expected once a patient reaches 5–6 cm of dilation [4] The second stage of labor refers to maternal pushing and delivery of the infant; in women without an epidural, the median time to delivery in nulliparous women is 0.6 h, with 2.8 h representing the 95th percentile; the median time to delivery in multiparous women is 0.2 h (95th percentile: 1.3 h) [4]. Use of an epidural extends these times.

Rupture of Membranes Rupture of the amniotic membrane around the fetus. Rupture of membranes is suggested by a history of leakage of fluid from the vagina, usually abrupt in onset and ongoing. The color of the fluid can further inform the clinical scenario. For example, dark red fluid may be secondary to a placental abruption (separation of placenta, a potentially highly morbid complication), while green fluid is a sign of fetal meconium (stool) passage, most commonly seen in late term pregnancies and an indicator of fetal distress.

Braxton-Hicks Contractions Mildly painful contractions that do not cause cervical change, often triggered by dehydration or other systemic infections.

Differential Diagnosis

Abdominal Pain in a Viable Pregnancy

- Labor
- Braxton-Hicks contractions
- Placental abruption
- Uterine rupture (particularly in women with prior uterine surgery)
- Chorioamnionitis (intrauterine infection)

(continued)

(continued)

Preeclampsia or hemolysis, elevated liver enzymes, and low platelet (HELLP) syndrome
Any causes of abdominopelvic pain, including ovarian torsion, urinary tract infection, pyelonephritis, nephrolithiasis, gastroenteritis, bowel obstruction, appendicitis, cholelithiasis, ovarian vein thrombosis, musculoskeletal pain and opiate withdrawal.

Leaking Fluid in a Viable Pregnancy

Rupture of membranes
Physiologic discharge
Passage of mucous plug
Vaginitis
Involuntary leakage of urine

When You Get the Call Ask for a complete set of vital signs and whether a physical exam and confirmation of fetal cardiac activity have been performed. Ask for the patient's parity and gestational age, if known. In an institution with pediatricians or neonatologists and obstetricians, be sure to alert these teams to the possibility of a laboring patient in the emergency room.

When You Arrive Assess whether the patient is having vaginal bleeding, and clinically assess the patient's degree of discomfort. View the full flow sheet of vital signs, assessing for fever or hemodynamic instability. Particularly if the patient has either bleeding or moderate to severe discomfort, ensure that the patient has intravenous (IV) access. Ask for an ultrasound or Doppler at the bedside, if available, to assess the fetal heart rate.

History

In stable patients, obtain an obstetric history and inquire about any complications with the current pregnancy. Also obtain a full past medical history, surgical history including

prior cesarean deliveries or other uterine or abdominal surgeries, medications, allergies, and social history including any active drug or alcohol use or intimate partner violence.

Perform an obstetric review of systems, asking the patient about vaginal bleeding, leakage of fluid, and fetal movement. Ask about the frequency and duration of her contractions. Review of systems should also inquire about any evidence of dehydration or infectious symptoms including gastrointestinal or genitourinary issues and complaints of persistent uterine tenderness between contractions.

Physical Examination

Assess for an appropriate fetal heart rate, which should be between 110 and 160 beats per minute [5]. A targeted maternal exam includes palpating the size of the uterus and assessing for any abdominal tenderness between contractions, which may suggest additional causes of pain including infection, uterine rupture or placental abruption. Also assess fetal lie (transverse or longitudinal in the uterus) and presentation (breech or cephalic); use of ultrasound to confirm this assessment is advisable.

The vaginal exam includes a speculum exam if the patient's history raises concern for rupture of membranes. Three tests are used to assess for **rupture of membranes**: (1) "the pool test" or visual inspection for a large pool of fluid in the vagina; (2) the pH of the vaginal fluid, as a pH of 6.5 or greater suggests the presence of amniotic fluid, though blood and semen can also affect pH; and (3) microscopic assessment of a thin film of fluid dried on a slide for the presence of "ferns," which is a characteristic crystal pattern (Fig. 12.1) [6, 7]. Patients with ruptured membranes will have a combination of a pool of fluid in the vagina of high pH and positive ferning.

Patients without a pool of fluid in the vagina, or a small pool, can be asked to cough, as Valsalva may expel fluid from the uterus. Physical examinations resulting in borderline findings can be repeated after having the patient rest supine, to

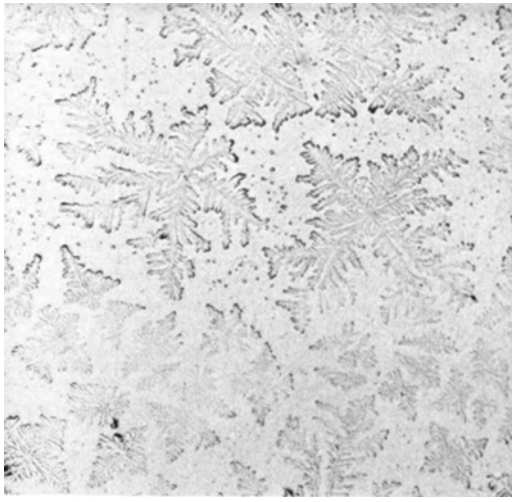

FIG. 12.1 Amniotic fluid ferning (Reprinted from Brookes C, Shand K, Jones WR, *A reevaluation of the ferning test to detect ruptured membranes*. Australian and New Zealand Journal of Obstetrics and Gynaecology, 2008, with permission from John Wiley & Sons, Inc., and the Royal Australian and New Zealand College of Obstetricians and Gynaecologists)

allow fluid to collect in the vagina. Confirmation of ruptured membranes may be helpful in supporting the diagnosis of active labor.

If a speculum exam is deferred, or if the cervix is not easily visible, a digital exam of the cervix is necessary to determine if the patient is in labor. Due to risk of introducing infection, digital exams should not be performed in patients with rupture of membranes prior to 34 weeks of gestational age, unless the patient appears to be in active, painful labor. Prior to an exam, confirm (either by ultrasound or from records) that the placenta is not overlying the cervical os or adjacent to the os (**placenta previa** and marginal previa, respectively). A digital exam of a patient with placenta previa can lead to massive hemorrhage and necessitate emergent delivery.

The elements of the exam are dilation, effacement, consistency, position, and station. Dilation of the internal cervical os is measured between 0 and 10 cm. Dilation to 10 cm is required for a term vaginal delivery (though a very small, preterm fetus could deliver through a less dilated cervix, which may also not be fully effaced). Effacement quantifies the thinning of the cervix; the cervix must be 100 % effaced in order for a vaginal delivery to occur. Consistency of the cervix is reported as firm, medium, and soft, and the position of the cervix is reported as posterior (closer to the sacrum, in early labor) to anterior (closer to the pubic bone, in progressive labor). Fetal station refers to the position of the fetal head—specifically the biparietal diameter—relative to the maternal ischial spines ("zero station"), which can be palpated vaginally. Fetal station is often reported from 5 cm above the ischial spines (negative 5) to 5 cm below the ischial spines (positive 5); the fetal head is typically visible at the perineum beyond "plus 3 station."

Diagnosis

The diagnosis of labor is made during the physical examination. The first stage of labor begins with cervical dilation and is complete with full dilation of 10 cm and 100 % effacement. On digital exam, the examiner feels only fetal head and no adjacent cervical tissue.

Management

The Emergency Medical Treatment and Active Labor Act requires hospitals accepting Medicare to provide care for emergency medical conditions (including contractions in pregnancy). A facility without sufficient obstetrical and neonatal services may transfer a pregnant woman only if she and the fetus are stable, transfer does not pose a risk to the patient or fetus, and delivery is not expected prior to completion of the transfer. Otherwise, care must continue at the initial facility.

If a transferring physician documents that benefits of transfer outweigh the risks to the patient and fetus, an unstable patient (i.e., in active labor) may be transferred [8]. In a hospital with obstetric services, the obstetrician or midwife may need to come to the emergency room to provide assessment and care of acutely unstable patients or those very near delivery [9].

Antibiotics should be administered to patients in whom rupture of membranes or active labor is confirmed, if they meet any of the following criteria: positive test for group B strep (GBS) by rectovaginal or urine culture during the current pregnancy, unknown GBS status at less than 37 weeks of GA, membranes ruptured for greater than 18 h, temperature greater than 100.4 °F, prior infant with invasive GBS infection [10]. Treatment regimens are shown in Table 12.1.

If labor is progressing faster than transfer can safely be arranged, and if the patient is determined to be fully dilated, management of the second stage of labor is recommended. At this point, the patient may begin to push. Effective pushing can be accomplished in a variety of ways, but frequently patients are encouraged to push with sustained effort for 8–10 s, repeated three times per contraction. As the fetal head approaches the perineum, the provider should prepare by wearing eye protection, mask, gown, and sterile gloves and should have available two Kelly clamps, sterile scissors, and a suction bulb. Additional providers should be available to assist with the newborn.

Table 12.1 Antibiotics for group B streptococcus prophylaxis

No penicillin allergy	Penicillin G (five million units IV, followed by 2.5–3 million units every 4 h) Ampicillin (2 g IV followed by 1 g IV every 4 h)
Mild allergy to penicillin	Cefazolin 2 g IV once, followed by 1 g IV every 8 h
Anaphylaxis to penicillin or cephalosporins	Consult GBS culture data or vancomycin (1 g IV every 12 h) or clindamycin (900 mg IV every 8 h)

Verani et al. [10]

The delivery of the head in a controlled fashion minimizes maternal perineal trauma. To facilitate this, apply one hand to the perineum to reinforce this tissue and minimize perineal lacerations, and one hand to the anterior aspect of the presenting fetal head to control delivery momentum. As the head delivers, apply gentle downward pressure to counteract extension of the fetal head and to prevent periurethral lacerations. Once the head is delivered, assess for the presence of the umbilical cord around the infant's neck, which should be released by gently slipping it over the fetal head.

The shoulders must be delivered next (Fig. 12.2). With flat hands applied to the anterior and posterior sides of the infant head, apply gentle downward pressure with a contraction and maternal pushing effort to deliver the anterior shoulder. Once the anterior shoulder is past the perineum, apply gentle upward effort to facilitate the delivery of the posterior shoulder. The infant can be delivered up to the maternal abdomen, or securely

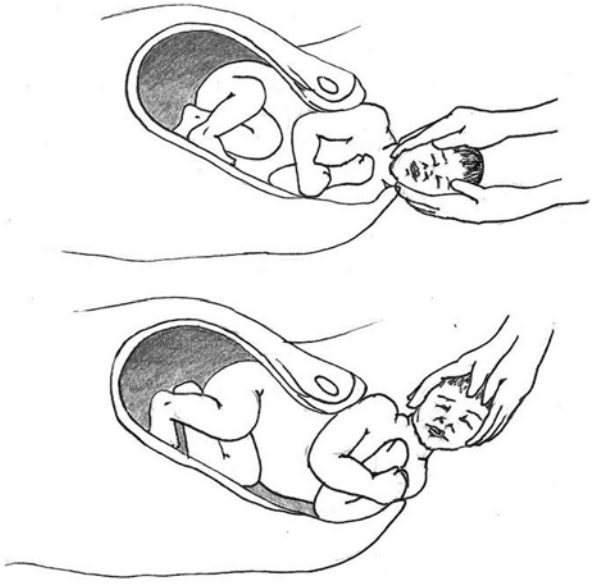

FIG. 12.2 Vaginal delivery. The anterior shoulder is delivered, followed by the posterior shoulder

held, with care taken not to put tension on the umbilical cord. Apply two Kelly clamps a few centimeters apart on the cord and cut the intervening section of the cord, in order to separate the infant from the mother. The infant should be dried with a warm towel and stimulated. Infant resuscitation is beyond the scope of the chapter, but a basic guideline is published by the World Health Organization for further reference [11].

The third stage of labor, following the delivery of the infant, involves the delivery of the placenta. The placenta commonly delivers within 30 min, though active management of the third stage of labor is associated with less blood loss [12, 13]. Massage the uterine fundus to ensure adequate contraction. Apply gentle pressure on the cord segment protruding from the vagina, while providing suprapubic pressure (above the pubic bone) to prevent uterine inversion [14]. Often, a small, abrupt increase in vaginal bleeding is noted when the placenta detaches from the uterine wall. Deliver the placenta in a controlled fashion, ensuring that trailing membranes are not separated from the placenta and retained in the uterus or vagina. With further fundal massage, the uterus should contract and be palpably firm on abdominal exam; vaginal bleeding is usually light.

Oxytocin is commonly administered to facilitate uterine involution and decrease the risk of hemorrhage. Whether to administer oxytocin before or after delivery of the placenta is unclear. Either way, oxytocin can be administered as ten units IM in patients without IV access, or 10–40 units IV in 500–1000 milliliters (mL) of a crystalloid solution, often administered over an hour [15].

Primary Obstetrical Hemorrhage

Definitions

Postpartum Hemorrhage Greater than 500 mL of blood loss following vaginal delivery, estimated to occur following 4–6 % of deliveries [16]. Postpartum hemorrhage is attributed primarily to uterine atony in 80 % of cases [16]. Risk factors for hemorrhage include prolonged or rapid labor, history of

prior postpartum hemorrhage, preeclampsia, overdistended uterus (multiple gestation, macrosomia, or polyhydramnios), chorioamnionitis, and Asian or Hispanic ethnicity [17, 18] After atony, lacerations and trauma account for the majority of cases with a minority attributed to coagulopathy.

Atony Failure of the uterus to contract appropriately, usually leading to hemorrhage. Affecting 1 in 20 deliveries, atony is a considerable cause of morbidity and mortality [19]. Risk factors for atony include uterine distension (multiple gestation, macrosomia, or polyhydramnios), high parity, induced or augmented labor, and prior postpartum hemorrhage [20]. Atony can be focal or diffuse and is diagnosed by an enlarged, boggy uterus.

Abnormal Placentation An abnormally adherent placenta, invading through the endometrium. Placenta accreta is defined as invasion through the endometrium; placenta increta describes invasion into the myometrium, while placenta percreta is defined as invasion through the myometrium to the uterine serosa or beyond. Abnormally adherent placentas are associated with prior uterine surgeries, including uterine curettage, myomectomy, and cesarean section [21]. The rate of placenta accreta increases with each successive cesarean section, up to 6.7 % in patients with five prior cesarean sections [22]. The further presence of a placenta previa (in which the placenta covers the cervical os), in women with prior cesarean sections, dramatically increases the risk of placenta accreta such that 39 % of women with a placenta previa and two prior cesarean sections are diagnosed with placenta accreta [23].

Uterine Rupture Transmural disruption of the uterus, most commonly associated with prior uterine surgeries or cesarean section. Uterine rupture is estimated to occur in 0.7 % of deliveries, the vast majority occurring in patients with a prior cesarean delivery [24].

Disseminated Intravascular Coagulation (DIC): Systematic activation of coagulation pathways causing diffuse fibrin deposition, leading to consumption of coagulation factors and platelets, and resulting in bleeding [25]. Conditions leading to

DIC include sepsis, malignancy, trauma, amniotic fluid embolism, placental abruption, retained intrauterine fetal demise, liver failure, and ABO incompatibility.

Differential Diagnosis

Atony
Abnormal placentation
Retained products of conception
Uterine inversion
Uterine rupture
Cervical laceration
Vaginal laceration
Infection
Hematologic abnormalities [26]

- Bleeding diathesis, such as von Willebrand disease
- Disseminated intravascular coagulation (DIC)
- Thrombocytopenia—caused by such etiologies as preeclampsia, HELLP, gestational thrombocytopenia, idiopathic thrombocytopenic purpura (ITP), and thrombotic thrombocytopenic purpura
- Anticoagulant medication

When You Get the Call Request IV access, a complete blood count, blood type and antibody screen, and coagulation labs (prothrombin time (PT) and activated partial thromboplastin time (aPTT), fibrinogen). Consider requesting blood products to be crossmatched or asking for emergency release O-negative blood to be delivered to the beside, particularly if the estimated blood loss is over 500 cc.

When You Arrive Ensure that the patient is hemodynamically stable. In patients with significant and ongoing hemorrhage on brief assessment, resuscitation should begin in parallel with diagnosis (see section "Management").

History

Review the patient's age and parity, and ask the delivering providers or first responders to provide details of the delivery, including intrapartum blood loss, any complications (including fever or shoulder dystocia), and ease of delivery of the placenta. Suspect adherent or retained placenta if removal of the placenta was difficult or if the placenta was not delivered within 30 min of delivery. A history of abdominal pain or vaginal bleeding preceding or during labor may raise suspicion for an abruption, which can lead to DIC (see section "Diagnosis" below).

Review the patient's obstetric history, and elicit any significant past medical history, including known bleeding diatheses, or prior episodes of excess bleeding with menses, surgery, or deliveries. Review whether the patient has a history of hypertension or asthma, as some uterotonic agents are contraindicated in these conditions.

Physical Examination

Patients with significant hemorrhage, particularly those with any vital sign changes including tachycardia, should be taken to the operating room for an exam under anesthesia. The lighting and instruments of an operating room are optimal for this examination and often necessary for adequate repair of deep or complex vaginal or cervical lacerations or to perform a dilation and curettage if needed.

In stable patients, request a stretcher or bed with stirrups to facilitate a thorough vaginal exam and repair of any lacerations. An abdominal and bimanual exam should be performed to assess fundal tone and evaluate for any clots or retained placenta. A bedside ultrasound can also be useful when performed by a skilled provider to assess for evidence of retained products of conception (Fig. 12.3). If the uterine fundus is difficult to palpate, ensure the patient's bladder is empty. A full or distended bladder can hinder uterine

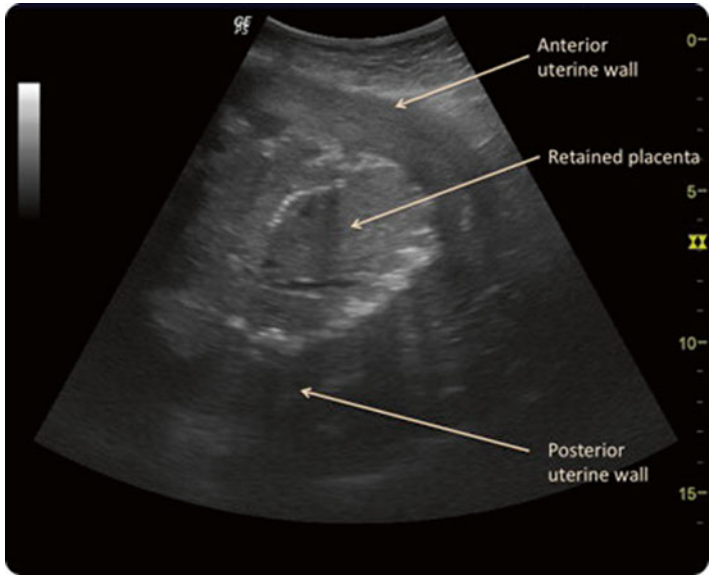

Fig. 12.3 Retained placenta. Ultrasound image of retained placenta in situ (Reprinted from Rosenstein and Vargas [27] with permission from Elsevier)

contraction as well as make the exam more difficult. In a hemorrhaging or unstable patient, a urinary catheter is indicated for monitoring of output.

Diagnosis

The amount of hemorrhage should be estimated; stages of hemorrhagic shock are shown in Table 12.2 [28]. In every patient with bleeding more than 500 mL postpartum and ongoing, a complete blood count, blood type and antibody screen, and coagulation labs (prothrombin time (PT) and activated partial thromboplastin time (aPTT), fibrinogen) should be collected.

The underlying cause of uterine hemorrhage may be suggested by the patient's medical history—including known

Table 12.2 Stages of hemorrhagic shock

Class I: blood volume lost <15 %	**Class II: blood volume lost 15–30 %**
Heart rate <100 beats per minute	Heart rate >100 beats per minute
Blood pressure normal	Blood pressure normal
Respiratory rate 14–20 breaths per minute	Respiratory rate 20–30 breaths per minute
Urine output >30 mL per hour	Urine output 20–30 mL per hour
Mental status normal	Mental status mildly anxious
Class III: Blood volume lost 30–40 %	**Class IV: Blood volume lost >40 %**
Heart rate >120 beats per minute	Heart rate >140 beats per minute
Blood pressure decreased	Blood pressure decreased
Respiratory rate 30–40 breaths per minute	Respiratory rate >35 breaths per minute
Urine output 5–15 mL per hour	Urine output negligible
Mental status anxious/confused	Mental status confused/lethargic
Often marks the onset of decompensated hypovolemic shock	

Committee on Trauma [28]

thrombocytopenia or clotting disorders—and is often confirmed by physical examination. **Uterine inversion** is suggested by depressed fundal height and part of the inverted uterus prolapsing into the vagina. An **abnormally adherent placenta** should be suspected in patients with a history of uterine surgery or prior placenta accreta or following difficult or piecemeal delivery of the placenta. **Atony** is suggested by an enlarged, boggy uterus. **Uterine rupture** should be suspected in patients with fetal bradycardia, abdominal pain independent of contractions, and vaginal bleeding, though hemorrhage may be concealed within the abdomen. Patients with uterine rupture may develop hypovolemic shock; bedside ultrasound may reveal complex free fluid in the abdomen resulting from intra-abdominal hemorrhage [29]. **Lacerations** are usually visualized by vaginal exam, which

should include a thorough assessment of the cervix, vaginal sulci, and periurethral area. A cervical laceration should be suspected if no vaginal laceration is identified and the uterus has appropriate tone, without suggestion of retained products of conception by ultrasound. There is usually insufficient time for a formal ultrasound, but bedside ultrasound can be helpful in diagnosing **retained products of conception** when performed by an experienced clinician (Fig. 12.3) [27].

Management

When postpartum hemorrhage is diagnosed, the available anesthesia and obstetrics staff should be notified.

In hemodynamically unstable patients, resuscitation should begin alongside the assessment. Most obstetric hemorrhage protocols utilize a 1:1 ratio in transfusing units of red blood cells to fresh frozen plasma, as obstetric hemorrhage can rapidly consume coagulation factors. Attention should also be paid to fibrinogen replacement (in the form of fibrinogen powder concentrate or cryoprecipitate), and a unit of apheresis platelets (usually composed of six units of random donor platelets) should be administered after every six units of packed red blood cells [30, 31]. Refer to Chap. 13, Preparing for Urgent and Emergent Surgery, for further resuscitation guidelines. For non-massive, goal-oriented resuscitation, goals include (1) hemoglobin greater than 7 g per deciliter (dL); (2) platelets above 50,000 per microliter (μL), particularly if surgery is planned; (3) an international normalized ratio (INR) less than 1.5; and (4) fibrinogen above 100 mg/dL [32, 33]. A patient's goal heart rate should generally be less than 100 beats per minute, with urine output at least 0.5 mL per kilogram per hour.

If the etiology of hemorrhage is diagnosed, management should focus on addressing that issue specifically. **Uterine inversion**, an uncommon cause of postpartum hemorrhage, can be diagnosed by physical exam immediately following delivery. Replace the uterus manually, as quickly as possible. Uterotonic medications should be stopped. Uterine relaxation

may be required, which can be achieved with 50 μg of intravenous nitroglycerin, repeated up to three times as needed [34]. Once the uterus is reverted, uterotonic agents should be given to prevent recurrence and to improve tone. If this is unsuccessful, surgical management may be required [35].

If **retained products of conception** or **abnormal placentation** (such as placenta accreta) is suspected, obstetricians may need to perform manual removal of the placenta or dilation and curettage, as needed. If a **cervical laceration** or deep sulcal vaginal tear is suspected, vaginal packing can be placed until the obstetrics team arrives; examination and repair in an operating room provides optimal visualization. If **uterine rupture** is suspected, the patient will require laparotomy for repair.

Intravenous access, emptying the bladder, fundal massage, and administration of uterotonics are first steps in the management of obstetrical hemorrhage (Table 12.3) [36–39]. If hemorrhage continues, particularly if the estimated blood loss reaches one liter, additional support should be requested (including other obstetricians, anesthesiologists, and potentially interventional radiologists or general surgeons). Repeat labs should be sent emergently, including blood count and coagulation studies (PT/INR, PTT, fibrinogen); transfusions are often initiated by this point.

Uterine tamponade can be established with a Foley catheter or Bakri® balloon (Cook Medical, Bloomington, IN), inflated with normal saline; a 30 mL Foley catheter can be inflated with 60 mL of normal saline, and a Bakri balloon can hold up to 500 mL [40, 41]. If these are not available, laparotomy sponges can be used.

If bleeding persists, more significant intervention should be considered, including uterine artery ligation, B-lynch sutures, or hysterectomy, all of which require open abdominal surgery. Interventional radiology may also perform uterine artery embolization, which can be helpful in the diagnosis and management of genital tract lacerations, vascular injuries or anomalies, refractory atony, and abnormal placentation (Fig. 12.4) [42, 43]. Transferring patients to interventional radiology, however, often requires time; for this reason,

Table 12.3 Uterotonic medications

Medication	Comment
Misoprostol 800–1000 μg PO, SL, PV or PR	Peak serum concentration of misoprostol is lower following rectal administration
Oxytocin 10 units IM or 10–40 units IV in 1 L of normal saline or lactated Ringer's	
Methylergonovine maleate (Methergine®, Novartis, East Hanover, New Jersey) 0.2 mg IM every 2–4 h, or PO every 6–8 h	Contraindicated in patients with hypertension
Carboprost tromethamine (Hemabate®, Pfizer, New York, NY) 0.25 mg IM every 15–90 min, maximum 8 doses	Contraindicated in patients with asthma or suspected amniotic fluid embolism

From: O'Connell et al. [37]; American College of Obstetricians and Gynecologists [17]
PO oral, *SL* sublingual, *PV* vaginally, *PR* rectally, *IM* intramuscular

interventional radiology should be contacted earlier in the process of managing postpartum hemorrhage.

After the immediate postpartum period, women with an initial or primary hemorrhage are at risk of secondary hemorrhage. Secondary hemorrhage can occur between 24 h and 6 weeks following delivery. Overall, secondary postpartum hemorrhage affects 0.5–2 % of deliveries; of these women, two-thirds will have experienced a primary hemorrhage [44]. In addition to the assessment indicated for primary hemorrhage, secondary hemorrhage should initiate coagulation studies to assess for von Willebrand disease and ultrasound imaging to assess for retained products of conception and vascular malformations of the uterus, including arteriovenous malformations and uterine artery aneurysms.

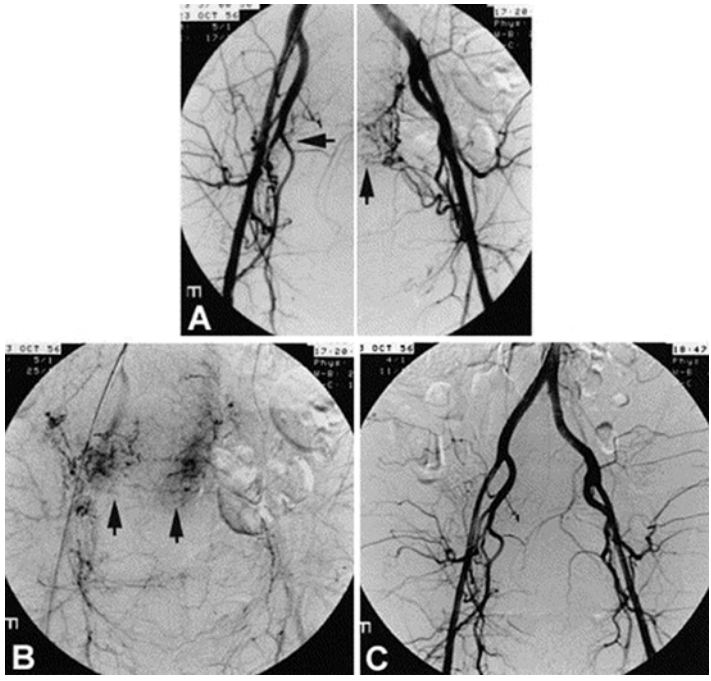

FIG. 12.4 Uterine artery embolization. Early (**a**) and delayed (**b**) digital subtraction angiogram of pelvis. Pelvic hypervascularity is clearly seen, with contrast blush at placental insertion sites (*arrowheads*). Contrast extravasation was present on right, at placental insertion site. (**c**), Angiogram obtained after embolic procedure shows complete embolization of the uterine arteries (Reprinted from the Hansch et al. [42] with permission from Elsevier)

Hypertensive Emergencies

Definitions

Hypertensive Disorders of Pregnancy Affecting up to 10 % of pregnancies, associated with significant maternal and fetal morbidity and mortality [45]. Risk factors for hypertensive disease in pregnancy include nulliparity, extremes of maternal age,

preeclampsia in prior pregnancy, obesity, pregestational diabetes, thrombophilias, chronic hypertension, renal disease, and multiple gestations [46]. Hypertension in pregnancy exists on a spectrum of clinical disease, from chronic hypertension (hypertension predating pregnancy) and gestational hypertension (new-onset hypertension without associated hematologic, hepatic, renal, or neurologic dysfunction) to preeclampsia and eclampsia (preeclampsia with seizure). Preeclampsia is defined as a syndrome of hypertension with proteinuria or with end-organ dysfunction [45]. Please see section "Diagnosis" for the diagnostic criteria of preeclampsia. Hemolysis, elevated liver enzymes, and low platelet (HELLP) syndrome is a related condition.

Delivery is usually curative for these diseases, and improvement of laboratory values occurs in the following days; hypertension usually improves within 48 h of delivery, but may rise again after 3–6 days or present for the first time after delivery. The incidence of postpartum preeclampsia is unknown, particularly as many hypertensive women are asymptomatic [47]. Preeclampsia could bring a woman to the emergency room as many as 6 weeks postpartum and should therefore not be overlooked, particularly if the presentation includes headache and associated hypertension.

Differential Diagnosis

Hypertension

- Chronic hypertension
- Gestational hypertension
- Preeclampsia
- HELLP syndrome
- Acute fatty liver of pregnancy (AFLP)
- Systemic lupus erythematosus
- Thrombotic microangiopathies (including thrombotic thrombocytopenic purpura and hemolytic uremic syndrome)

(continued)

(continued)

Renal artery stenosis
Pheochromocytoma
Drug effect: illicit drugs such as cocaine and amphetamines and withdrawal from antihypertensive medication or alcohol

Postpartum Seizure

Eclampsia
Underlying seizure disorder
Withdrawal from alcohol or benzodiazepines
Central nervous system lesions, including bleeding arteriovenous malformations or ruptured aneurysms

When You Get the Call Ask for a full set of vital signs. Pregnant patients with hypertension, particularly those at least 20 weeks of gestational age, should be transferred to the hospital's Labor and Delivery unit for maternal and fetal assessment. More commonly, a postpartum patient may present to an emergent care setting without immediately available Labor and Delivery facilities and will require initial assessment and stabilization in the emergency room [48]. If possible, however, patients within acute hypertension within 6 weeks postpartum should also be seen and assessed in a Labor and Delivery Triage unit, given obstetricians' expertise with this issue.

When You Arrive Review the full vital signs flow sheet. If severe range blood pressures are present (systolic blood pressure of at least 160 mmHg or diastolic blood pressure of at least 110 mmHg), repeat the blood pressure with a manual cuff to confirm. The length of an appropriately sized blood pressure cuff is 1.5 times the circumference of the upper arm. If severe blood pressure is confirmed, request IV access in anticipation of potentially administering parenteral medication.

History

Upon arrival, if the patient is conversant and well appearing, proceed with a full past obstetrics and medical history, including hypertensive, renal, hepatic, pulmonary, and autoimmune disease. Review any complications in this pregnancy or hypertensive diseases in a prior pregnancy. Review whether the patient has a history of epilepsy or recent head trauma. If the patient is postpartum, review her delivery date and course, and review any complications or hypertensive issues intrapartum.

Complete a review of systems, including questions about headache, visual disturbances, nausea, vomiting, shortness of breath, right upper quadrant (RUQ) pain, and acutely worsened edema, particularly in the face and hands [45]. In pregnant patients, obtain a routine obstetrical review of systems including fetal movement, vaginal bleeding, rupture of membranes, or abdominal pain.

Physical Examination

A complete physical exam should be performed, including cardiac and pulmonary exams, an abdominal exam assessing for RUQ and uterine tenderness, and a neurologic exam to assess for evidence of hyperreflexia and clonus; note edema of the upper and lower extremities and face. In pregnant patients with viable fetuses, continuous fetal monitoring is preferred during the acute assessment and blood pressure treatment. While the patient's transfer to a Labor and Delivery unit is facilitated, if possible, assessment with Doppler or ultrasound should be performed to document the fetal heart rate. An appropriate fetal heart rate is between 110 and 160 beats per minute [5].

Diagnosis

Initial laboratory assessment of a pregnant or postpartum patient presenting with new or acutely worsened hypertension

or seizure includes a complete blood count, complete metabolic panel (including liver function tests and creatinine), uric acid, lactate dehydrogenase, and a urine sample to allow for calculation of the protein to creatinine ratio. Also consider sending a urine toxicology screen as drugs of abuse can elevate blood pressure. Patients with acute focal neurologic symptoms may require emergent head computed tomography (CT) to assess for stroke. In women with preeclampsia, a CT scan may show hypodense lesions in the occipital lobes, at the gray-white matter junction [49]. In pregnant women with new-onset hypertension, a formal obstetrical ultrasound should be obtained to confirm normal fetal growth and umbilical artery Doppler flow, as fetal growth restriction is more common in hypertensive disorders of pregnancy [45].

Gestational Hypertension is diagnosed as systolic blood pressure greater than or equal to 140 mmHg or diastolic blood pressure greater than or equal to 90 mmHg on two occasions at least 4 h apart, after 20 weeks of gestation in a woman with previously normal blood pressure [45]. Women presenting with severely elevated blood pressures—a systolic blood pressure of 160 mmHg or more and/or a diastolic blood pressure of 110 mmHg or more—can receive the diagnosis within a shorter interval (minutes) to facilitate timely antihypertensive therapy. Patients diagnosed with gestational hypertension should have no other laboratory abnormalities or neurologic symptoms.

Preeclampsia is diagnosed by the same blood pressure limits as gestational hypertension, in combination with either a protein to creatinine ratio greater than or equal to 0.3 in a urine sample or a urine dipstick reading of 1+ if other quantitative methods are not available [45]. A 24-h urine collection can also be used—with 300 mg or more considered a positive finding—but this result is frequently not available in the setting of an acute presentation. In the absence of proteinuria, new-onset hypertension with the new onset of thrombocytopenia, renal insufficiency, or elevated liver enzymes is consistent with preeclampsia. Preeclampsia with

severe features, specifically, applies to patients with new-onset hypertension and any of the following:

- Thrombocytopenia: Platelet count less than 100,000/μL
- Progressive renal insufficiency: Serum creatinine concentration greater than 1.1 mg/dL or a doubling of baseline serum creatinine in the absence of other renal diseases
- Impaired liver function: Elevated serum concentrations of liver transaminases to twice normal levels, severe right upper quadrant or epigastric pain unresponsive to medication and not accounted for by alternative diagnoses, or both
- Pulmonary edema
- New-onset cerebral or visual disturbances

HELLP syndrome is further defined as the presence of thrombocytopenia with platelets less than 100,000 /μL, elevated liver enzymes with AST greater than or equal to 70 IU per liter (L), and evidence of hemolysis, including schistocytes on peripheral blood smear, lactate dehydrogenase greater than or equal to 600 IU/L, or bilirubin greater than or equal to 1.2 mg/dL [50].

Clarifying the etiology of a seizure acutely can be difficult. Idiopathic seizure disorders or intracranial pathology may be more likely as the cause of seizures after 48–72 h postpartum or if the patient is already receiving magnesium prophylaxis for the diagnosis of eclampsia [45]. In patients with known seizure disorders, serum levels of patients' antiepileptic medications should be sent to ensure serum levels are in the therapeutic range, though results are not immediately available.

Management

In pregnant patients presenting with acute or worsening hypertension, fetal considerations include reducing blood pressure to prevent placental abruption, while not reducing blood pressure so quickly as to cause placental hypoperfusion

and fetal distress. Continuous fetal monitoring during the acute diagnosis and treatment of severe hypertension or eclampsia is preferable. Of note, fetal bradycardia will often occur during maternal seizure activity and most often resolves with maternal stabilization [45].

In women with viable fetuses presenting before 34 weeks GA with preeclampsia with severe features or eclampsia, betamethasone (12 mg IM every 24 h for two doses) or dexamethasone (6 mg PO every 12 h for four doses) should be administered to promote fetal lung maturity. Delivery should not be delayed to allow for the full steroid course in the presence of uncontrollable hypertension, seizure, pulmonary edema, placental abruption, disseminated intravascular coagulation, or nonreassuring fetal status [45].

Recommendations for the timing and mode of delivery in women with hypertensive diseases of pregnancy are beyond the scope of this chapter. These guidelines are outlined in "Hypertension in Pregnancy," published by the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy [45]. In general, stable women with gestational hypertension or preeclampsia without severe features without other indications for delivery are delivered at 37 0/7 weeks GA. Delivery is usually recommended at 34 0/7 weeks GA in pregnant patients with preeclampsia with severe features without indications for earlier delivery. Delivery may be indicated prior to 34 0/7 weeks GA due to maternal or fetal instability, including uncontrollable hypertension, seizure, pulmonary edema, placental abruption, disseminated intravascular coagulation, or nonreassuring fetal status [45].

Hypertension

Pregnant patients with hypertension, particularly those at least 20 weeks of gestational age, should be transferred to the Labor and Delivery unit within the hospital for maternal and fetal assessment. On a Labor and Delivery unit, continuous

fetal monitoring can be performed while blood pressure medications are administered, which can result in decreased placental perfusion and fetal distress. Similarly, postpartum patients with acute hypertension within 6 weeks of their delivery are ideally assessed in a Labor and Delivery Triage unit, given obstetricians' expertise with this issue.

Once the diagnosis of a hypertensive disorder related to pregnancy is made in the emergent setting, the need for antihypertensives and intravenous magnesium sulfate for seizure prophylaxis should be determined, while arranging transfer to an appropriate obstetric service. Antihypertensive medications are indicated in women with blood pressures consistently in the severe range, defined as systolic blood pressures of 160 mmHg or more or diastolic pressures of 110 mmHg or more. The goal is to reduce blood pressure to below 160/110 mmHg, keeping in mind that an excessive decrease in blood pressure in pregnancy can restrict placental perfusion and cause fetal distress [48].

Labetalol is considered the first-line medication for the management of hypertensive diseases of pregnancy (Table 12.4) [45]. Drug choice should also be based upon maternal comorbid conditions, possible adverse effects, and clinician's comfort and experience with the medications.

The range of acceptable medications is broader in the postpartum period. In addition to these, please see Chap. 14, Common Postoperative and Inpatient Issues, for additional antihypertensives that could be used in postpartum patients. Angiotensin-converting enzyme inhibitors, in particular, are not recommended in pregnancy, but are safe for breastfeeding patients (as are labetalol, hydralazine, and nifedipine) [52].

For women with preeclampsia with severe features, seizure prophylaxis with magnesium sulfate is indicated [53]. Magnesium sulfate reduces the incidence of eclamptic seizures by 50 % in patients with preeclampsia [54]. Dosing regimens vary; commonly, a loading dose of 4–6 g IV is administered, followed by 1–2 g per hour as a continuous IV

Table 12.4 Antihypertensive medications in pregnancy

Antihypertensive	Dose	When to consider alternatives
Labetalol	10–20 mg IV, doubled up to 80 mg every 10–20 min, to a maximum daily dose of 300 mg	Heart block Bradycardia Acute heart failure Bronchoconstrictive disease
Hydralazine	5 mg IV or IM, redosed up to 10 mg every 20–40 min	Increased intracranial pressure Myocardial ischemia Aortic dissection May cause reflex tachycardia, headaches, hypotension
Nifedipine	10–20 mg orally, repeated in 30 min as needed	May cause reflex tachycardia or headaches

American College of Obstetricians and Gynecologists [45, 48], Johnson et al. [51], Duley et al. [54]

infusion. In pregnant patients, magnesium sulfate is continued during delivery and 24 h postpartum; in postpartum patients, magnesium sulfate is generally administered for at least 24 h [45]. In patients receiving magnesium sulfate, regular assessments of mental status, reflexes, respiratory status, and urine output should be performed to monitor for magnesium toxicity; altered mental status, loss of the patellar reflex, and depressed respiratory rate are signs of magnesium toxicity. Additionally, magnesium sulfate is contraindicated in women with heart block or myocardial damage and must be used with caution in patients with myasthenia gravis or significant renal impairment, as magnesium is renally excreted [55].

Seizure

Comprehensive management of a seizing patient is beyond the scope of this chapter, except to note that eclampsia should be very strongly considered in any pregnant patient or postpartum patient within 6 weeks of her delivery. Postpartum eclamptic seizures are more common in the first 48–72-h postpartum [45].

Eclamptic seizures are typically self-limited. Initial interventions include supportive care, airway protection to prevent aspiration, and prevention of maternal injury, while also initiating magnesium sulfate and blood pressure control. The goal is to stabilize the patient for transfer to an appropriate obstetric service.

Magnesium sulfate is administered for the indication of prevention of recurrent seizure and is a more effective prophylaxis against recurrent seizure in the eclamptic population than either phenytoin or diazepam [56]. In patients with IV access, magnesium sulfate is administered at a dose of 4–6 g IV, followed by 1–2 g per hour as a continuous IV infusion. If IV access is not yet established, deep IM administration of 10 g of magnesium sulfate (5 g IM into each buttock) can also be used [56]. Women with eclampsia should also receive antihypertensives to control elevated blood pressures to levels below 160/110 mmHg.

In rare cases, women have seizures despite magnesium sulfate treatment. An additional bolus of magnesium (2–4 mg IV) can be administered in the event of recurrent seizure, provided the patient does not have signs of magnesium toxicity [56]. In the event of refractory seizures, benzodiazepines can also be used, such as lorazepam (0.1 mg/kg IV, maximum 2 mg/min), allowing one minute to assess effect before redosing [57].

Trauma in Pregnancy with a Viable Fetus

Definitions

Trauma in Pregnancy Affects approximately 1 in 12 pregnancies and is the leading non-obstetrical cause of maternal death [58]. Trauma in pregnancy is also a considerable cause of fetal

morbidity and mortality, primarily through placental abruption and preterm birth [58, 59]. Motor vehicle collision (MVC) is a common cause of trauma, affecting 207 per 100,000 pregnancies [60]. The primary obstetrical concern with MVC is strain on the uterus, which may result in placental abruption through sheer force and tensile failure (countercoup) [61]. Intentional trauma during pregnancy is most commonly due to intimate partner violence, which increases the risk of preterm birth by 2.7-fold and of low birth weight by 5.3-fold [62].

The scope of this section is limited to non-catastrophic blunt trauma as well as a brief discussion of catastrophic trauma in pregnancy at gestational ages of fetal viability.

When You Get the Call Ask for the patient's gestational age and whether the patient is hemodynamically unstable or gravely injured. Consider enlisting available resources if significant or catastrophic injuries are suspected. Obtain a cesarean section operative kit to bring to the emergency room if the patient is reported to be gravely injured.

When You Arrive Assess the patient's mental status and hemodynamic stability. Review the patient's gestational age; if the fetus is viable, urgently request Doppler or ultrasound confirmation of fetal cardiac activity.

History

In a hemodynamically stable patient, obtain a history of the circumstances surrounding the trauma. After MVC, inquire about collision speed, whether airbags were deployed, and whether the patient was wearing a seatbelt or driving (as the steering wheel may cause direct trauma to the uterus). Ask where on her body the patient sustained impact, and inquire about ongoing symptoms of pain. Obtain an obstetrical review of systems including fetal movement, vaginal bleeding or loss of fluid, or contractions. Additionally, screen for intimate partner violence. Obtain a full past medical and surgical history as well as an obstetrical history including current gestational age and complications of the pregnancy.

Physical Examination

An initial evaluation of a pregnant woman who has suffered trauma should follow non-obstetric guidelines for trauma assessment. The patient should also be positioned in the left lateral position to reduce compression of the aorta by the gravid uterus. Assessment of fetal status should include confirming gravid state and evidence of ongoing fetal life, usually with bedside ultrasound.

Management

The primary management goal is to stabilize the condition of the mother, as fetal outcomes are directly correlated with early and aggressive maternal resuscitation (Fig. 12.5) [61, 63]. In pregnant patients who have sustained significant trauma, initial interventions include placing the patient in the full left lateral position, administering 100 % oxygen, and establishing IV access above the diaphragm [64]. Lateral positioning shifts the gravid uterus off the inferior vena cava, improving cardiac return. Hypotension, defined as a systolic blood pressure below 100 mmHg or less than 80 % of baseline, should be avoided, to ensure adequate placental perfusion.

For women who are clinically stable and well appearing following blunt trauma, an initial period of continuous fetal monitoring with fetal heart rate monitoring and tocometer to assess for contractions should be conducted over 4 h [61]. In the absence of worsening pain or evidence of six or more contractions per hour, the patient may be discharged with strict instructions to return if she develops worsening pain or vaginal bleeding. If six or more contractions per hour are documented, the patient should be observed with continuous fetal monitoring for a period of at least 24 h given the concern for possible evolving placental abruption or preterm labor. In these patients, consider checking a complete blood count, coagulation labs, and potentially a formal ultrasound, to assess for occult placental abruption.

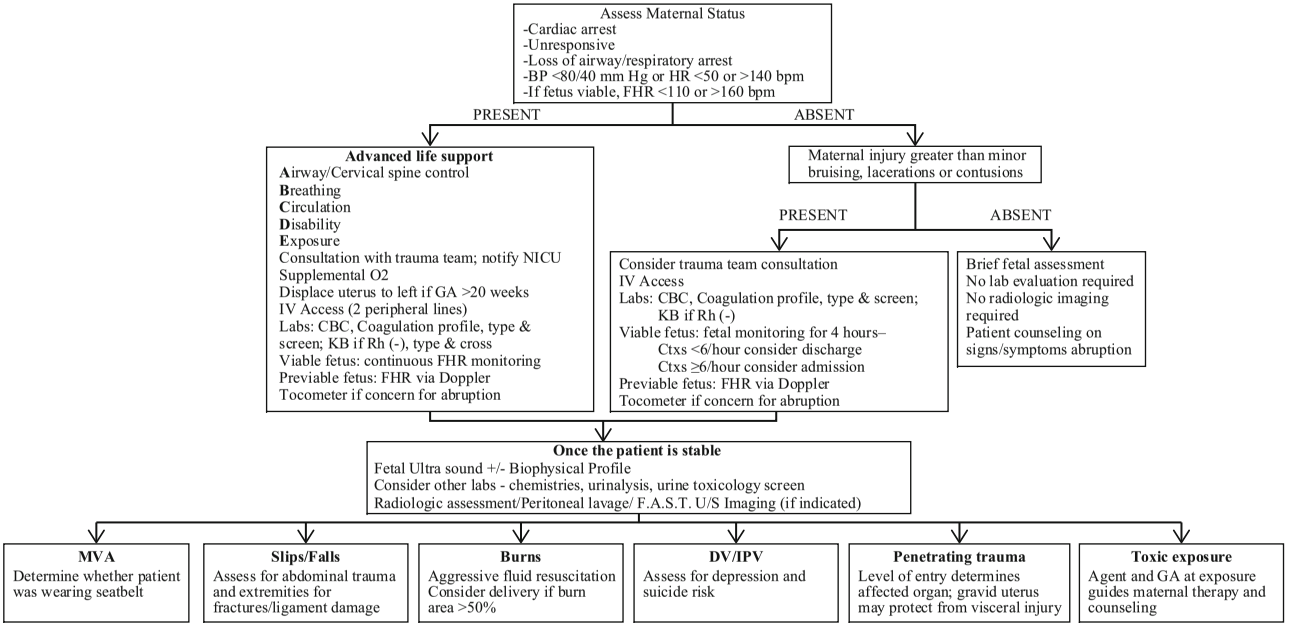

FIG. 12.5 Management algorithm for trauma in pregnancy. *BP* blood pressure, *CBC* complete blood cell count, *Ctxs* contractions, *DV* domestic violence, *FAST* focused assessment with sonography for trauma, *FHR* fetal heart rate, *GA* gestational age, *HR* heart rate, *IPV* intimate partner violence, *ISS* injury severity score, *IV* intravenous, *KB* Kleihauer-Betke, *MVA* motor vehicle accident, *NICU* neonatal intensive care unit, *O2* oxygen, *U/S* ultrasound (Reprinted from the Mendez et al. [61] with permission from Elsevier)

Women who are Rhesus factor (Rh) negative are at risk for isoimmunization if fetomaternal hemorrhage occurs. Though the true incidence is unknown, it is estimated that fetomaternal hemorrhage occurs in 8–30 % of pregnant women involved in trauma [65]. It is recommended that all Rh-negative mothers who present with a history of abdominal trauma should receive one 300 mg prophylactic dose of Rho(D) immune globulin within 72 h of the traumatic event, if they have not received a dose within the prior 12 weeks [61]. A Kleihauer-Betke (KB) test can be sent to quantify fetomaternal hemorrhage, chiefly to determine if additional doses of Rho(D) immune globulin are indicated [61].

In the event of cardiac arrest associated with catastrophic trauma, the 2010 American Heart Association guidelines account for the altered anatomy and physiology of pregnancy, recommending prompt airway management and performance of chest compressions slightly higher on the sternum than usual, in the supine position with manual left uterine displacement [64]. If manual leftward displacement of the uterus does not result in successful resuscitation, the patient can be positioned in a leftward tilt, up to 30° [66]. Defibrillation may be used as needed, as no studies have documented maternal or fetal harm from this intervention; recommended drug dosages need not be altered due to pregnancy [64].

If these interventions fail to resuscitate a patient after 4 min of chest compressions, the treatment team must move forward with cesarean delivery so as to optimize cardiopulmonary resuscitation (CPR) and survival of mother and infant. Cesarean section should be considered in any pregnancy at 20 weeks GA or more, or in any pregnancy in which the fundus reaches the umbilicus, due to aortocaval compression [64]. Effective maternal resuscitation is not possible until optimal cardiac output and venous return are restored by delivery of the fetus [67]. Given the possible need for emergent cesarean, preparations for the procedure should commence at the onset of CPR.

Postpartum Infectious Complications

Differential Diagnosis

Fever

- Wound infection (perineal or cesarean wound)
- Endomyometritis
- Pelvic hematoma or abscess
- Mastitis or breast abscess
- Cystitis
- Pyelonephritis
- Necrotizing fasciitis
- Septic pelvic thrombophlebitis
- Ovarian vein thrombosis
- Deep vein thrombosis (DVT)
- Pulmonary embolism (PE)
- Pneumonia
- Medication effect (drug fever)
- *Clostridium difficile* colitis
- Urinary tract or bowel injury at cesarean section
- Retained foreign body at cesarean section

Definitions

Endomyometritis A polymicrobial infection of the decidua or myometrium and parametrial tissues. Endomyometritis accounts for approximately 2 % of postpartum patient presentations to the emergency room [68]. Risk factors for postpartum endomyometritis include cesarean delivery, lower socioeconomic status, obesity, young maternal age, nulliparity, prolonged labor induction, and meconium-stained amniotic fluid [69].

Mastitis Occurs in up to 10 % of lactating women, usually occurring 2 weeks after delivery [70, 71]. Mastitis is most often caused by methicillin-sensitive *Staphylococcus aureus*,

though methicillin-resistant *Staphylococcus aureus*, *Streptococcus pyogenes, Escherichia coli*, and coagulase-negative staphylococci are also causal organisms [72]. Patients may report a history of difficult or inconsistent breastfeeding or cracked nipples, both of which predispose women to mastitis [73].

When You Get the Call Ask for a complete set of vital signs to assess for hemodynamic instability. Begin to formulate a differential diagnosis regarding the possible source of the infection.

When You Arrive Review the patient's vital signs to assess for hypotension, tachycardia, or hypoxia. Review the patient's discharge summary and cesarean section operative report if available, including the extent of dissection, complications, administration of perioperative antibiotics, and use of thromboprophylaxis.

History

Review with the patient when her primary symptoms began, and any associated symptoms, including but not limited to fever, localizing pain, nausea, vomiting, diarrhea, dysuria, urinary frequency, or foul-smelling vaginal discharge. Ask the patient for the date and mode of her delivery, and review any complications of the delivery including infections, retained products of conception, postpartum hemorrhage, postpartum dilation and curettage, or other interventions. For patients who had vaginal deliveries, review whether the patient had an episiotomy or perineal laceration. Ask whether the patient is breastfeeding and whether she recently stopped breastfeeding or changed the duration or frequency of feeding. Ask the patient whether she resumed sexual activity since her delivery, which is usually prohibited until 6 weeks postpartum due to risk of ascending infection.

Review the patient's obstetrical history and her full medical history, including risk factors for infection such as obesity, diabetes, and immunosuppression [74]. Ask the patient

whether she has a history of venous thromboembolism or known thrombophilia, though patients are hypercoagulable in the postpartum period regardless. Review her prior surgical history, as prior surgeries may increase the risk of adhesions and intraoperative injury to other organs. Make note of any current medications, including immunosuppressant medications or anticoagulant therapy.

Physical Examination

In the setting of fever, the patient should have a head-to-toe assessment, including assessments of the oropharynx, heart, lungs, abdomen, skin, and lower extremities. An abdominal exam should focus on the cesarean section incision, if applicable, assessing for erythema, drainage or fluctuance, and the uterine fundus, assessing for tenderness. A bimanual exam may be helpful in the assessment of endomyometritis—noting fundal tenderness, cervical motion tenderness, or malodorous discharge—but may be far too uncomfortable for recently postpartum patients. Any perineal laceration or episiotomy repair should be inspected, using a gynecology bed with stirrups for better visualization. In addition, a thorough breast exam should be performed to assess for erythema, skin breakdown, or fluctuance to suggest the presence of an abscess.

In some cases of wound breakdown, it may be necessary to administer topical or local anesthetics, or even light sedation, in order to fully explore the extent of wound breakdown. Cesarean incisions with significant drainage or skin separation should be probed for fascial dehiscence.

Diagnosis

A temperature of 100.4 °F (38 °C) on two occasions more than 4 h apart or a single temperature of 101 °F (38.5 °C) constitutes a fever [75]. Patients with significant complications, such as severe wound infection or pelvic abscess, may present with septic physiology—including tachycardia,

tachypnea, hypotension, and/or oliguria—which must be identified and treated quickly (Table 12.1) [76–78]. For further management of sepsis, see Chap. 1, Acute Pelvic Pain.

Laboratory testing should include a complete blood count with a differential and urinalysis. In patients with a fever of 38.5 °C (101 °F) or more, consider collecting blood cultures in addition to a urine culture, and cultures of any purulent wound exudate. Many diagnoses can be made without imaging in the postpartum population (including mastitis, endomyometritis and superficial wound complications). Abdominal CT may be indicated in ill-appearing patients, particularly after cesarean section, or those who have failed outpatient management. Of note, hemostatic agents (such as Gelfoam®, Pfizer, New York, NY) placed at the time of cesarean section may appear as an abscess on imaging. Diagnosis and management of the most common postpartum infectious complications—breast infections, endomyometritis and wound infections—are discussed together in the next section.

Management

Please see Chap. 16, Complications of Minimally Invasive Gynecologic Surgery, for the diagnosis and management of pelvic abscess and hematoma, cystitis, pyelonephritis, necrotizing fasciitis, septic pelvic thrombophlebitis, and ovarian vein thrombosis.

Breast Infections

Women with mastitis or breast abscess typically report tenderness and erythema of the affected breast, often associated with fever, fatigue, and headaches [73]. Women with breast engorgement, which is a noninfectious process, may present similarly. Breast engorgement is, however, typically a bilateral process characterized by breast firmness and warmth, without erythema or high fever [71]. Breast engorgement usually begins within 48–96 h postpartum [79].

Patients with the diagnosis of mastitis suggested by exam can be started on antibiotics. In patients with refractory or hospital-acquired cases of mastitis, a culture of the breast milk may help guide treatment [73]. Patients with refractory mastitis or palpable mass on exam should have a breast ultrasound to assess for abscess. Empiric treatment of uncomplicated mastitis is dicloxacillin (500 mg PO every 6 h), cephalexin (500 mg PO every 6 h), or amoxicillin-clavulanate (875 mg PO every 12 h) [73]. If MRSA is suspected, trimethoprim-sulfamethoxazole (160–800 mg, PO every 12 h) or clindamycin (300 mg PO every 6 h) can be prescribed. Optimal length of therapy has not been described; commonly antibiotics are prescribed for 10–14 days.

In patients diagnosed with mastitis, use of warm compresses and breast massage at initiation of breastfeeding may be helpful. Nonsteroidal anti-inflammatory medications can be used for pain. Patients with either mastitis or engorgement often stop breastfeeding due to concerns over infecting their infant, and this can exacerbate the problem. Women with mastitis should breastfeed or pump every 2–3 h [80].

Breast abscess is initially managed with needle aspiration and antibiotics [81]. The needle aspiration is increasingly performed by interventional radiologists [82]. Large, multiloculated, or refractory cases may require surgical consultation for incision and drainage.

Endomyometritis

Women with postpartum endomyometritis typically present with abdominal pain and fevers and may report vaginal bleeding or foul-smelling discharge. On physical examination, significant fundal tenderness along with fever is highly suggestive of endomyometritis, and the diagnosis is usually made clinically.

Most women with postpartum endometritis and fever generally require admission for IV antibiotic therapy. Commonly used regimens include (1) gentamicin (4–7 mg/kg IV daily), clindamycin (900 mg IV every 8 h), and ampicillin

(2 g IV every 6 h) and (2) ampicillin-sulbactam (3 g IV every 6 h) [83]. Improvement in symptoms typically occurs within 48–72 h of treatment in the majority of women. For women without improvement, pelvic ultrasound should be considered to assess for abscess or septic pelvic thrombophlebitis, and consultation with obstetrics, interventional radiology, or general surgery (depending on the suspected infectious source) may be indicated for further management.

Physicians should maintain a high index of suspicion for a rare but potentially lethal cause of postpartum endometritis: *Streptococcus pyogenes*, also called group A streptococcus (GAS), which is associated with a mortality rate of 2 % [84]. Once patients develop fulminate sepsis, mortality ranges from 30 to 70 % [85]. Most patients present within days of delivery, though patients may also develop GAS endometritis 2 weeks or more postpartum [86]. Patients with GAS endometritis usually have high fevers (above 102 °C) and flu-like symptoms, including myalgias, nausea, and vomiting [87]. Patients may have little fundal tenderness on exam, though they may report severe general abdominal pain [87]. An endometrial culture (or at least cervical/vaginal culture) should be obtained to confirm the diagnosis. Patients with GAS endometritis should receive penicillin (2–4 million units IV every 4–6 h) and clindamycin (600–900 mg every 8 h intravenously) for 10–14 days [88]. Patients with severe penicillin allergies can receive vancomycin (30 mg/kg per day IV in two divided doses) and clindamycin. Women without improvement, or who are developing signs of sepsis, require prompt surgical management—usually hysterectomy—to control the source of infection [86, 87].

Wound Infections

Worsening pain at an incision, accompanied by warmth, erythema, or induration, is suggestive of a surgical site infection. Complications of cesarean incisions, including infection, hematoma, and dehiscence, occur in 1–2 % of patients [89].

Forty percent of these wound infections present after discharge from the hospital [90]. In patients with possible infection of the cesarean incision, if examination or imaging suggests the presence of a fluid collection under the skin—seroma, hematoma, or purulence—or purulent fluid is expressed from the incision, a wound should be opened, irrigated, and managed with wet-to-dry dressings [91–93]. In instances of fluid collection and breakdown, the wound should be carefully probed to ensure that the fascia is intact. Fascial dehiscence may also be suggested by abdominal CT. If there is any concern for fascial dehiscence, the patient should be transferred to Labor and Delivery if available; otherwise, a general surgery consultation should be obtained, to arrange for wound exploration and repair [93].

While opening a superficial collection in a cesarean wound can be a sufficient management, if surrounding erythema is observed, or fever and/or leukocytosis is documented, antibiotics should be given. For mild symptoms, cephalexin (500 mg PO every 6 h) or trimethoprim-sulfamethoxazole double strength (160–800 mg PO every 6 h) can be used [88]. Trimethoprim-sulfamethoxazole and clindamycin (300–450 mg PO every 6 h) provide coverage for methicillin-resistant *Staphylococcus aureus* [94]. Evidence of severe or systemic infection requires admission for parenteral antibiotics.

Wound infections of the perineum can occur after laceration or episiotomy. The rate of perineal wound complications is estimated to be 0.5–6 % [51, 83]. Pain and dysuria are the most common presenting symptoms, with or without fevers and malaise. Thorough examination, including a rectal exam, is needed to determine the extent of the infection and/or breakdown; local or general anesthesia may be required to fully explore the wound.

Treatment of infected perineal wounds involves establishing drainage, typically through removing sutures and debriding the infected wound. Broad-spectrum antibiotic coverage should be initiated for severe perineal wound infections; regimens used for endomyometritis can be applied. In addition to IV antibiotics, further wound exploration may be warranted

with debridement of any necrotic tissue. There is currently insufficient evidence to determine whether healing by secondary intention or reoperation is superior [96]. If there is any clinical suspicion for severe, life-threatening infection such as necrotizing fasciitis, aggressive and immediate surgical exploration is warranted; please see Chap. 16, Complications of Minimally Invasive Gynecologic Surgery, for more information.

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Chapter 13
Preparing for Urgent or Emergent Surgery

Paula C. Brady and Julianna Schantz-Dunn

Definition

Emergent Surgery Typically scheduled within 6 h [1]. In gynecology, emergent operative cases usually involve ovarian torsion, intra-abdominal hemorrhage, severe intra-abdominal infection, intrauterine infection, or vaginal hemorrhage. Urgent surgery is typically scheduled within 6–24 h.

Surgical Risk

Medical conditions conferring increased risk of surgically related severe complications and mortality include diabetes, hypertension, malignancy, prior cardiac events or congestive heart failure, severe chronic obstructive pulmonary disease (COPD), current smoking, dialysis and/or renal failure, and obesity. The presence and severity of these conditions should be considered when determining whether a surgical case should be scheduled emergently or can be delayed to provide

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time for medical optimization. The American College of Surgeons incorporates these factors into a risk calculator, providing estimated risks of cardiac, thromboembolic, renal, and infectious complications and death; the calculator is available at http://riskcalculator.facs.org [2].

Many grading systems have attempted to quantify the risk of adverse cardiac events, specifically related to surgery. Intraperitoneal surgeries are classified as intermediate risk, with reported risk of cardiac death or nonfatal myocardial infarction of 1–5 %, while endoscopic, superficial, or ambulatory surgery is generally associated with a cardiac risk of less than 1 % [3]. Emergency surgeries generally carry higher risk of adverse events. Particularly high-risk cardiac conditions, which will result in the delay or cancellation of nonemergent cases, include unstable coronary syndromes, decompensated heart failure, significant arrhythmias (including high-grade atrioventricular block, new or symptomatic ventricular arrhythmias, supraventricular arrhythmias with a heart rate greater than 100 beats per minute, and symptomatic bradycardia), and severe aortic or mitral stenosis [3].

Careful consideration should also be given to surgical planning in obese patients. Moderately obese patients (class II obesity or body mass index (BMI) greater than 35 kg/m^2) have a higher risk of surgical complications, venous thromboembolism, and wound infections than their normal weight counterparts [4]. Similar to normal weight patients, obese patients have improved outcomes with minimally invasive surgery. Minimally invasive surgery, however, comes with its own set of challenges in the obese patient. Positioning and retracting as part of vaginal surgery may be difficult, while ventilating a morbidly obese patient while in Trendelenburg position can be challenging [5]. Consider asking the operating room to prepare long instruments and trocars, and a bariatric bed and stirrups, as needed.

In patients with these medical conditions, medicine consult should be obtained for clearance. The anesthesia team should also be contacted as soon as possible to discuss the patient's current condition and medical history.

Preoperative Testing

The vast majority of gynecology patients requiring urgent or emergent surgery will have had a complete blood count collected as part of their assessment. A complete blood count should be collected in any patient with active bleeding, anemia, chronic illness, or a high likelihood of blood loss at the time of surgery [6].

A basic metabolic panel, including serum creatinine, is not routinely recommended but should be collected in patients with chronic illness or taking medications that predispose to electrolyte abnormalities or renal dysfunction, including diuretics, digoxin, angiotensin-converting enzyme inhibitors, and angiotensin receptor blockers [4]. A blood type and antibody screen should be collected in all pregnant patients, patients with preoperative anemia, ongoing bleeding, or those who will undergo surgery with moderate to high risk of bleeding, such as resection of an ectopic pregnancy [7]. Coagulation testing (prothrombin time (PT) and activated partial thromboplastin time (aPTT)) is only strictly indicated in patients receiving anticoagulation, those with a history of bleeding after procedures, or with coagulation abnormalities, such as coagulation factor deficiencies, von Willebrand disease, liver disease, and disseminated intravascular coagulation [4]. A pregnancy test should be checked in any woman who is not yet postmenopausal [8].

A 12-lead electrocardiogram (ECG) is recommended for patients with known coronary artery disease, significant arrhythmia, peripheral arterial disease, cerebrovascular disease, or other significant structural heart diseases [1]. Routine screening ECGs can also be considered in asymptomatic patients, particularly over age 50 years, undergoing intermediate- or high-risk surgery [9].

Chest radiograph may be considered in patients who smoke or those with recent upper respiratory tract infections, known chronic obstructive pulmonary disease (COPD), or cardiac disease, though radiographs are not strictly required in patients with stable COPD or cardiac disease or resolved respiratory infection [6]. The American Heart Association suggests obtaining chest radiographs in patients with significant obesity (BMI greater than 40 kg/m^2) [10].

Consent

The consent process involves discussing the risks, benefits, and alternatives of the planned procedure. The discussion of the management options should include medical, surgical, and expectant management. Include all possible procedures on the consent form, such as ovarian cystectomy and unilateral salpingo-oophorectomy for a patient scheduled for a diagnostic laparoscopy for suspected ovarian torsion. In addition, for diagnostic laparoscopies, include the possibility of a negative laparoscopy (the absence of identifiable pathology). Always include a provision for reparative surgery in the event of iatrogenic injury. During the consent process, specify whether the patient is willing to accept blood products.

Medicaid laws require that federally insured women undergoing hysterectomy or other procedures resulting in sterility sign a sterilization or hysterectomy consent form prior to the procedure. Typically these consents require a 30-day waiting period, though exceptions are made in cases of emergency abdominal surgery. State-specific forms can be found online or on the Department of Health and Human Services website at http://www.hhs.gov/opa/pdfs/consent-for-sterilization-english-updated.pdf. If time allows, the patient should also complete a health care proxy form.

Antibiotic Prophylaxis

For reference, most gynecologic operative cases are considered "clean" or "clean-contaminated," which is defined as controlled entry into the gastrointestinal, genital, or urinary tract [11]. "Contaminated" cases involve accidental wounds, major breaks in sterile technique, spillage of gastrointestinal contents, or presence of acute nonpurulent inflammation. "Dirty" cases are those involving clinical infection, perforated viscera. Recommended antibiotic prophylaxis, to be given immediately preoperatively, is shown in Table 13.1 [12].

Multiple studies have demonstrated a reduction in vaginal cuff complications in women with bacterial vaginosis (BV)

Table 13.1 Recommended antibiotic prophylaxis

Procedure	Antibiotics
Hysterectomy	Cefazolin 1–3 g IV (weight based)
Urogynecology procedures, including mesh placement	• Clindamycin 600 mg IV plus gentamicin 1.5 mg/kg IV or quinolone (ciprofloxacin, levofloxacin, moxifloxacin) 400 mg IV or aztreonam 1 g IV • Metronidazole 500 mg IV plus gentamicin 1.5 mg/kg IV or quinolone 400 mg IV
Dilation and evacuation of pregnancy	• Doxycycline 200 mg PO or IV • Azithromycin 1 g PO or IV plus metronidazole 500 mg PO or IV
Laparoscopy	None
Laparotomy	None
Hysteroscopy	None
IUD insertion	None
Endometrial biopsy	None

American College of Obstetricians and Gynecologists [12]
Please see Chap. 8, Spontaneous Abortion, for more information on antibiotic prophylaxis for dilation and evacuation.

who were treated preoperatively with metronidazole. While urgent surgery may not afford the ideal preoperative treatment time of 5–7 days, a dose of metronidazole (500 milligrams (mg) IV) preoperatively in women with current BV is an option [13].

Thromboprophylaxis

Risk factors for venous thromboembolism include but are not limited to increasing age, immobility, sepsis, malignancy, pregnant or postpartum state, use of estrogen-containing medications or selective estrogen receptor modulators, respi-

ratory failure, inflammatory bowel disease, nephrotic syndrome, indwelling venous catheters, varicose veins, obesity, and smoking [14, 15]. Cardiovascular issues placing patients at high risk of thromboembolism include artificial cardiac valves, prior stroke, transient ischemic attack or venous thromboembolism, thrombophilias (including factor V Leiden, prothrombin variant 20210A, antiphospholipid antibodies, deficiency of antithrombin, protein C, or protein S) and other hematologic abnormalities including heparin-induced thrombocytopenia and myeloproliferative disorders such as polycythemia vera [16, 17].

According to the American College of Obstetricians and Gynecologists, surgeries that are low risk for thromboembolism are defined as those lasting less than 30 min, in patients 40 years of age or less without additional risk factors; these patients do not require additional thromboprophylaxis beyond early ambulation postoperatively [15]. Sequential compression boots should be placed at the time of surgery for all other patients, except on an extremity with known deep vein thrombosis, due to theoretical risk of embolism [18]. For the highest-risk patients, particularly those with active malignancy, hypercoagulable state, or prior thromboembolism, a single dose of heparin 5000 units can be given subcutaneously preoperatively, which has not been associated with additional blood loss intraoperatively [19].

For patients admitted to the hospital after surgery, thromboprophylaxis should be continued postoperatively and should be decided by the surgical team based on the patient's risks of thromboembolism and postoperative bleeding. Postoperative thromboprophylaxis can include sequential compression boots, heparin (5,000 units subcutaneously every 8–12 h), dalteparin (2500–5000 units subcutaneously daily), or enoxaparin (40 mg subcutaneously daily) [15]. Unfractionated heparin is preferable to dalteparin and enoxaparin in patients with renal insufficiency. Pharmacologic thromboprophylaxis can typically start 12 h postoperatively; the anesthesiologist should be involved in this decision making for patients receiving neuraxial anesthesia, which may require withholding anticoagulation (particularly for epidural catheter removal).

Anticoagulation Reversal

In patients requiring urgent or emergent surgery—particularly intra-abdominal surgery—while anticoagulated, reversal of their anticoagulation medications is usually necessary to minimize intraoperative bleeding. The risk of intraoperative bleeding, however, must be balanced against thromboembolic risk, ideally in consultation with the patient's hematologist or cardiologist.

Warfarin can be reversed with administration of vitamin K (5–10 mg IV), fresh frozen plasma or prothrombin complex concentrates with a target INR of 1.5 or less [20]. Prothrombin complex concentrates (such as Kcentra®, CSL Behring GmbH, King of Prussia, PA) confer the advantages of rapid infusion and no need for thawing, but are reserved for life-threatening hemorrhage due to elevated risk of thromboembolism [21]. For the oral direct thrombin inhibitor, dabigatran, the only antidote is a monoclonal antibody called idarucizumab that can be administered in 2 doses of 2.5 g IV each, given 15 mins apart [22]. No antidotes exist for the factor Xa inhibitors (rivaroxaban, apixaban, and edoxaban); antifibrinolytic medications (such as tranexamic acid) can be used in patients with active bleeding, while prothrombin complex concentrates are reserved for refractory severe hemorrhage, due to increased risk of thromboembolism [23].

Unfractionated heparin has a short half-life, (approximately 60 mins) but if necessary, 1 mg of protamine sulfate will reverse 100 units of heparin [24]. Low molecular weight heparin (LMWH) is incompletely reversed with protamine sulfate, but for clinically significant bleeding or high risk of intraoperative bleeding in the setting of LMWH given within the past 8 h, 1 mg protamine sulfate can be given for each milligram of enoxaparin. Less protamine sulfate is needed if the LMWH was given more than 8 h prior [21]. If necessary, residual anticoagulant activity can be assessed by checking an aPTT in patients who received unfractionated heparin, while an anti-Xa level will reflect LMWH activity. Please refer to 13.2 for more information.

TABLE 13.2 Emergent anticoagulation reversal

Medication	Mechanism of action	Laboratory monitoring	Half-life in healthy individuals	Antidote	Antidote dose	Side effects of antidote (including, not limited to)
Warfarin	Blocks hepatic synthesis of vitamin K-dependent clotting factors (II, VII, IX, X)	PT, INR	Varies (mean 40 h)	Vitamin K	5–10 mg IV	Hypersensitivity
				Fresh frozen plasma (FFP)	Depends on starting INR	Infection Febrile or allergic reaction Volume overload
				For life-threatening bleeding: prothrombin complex concentrates, such as Kcentra® (CSL Behring GmbH, King of Prussia, PA), containing factors II, VII, IX, X, protein C and S	Kcentra®: INR 2 to <4: 25 units/kg, max 2500 units INR 4–6: 35 units/kg, max 3500 units INR >6: 50 units/kg, max 5000 units	Hypersensitivity Thromboembolism (similar to FFP, 3–4 %) May contain heparin; contraindicated in patients with heparin-induced thrombocytopenia

Dabigatran	Direct thrombin inhibitor	None, though aPTT may be elevated	12–17 h	Oral charcoal if taken in the last 2 h, or dialysis Idarucizumab for severe hemorrhage	5 g IV (two 2.5 g doses 15 min apart)	Hypersensitivity Rebound elevation in coagulation parameters (in as little as 1–4 h) Thromboembolism Use with care in hereditary fructose intolerance
Rivaroxaban, apixaban, edoxaban	Factor Xa inhibitor	None routinely, though Anti-Xa can be checked	Rivaroxaban (5–9 h, prolonged to 11–13 h in elderly) Apixaban (11.5 h) Edoxaban (10–14 h)	None – Oral activated charcoal if medication taken in the last 2 h – Consider antifibrinolytic medications (such as tranexamic acid or aminocaproic acid). Little data and off-label, but risks are low – For life-threatening ongoing hemorrhage despite transfusion and antifibrinolytic medication, can consider prothrombin complex concentrates (off-label)	Tranexamic acid: 10 mg/kg up to 1 g, or 1 g presumptively	Adjust for renal impairment Color vision change, visual loss Thromboembolism (controversial, use with caution) Contraindicated in DIC and subarachnoid hemorrhage

(continued)

TABLE 13.2 (continued)

Medication	Mechanism of action	Laboratory monitoring	Half-life in healthy individuals	Antidote	Antidote dose	Side effects of antidote (including, not limited to)
Unfractionated heparin	Potentiates antithrombin activity (inhibiting Xa and thrombin)	aPTT and/or anti-Xa	Variable IV: 30–60 min (longer for larger loading doses) Subcutaneous: 1–2 h	Protamine sulfate (PS)	Maximum 50 mg Heparin <30 min prior: 1 mg PS per 100 units of heparin Heparin 30 min – 2 h prior: 0.5–0.75 mg PS per 100 units of heparin Heparin >2 h prior: 0.25 mg PS per 100 units of heparin Continuous IV heparin: calculate PS dose based on cumulative heparin dose given in last 2–3 h	Hypersensitivity/ anaphylaxis, particularly in patients with severe fish allergy or diabetics with prior exposure to protamine-containing insulin (NPH) Heparin "rebound" may occur, and repeat PS dosing may be required in 2–4 h

Low molecular weight heparin (enoxaparin, dalteparin)	Potentiates antithrombin activity (inhibiting Xa and thrombin to a lesser extent)	None routinely, though Anti-Xa can be checked	Subcutaneous enoxaparin (4.5 h) Subcutaneous dalteparin (3–5 h)	Protamine sulfate (PS) provides incomplete neutralization (off-label)	Maximum 50 mg Enoxaparin <8 h prior: 1 mg PS per 1 mg enoxaparin Enoxaparin ≥8 h prior: 0.5 g PS per 1 mg enoxaparin Dalteparin: 1 mg PS per 100 anti-Xa units of dalteparin	Hypersensitivity/ anaphylaxis, particularly in patients with severe fish allergy or diabetics with prior exposure to protamine-containing insulin (NPH) Heparin "rebound" may occur, and repeat PS dosing may be required in 2–4 h

Citations are provided in the text

Please see Chap. 2, Vaginal Hemorrhage, for the management of bleeding attributed to coagulation disorders, including disseminated intravascular coagulation and von Willebrand disease.

Resuscitation and Blood Products

For patients with active bleeding that will be managed surgically, active resuscitation should begin while preparing to proceed to surgery. Crystalloids, such as normal saline and lactated Ringer's solution, are used as first line for maintaining hemodynamic stability, but each additional liter of crystalloid transfused will further dilute the concentration of packed red blood cells—thereby lowering oxygen-carrying capacity to target tissues—and coagulation factors.

In patients with hemorrhagic shock who are too unstable to wait for cross-matched products, the use of emergency release O-negative blood is recommended. Please refer to Chap. 1, Acute Pelvic Pain, for more information on the diagnosis of hemorrhagic shock [25]. In rare cases of gynecology patients requiring massive transfusion, recommendations extrapolated from the trauma literature include a 1:1:1 transfusion ratio of packed red blood cells, fresh frozen plasma, and platelets, meaning 6 units of pooled random donor platelets (which equals one apheresis platelet unit) should be given for every 6 units of red blood cells and 6 units fresh frozen plasma [26–28].

Complications of blood transfusions include hemolytic and non-hemolytic (immune-mediated) reactions, sepsis, Transfusion-Associated Circulatory Overload (TACO) and Transfusion-Related Acute Lung Injury (TRALI). TACO and TRALI are discussed in Chap. 15, High-Acuity Postoperative and Inpatient Issues. In general, if an acute reaction to a blood product is suspected (particularly in patients with acute fever, flank pain and hypotension), the infusion should be stopped, followed by IV hydration, confirmation of patient and blood product identifiers, and blood bank notification.

Most hemorrhage encountered in gynecologic patients can be managed in a goal-oriented manner. Resuscitation goals include hemoglobin of at least 7 g per deciliter (dL), platelets above 50,000 per microliter (μL), fibrinogen above 100 mg/dL, and an INR less than 1.5 [29–32]. Blood products and their effects on laboratory parameters are shown in Table 13.3. The patient's blood pH and electrolytes (particularly calcium and potassium) should be closely monitored in the setting of multiple transfusions.

Certain physiologic goals of resuscitation can also be observed. A patient's goal heart rate should generally be less than 100 beats per minute, with urine output at least 0.5 mL per kilogram per hour. Maintaining a normal core temperature is also vital to resuscitation; patients who are hypothermic will have impaired coagulation [33]. Removing wet blankets or towels and using fluid warmers and warming blankets can help maintain a safe core temperature.

In addition to allogeneic blood transfusion, consideration should be given to autologous blood transfusion, which can be accomplished with intraoperative blood salvage; Cell Saver® (Haemonetics Corporation, Braintree, MA) is one such device. Intraoperative blood salvage requires coordination with a perfusionist. Advantages to autologous blood transfusion include avoiding allogeneic blood transfusion—and associated reactions and infections—as well as decreased time to prepare blood products [34]. Blood salvage is contraindicated in cases with bacterial contamination or malignancy. Pregnancy is not a contraindication, and studies have demonstrated the benefit of autologous blood transfusion in the setting of ruptured ectopic pregnancies [35, 36].

As an adjunct to treatment of acute bleeding, intravenous tranexamic acid, an antifibrinolytic medication, can be used to reduce blood loss. Tranexamic acid is administered in a dose of 10 mg/kg for a maximum of 1 g, or 1 g presumptively (extrapolating from the trauma literature) intravenously over 10 min and repeated every 8 h as needed [37–40]. Contraindications of tranexamic acid include, but are not limited to, acquired defective color vision and active intravascular clotting. The risk of thromboembolism associated with

TABLE 13.3 Blood products

Blood product	Lab indicator	Contains	Typical effect
Packed red blood cells (PRBC)	Hemoglobin below 7 g/dL or hematocrit below 21 %	Packed red cells	1 unit will raise hemoglobin by 1 g/dL or hematocrit by 3 %
Platelets	Platelets below 50,000/μL	Platelets	1 apheresis unit of platelets (usually a 6 pack of pooled donor platelets) will raise platelets by 30,000–50,000
Fresh frozen plasma (FFP)	INR above 1.5	All clotting factors and 500 mg of fibrinogen	Use of FFP (may require multiple units) will correct an INR to 1.3 at best
Cryoprecipitate	Fibrinogen below 100 mg/dL	1 bag (five units) contains 1000 mg fibrinogen as well as factor VIII, factor XIII, and von Willebrand factor	Will raise fibrinogen approximately 40 mg/dL
Fibrinogen concentrate (available commercially in the United States as RiaSTAP®, CSL Behring GmbH, King of Prussia, PA)	Fibrinogen below 100 mg/dL	1 vial (mixed in 50 cc sterile water) contains 900–1300 mg of fibrinogen	Will raise fibrinogen approximately 40 mg/dL

Santoso et al. [42], Arya et al. [43], Sharma et al. [29], Bell et al. [44]

tranexamic acid is controversial; overall, this medication should be used with caution in patients at high risk for thromboembolism, including those with known thrombophilia or a history of venous thromboembolism [41]. Dosing should be adjusted in patients with renal dysfunction.

Aminocaproic acid is another anti-fibrinolytic medication that can be used instead of tranexamic acid; aminocaproic acid is given as 4–5 g IV (in 250 mL of diluent over 1 h), then 1 g IV per hour until bleeding is controlled [38, 45, 46]. Studies have also reported using desmopressin in cases of severe hemorrhage; desmopressin (0.3 μg/kg subcutaneously or IV) is typically given in the setting of platelet dysfunction or type I von Willebrand disease. Though data are lacking, it is sometimes given as adjunct treatment to enhance platelet function in the setting of hemorrhage, as the risk of thromboembolism has been shown to be low; side effects include vasoconstriction [40, 46].

In cases of life-threatening hemorrhage in patients taking warfarin or oral direct anticoagulants who have failed more conservative measures, prothrombin complex concentrates such as Kcentra® (CSL Behring GmbH, King of Prussia, PA) have been used [46, 47]. Prothrombin complex concentrates are contraindicated in patients with DIC and heparin-induced thrombocytopenia. The risk of thrombosis with prothrombin complex concentrates has been shown to be similar to the risk with FFP (3–4 %) [47]. This thromboembolism risk likely also reflects the underlying condition requiring anticoagulation.

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Part II
Inpatient and Post-procedural Care

Chapter 14
Common Postoperative and Inpatient Issues

Paula C. Brady and J. Sawalla Guseh

Fever and incisional erythema or ecchymosis are common postoperative calls. Please refer to Chap. 16, Complications of Minimally Invasive Gynecologic Surgery, for more information.

Oliguria

Definitions

Oliguria Urine output of less than 0.3–0.5 mL per kg per hour or less than 300–500 mL per day [1]. Urine output is reliant on adequate circulation to the kidneys, intrinsic renal function, and unobstructed urine drainage from the kidneys, ureters and bladder. Oliguria may be the first marker of hemorrhage and impending hemodynamic instability, particularly in a

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young healthy woman, and should be thoughtfully assessed when it occurs.

"Third Spacing" Extravasation of fluid from the intravascular space, commonly seen in patients with advanced malignancy, sepsis, and ovarian hyperstimulation syndrome (OHSS). Patients commonly have peripheral edema, ascites, pleural effusion and/or weight gain. In patients with critical medical illness or advanced malignancy (particularly ovarian cancer), third spacing is due to low albumin, which results in low intravascular oncotic pressure. Inflammation and vasodilation due to sepsis and ovarian hyperstimulation syndrome lead to capillary leakage [2].

In general, while patients with sepsis require aggressive fluid replacement, women with advanced malignancy or OHSS are at risk of pulmonary edema, effusions and ascites due to excessive IV fluid replacement. Low or borderline urine output is expected in these patients. Thoughtful and restrained use of IV hydration is vital; daily weights and electrolyte monitoring, for the purposes of assessing fluid shifts, are recommended. Please see Chap. 1, Acute Pelvic Pain, for the diagnosis and management of sepsis, and Chap. 20, Reproductive Endocrinology and Infertility for more information on OHSS.

Differential Diagnosis

1. Prerenal: Essentially meaning inadequate renal perfusion, usually due to hypotension or hypovolemia. A mean arterial pressure of 60–65 millimeters of mercury (mmHg) is usually sufficient for renal perfusion in a patient without preexisting hypertension [3–5]. Causes of poor perfusion include bleeding, sepsis, inadequate resuscitation intraoperatively, excess vomiting or diarrhea, severe hepatic or renal disease and "Third spacing." Medications can also affect renal inflow and commonly include nonsteroidal anti-inflammatory drugs (NSAIDs), angiotensin converting enzyme inhibitors and angiotensin II receptor blockers. Less immediately related to gynecology, cardiogenic shock,

aortic or renal artery dissection (particularly in women with fibromuscular dysplasia) are possibilities as well [1].
2. Intrinsic renal: Referring to a parenchymal renal insult due to medication toxicity or intravenous contrast exposure, ischemia due to hypovolemia or hypoperfusion (such as in hemorrhage or sepsis). Intrinsic renal injury is most often acute tubular necrosis (ATN), due to prolonged ischemia or nephrotoxins [5].
3. Postrenal: Urinary outflow tract obstruction, including Foley catheter malfunction due to kinking or obstruction, urinary retention, or urinary tract injury [5].

When You Get the Call Ask for a full set of vital signs, and ask the nurses to flush or even exchange the Foley catheter, to ensure that kinking or obstruction of the catheter is not the primary issue.

When You Arrive Review the vital sign flow sheet; if the patient has signs of infection or hemodynamic instability, efforts may need to be redirected to emergent diagnosis and stabilization. Please see Chap. 1, Acute Pelvic Pain, for the diagnosis and management of sepsis.

In a stable patient, check the urimeter attached to the Foley to ensure that the reported urine output is accurate. Note whether the urine is highly concentrated (suggestive of hypovolemia) or bloody, which may occur after extensive pelvic surgery; significant bladder hemorrhage may lead to anemia and/or clots occluding the Foley catheter. Check the patient's intake and output for past 2–3 days and assess the overall trend and fluid balance. Review the duration of surgery, surgical approach (vaginal, laparoscopic or open), and note the amount of intravenous resuscitation and blood loss.

History

Ask whether the patient is having lower pelvic pressure or intense urge to void, which suggests bladder distention and urinary retention. Ask the patient whether she has chest pain, newly worsened abdominal pain, or any other new or concerning symptoms.

Review whether the patient is being treated for OHSS or advanced malignancy (refer to "Third Spacing," above). Review whether the patient has chronic cardiac or hepatic dysfunction, which may contribute to renal hypoperfusion. Patients with any of these conditions are at risk of pulmonary edema with administration of excessive IV fluid. Review whether the patient is at risk of acute renal dysfunction, due to chronic renal disease or recent exposure to intravenous radiocontrast media or other nephrotoxins (including chemotherapy).

Physical Examination

Palpate the patient's abdomen for distention, which may represent ascites (in patients with malignancy or OHSS), or hemorrhage or visceral complication in a postoperative patient. Palpate the patient's suprapubic region for a distended bladder. Examine the surgical sites and drains for signs of bleeding. Assess the patient's mucous membranes for dryness, as a clinical marker of hypovolemia. Conversely, peripheral edema and decreased breath sounds may be suggestive of "Third spacing."

Diagnosis

In patients with evidence of sepsis or postoperative bleeding, diagnosis and management should be quickly tailored to these acute issues. Having a low threshold to order a complete blood count in a recently postoperative patient (particularly one with tachycardia, worsening pain or abdominal distention) to assess for bleeding is prudent. In patients with chronic renal disease, check a serum creatinine to assess for worsening of baseline function. In stable patients with unexplained oliguria, the following steps can be taken.

In a patient with a Foley catheter in place (particularly a well-appearing patient with anuria), first flush and adjust the Foley catheter to rule out catheter dysfunction as a cause. A bladder scan can be performed for assessment of contin-

ued urinary accumulation in the bladder despite the presence of a Foley catheter [6].

In a patient without a Foley, an accumulation of 600 mL without the urge to void, or over 150 mL immediately after voiding, is indicative of retention [7, 8]. Urinary retention occurs following 7–15 % of hysterectomies and 4 % of general surgical procedures [9, 10]. Consider sending a urinalysis, as infection is associated with postoperative urinary retention.

If urinary retention is excluded and a patient does not appear fluid overloaded, consider prerenal etiology as a possible cause; a fluid bolus challenge (usually 500 mL to start, except in patients at high risk of fluid overload, such as those with significant cardiac or hepatic disease, advanced malignancy and OHSS) can be both diagnostic and therapeutic [5]. If a patient does not respond to a fluid bolus, check a complete blood count (as indicated) and a basic metabolic panel, to assess for acute anemia or renal dysfunction, respectively.

Urine studies are also helpful in diagnosing the cause of oliguria. Using urine electrolytes paired with serum electrolytes, the fractional excretion of sodium (FeNa) can be calculated as the product of urine sodium concentration ($Urine_{Na}$) and serum creatinine concentration ($Serum_{Cr}$), divided by the product of the serum sodium concentration ($Serum_{Na}$) and urine creatinine concentration ($Urine_{Cr}$). Essentially FeNa is calculated as follows: $(Urine_{Na} \times Serum_{Cr})/(Serum_{Na} \times Urine_{Cr}) \times 100$. A value of less than 1 % indicates prerenal etiology, while a value greater than 2 % is indicative of acute tubular necrosis (intrinsic renal injury) [11]. Also check a urinalysis to assess not only for infection but also for hematuria, which may indicate urinary tract injury or, most commonly, muddy brown casts suggestive of acute tubular necrosis.

Intraoperative urinary tract injuries may only present days after surgery. However, in patients with extensive ureteral or bladder dissections intraoperatively, or those complaining of acutely worsening abdominal or flank pain, particularly in conjunction with hematuria, assessment of a possible urinary tract injury is prudent. A renal ultrasound is a helpful first step, as a low cost study without radiation that can reveal

hydronephrosis, absent ureteric jets, and peritoneal fluid suggestive of urinary tract leak [12]. For suspected ureteral injury, abdominopelvic CT with IV contrast or a CT urogram can be considered, while bladder injuries are diagnosed with cystoscopy, CT cystography, or abdominopelvic CT with IV contrast [12, 13]. The decision to pursue CT scanning with IV contrast is tempered by a risk of contrast nephropathy.

Management

Please refer to Chap. 13, Preparing for Urgent and Emergent Surgery, for management of bleeding complications and transfusion. In stable patients without evidence of bleeding but with clinical evidence of hypovolemia or a FeNa <1 %, fluid replacement is required. The exception is in patients with malignancy, OHSS or other significant medical illness associated with low intravascular volumes but high risk of worsening fluid extravasation (e.g. pulmonary edema) with IV hydration. In these patients, low or borderline urine output is tolerated, while daily weights and electrolyte monitoring are recommended to monitor fluid shifts.

Urinary retention is managed with replacement of the Foley catheter, usually for 24–72 h. Patients may also be discharged home with their catheters or, if they prefer, intermittent catheterization, ideally 4–5 times per day [10, 14]. Antibiotics are not required for either an indwelling Foley or intermittent self-catheterization.

In patients with renal injury—ATN or otherwise elevated creatinine—nephrotoxic medications, such as nonsteroidal anti-inflammatory drugs, should be discontinued, and doses of all necessary medications metabolized in the kidneys should be adjusted accordingly. Electrolytes should be checked daily to assess for hyperkalemia. ATN is usually self-limited; close assessment of urine output and daily serum creatinine levels should be performed.

For patients diagnosed with urinary tract injuries, please see Chap. 16, Complications of Minimally Invasive Gynecologic Surgery, for more information.

Tachycardia

Definitions

Tachycardia Heart rate above 100 beats per minute. Tachycardia can result in decreased cardiac output as the heart does not have time to fill, potentially causing hypotension, syncope, or cardiac ischemia (particularly in those with pre-existing cardiac or coronary artery disease) [1].

Atrial Fibrillation Irregular heart rhythm, due to aberrant electrical activity (classically in the left atrium arising from the pulmonary veins). The hallmark is an "irregularly irregular" rhythm without clear P waves on an electrocardiogram (ECG, Fig. 14.1). Atrial fibrillation is the most common arrhythmia, affecting over 4 % of noncardiothoracic postoperative patients—most often in the first 4 days postoperatively—and over 10 % of critically ill patients [15, 16]. Risk factors for the development of atrial fibrillation include advanced age, hypertension, electrolyte abnormalities, and pulmonary edema [17]. Underlying cardiac disease, hypervolemia, anemia, hypothermia, hypoxia, and sepsis can also contribute to the development of atrial fibrillation, particularly in postoperative patients [17, 18]. Atrial fibrillation may result in decreased cardiac output, cardiac ischemia (particularly in patients with coronary artery disease), hypotension, and syncope [1].

Pulmonary Embolism (PE) Embolization of a preformed thrombus, usually from the lower extremities or, in gynecologic surgery, the pelvic vasculature, to the pulmonary arteries. Risk factors include age over 40 years, obesity, smoking, immobility, malignancy, acute medical illness, diabetes, cardiac disease, chronic pulmonary disease, prior venous thrombosis, pregnancy or the postpartum period, or inherited or acquired thrombophilias (including factor V Leiden mutation, prothrombin gene mutation, and antiphospholipid antibody syndrome) [19]. This is a potentially highly morbid complication, with a mortality rate up to 2.3 %, with increased risk of death reported in patients over 80 years and those with malignancy or chronic cardiac or pulmonary disease [20, 21].

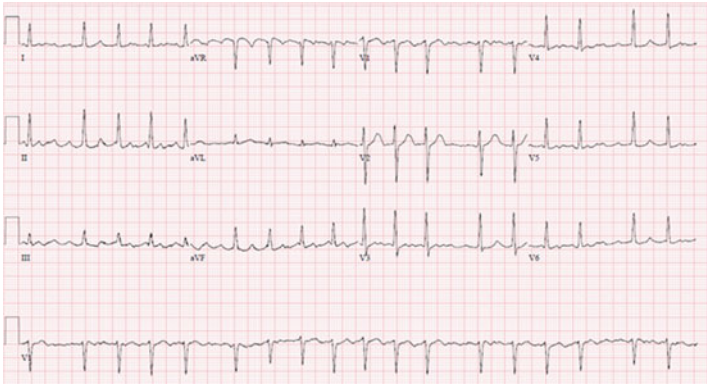

Fig. 14.1 ECG reveals coarse atrial fibrillation with a rapid ventricular response of 108 beats per minute. Note the irregularity of the QRS complexes

Differential Diagnosis [1, 22]

Hypovolemia
Hemorrhage (intra-abdominal or vaginal)
Anemia
Pulmonary embolism (PE)
Hypoxemia
Fever, infection and/or sepsis
Arrhythmia
Cardiovascular disease (including acute coronary syndrome)
Electrolyte derangement (particularly potassium and magnesium)
Medication effect (including cessation of home medications such as beta-blockers)
Thyroid dysfunction
Alcohol and opiate withdrawal
Nausea and vomiting
Pain
Anxiety
Delirium

When You Get the Call Ask for a full set of vital signs to assess for hemodynamic instability. Ask for an electrocardiogram (ECG) to be performed, if it has not been done already.

When You Arrive Confirm the heart rate on exam. Review the full vital signs flow sheet to assess the heart rate trend, and note hypoxemia, fever, or signs of hemodynamic instability. In stable patients, review outpatient records for a reference heart rate, for comparison. Assess the record of intake and output, to review urine output and fluid balance; tachycardia paired with oliguria should raise concern for such conditions as hypovolemia, hemorrhage or sepsis. Review risk factors for hypercoagulability, including obesity, prolonged immobility, pregnancy, recent postpartum status, and known thrombophilia such as factor V Leiden. Also review the patient's medications, including therapeutic anticoagulation and prophylactic measures against deep vein thrombosis (pneumatic compression boots or subcutaneous heparin). Review the operative report and record, including surgical duration, intraoperative fluid resuscitation and blood loss.

History

Ask the patient if she feels chest pain (particularly if it is pleuritic and worse with deep inspiration), palpitations, dizziness, shortness of breath, or any other new and concerning symptoms. If she is recently postoperative, assess whether her surgical pain is well controlled. Review her medical history, including active cancer, current or recent pregnancy, prior thrombosis (particularly within the last 3 months), cardiac disease, anxiety history or panic attacks [18].

Physical Examination

Confirm that the patient has IV access. Make note of whether she appears to be anxious or in pain and whether she is alert

and oriented. Perform a cardiopulmonary exam, confirming the cardiac rate and noting the regularity of the rhythm, while also assessing for lung consolidations, crackles, or other signs of pulmonary pathology. Assess whether the patient's abdomen is distended and whether she has signs of peritonitis; in a postoperative patient, this may be a sign of visceral injury or bleeding, while in a nonoperative patient, this may be a sign of worsening infection or a new complication, including bowel perforation or ischemia. Check the patient's extremities for signs of deep vein thrombosis, which include asymmetric edema and pain.

Diagnosis

An ECG and a basic metabolic panel should be ordered. Cardiac arrhythmias will be diagnosed by ECG. The ECG of a patient with atrial fibrillation is shown in Fig. 14.1. If the patient is postoperative or otherwise at risk for bleeding, obtain a complete blood count. If a patient has signs of sepsis, a complete blood count with a differential should be obtained, in addition to a complete metabolic panel and lactate level. If the patient is anticoagulated, check a complete blood count and coagulation studies. If the patient does not have a recent thyroid function test, particularly if she has a history of thyroid dysfunction, check a thyroid stimulating hormone level.

The diagnosis of **pulmonary embolism** should be suspected in any patient with tachycardia with risk factors for PE, particularly in conjunction with hypoxemia [23]. Please see Chap. 15, High-Acuity Postoperative and Inpatient Issues, section "Hypoxemia", for the diagnosis and management of pulmonary embolism.

A patient report of chest pain alters the differential diagnosis; please see Chap. 15, High Acuity Postoperative and Inpatient Issues, section "Chest pain" for the diagnosis of acute coronary syndromes.

Alcohol withdrawal is associated with symptoms of anxiety, tachycardia, tachypnea, hypertension, pyrexia, and hand tremors, and can result in seizures [24]. After alcohol cessation, symptoms may begin within 8 h, peak in 72 h, and begin to resolve within 5–7 days [25]. Please see Chap. 15, High-Acuity Postoperative and Inpatient Issues, section "Altered mental status," for the diagnosis and management of alcohol withdrawal.

Opiate withdrawal is often suggested by the patient's history. Physical findings of opiate withdrawal include hypertension, tachycardia, myalgias, rhinorrhea, lacrimation, emesis and diarrhea; this condition is managed with opiate or nonopiate replacement.

In a stable patient without arrhythmia or other significant systemic illnesses, particularly those who develop tachycardia with exertion, consider the documentation of orthostatic vital signs by checking the patient's blood pressure and pulse while lying down then standing [26]. A positive finding is a decrease in systolic blood pressure by at least 20 mmHg or diastolic blood pressure by at least 10 mmHg within 3 min of standing, usually accompanied by compensatory tachycardia. Conditions associated with orthostasis are hypovolemia—such as due to hemorrhage, dehydration from vomiting/diarrhea, or inadequate resuscitation in the operating room—deconditioning, and medications such as diuretics and narcotics.

Inadequate pain control, anxiety and delirium are diagnoses of exclusion and suggested by the patient interview and examination.

Management

Please see Chap. 1, Acute Pelvic Pain, for further information on the diagnosis and management of sepsis. Urgent resuscitation of hemorrhage is addressed in Chap. 13, Preparing for

Urgent or Emergent Surgery. Please refer to Chap. 15, High-Acuity Postoperative and Inpatient Issues, for the management of pulmonary embolism, acute coronary syndromes, alcohol withdrawal, and delirium.

In patients with **atrial fibrillation**, rate control is preferable, but a clinically unstable patient may require immediate cardioversion [27]. An optimally controlled heart rate is less than 110 beats per minute [28]. A selection of medications for acute and chronic rate control of atrial fibrillation is shown in Table 14.1 [18, 27]. These medications should be used with caution in patients with hypotension or heart failure, and beta-blockers should also be used with caution in patients with heart block, bradycardia, and bronchoconstrictive disease [27, 29]. Patients who are hemodynamically unstable, including a heart rate above 110 beats per minute, or unable to tolerate oral medications should be treated with

Table 14.1 Medications for acute-onset atrial fibrillation

Medication	Intravenous	Oral
Metoprolol	2.5–5 mg IV every 5 min for up to 3 doses	12.5–25 mg PO every 6 h; the dose can be uptitrated every 24 h
Diltiazem	0.25 mg/kg IV over 2 min, followed by a drip of 5–15 mg/h	30 mg PO every 6 h. Titrate dose every 24 h, to a maximum total daily dose of 360 mg
Digoxin	1 mg IV over 24 h in fractionated doses: 0.5 mg as initial dose, followed by 0.25 mg in 6–8 h intervals with ECGs to assess for toxicity (ventricular tachycardia or heart block)	

From (1) Danelich et al. [18]. (2) Fuster et al. [27]

intravenous medications [18]. Asymptomatic, stable patients may receive oral medications for ventricular rate control. Beta-blockers may be an advisable first step in postoperative patient due to these patients' high adrenergic tone [18, 30]. Consider anticoagulation in patients with atrial fibrillation over 48 h and with risk factors for stroke [18].

Thyroid dysfunction and electrolyte abnormalities must be addressed. In patient with orthostasis, intravenous resuscitation should be provided as needed, and potentially causal medication adjusted (including opiates, diuretics, and vasodilators). Until fully resuscitated, patients with orthostasis should be accompanied when standing and may ultimately benefit from physical therapy consultation depending on their functional capacity.

Sinus Bradycardia

Definition

Bradycardia Heart rate less than 60 beats per minute. Bradycardia leads to decreased cardiac output and can result in hypotension or syncope [1]. Sinus bradycardia is common postoperatively due to anesthetic effects, hypothermia, or epidural anesthesia. Patients may also develop bradyarrhythmias, such as atrioventricular block.

Differential Diagnosis

Medications (including acetylcholinesterase inhibitors for reversal of muscle relaxants, beta-blockers, calcium channel blockers, amiodarone, digoxin, and narcotics)

Obstructive sleep apnea
Hypothermia

(continued)

(continued)

Epidural anesthesia
Increased intracranial pressure
Acute coronary syndrome
Bradyarrhythmia, such as heart block
Vagal reflex (such as due to urinary retention)

When You Get the Call Ask for a full set of vital signs, to assess for hemodynamic stability. Ask for an ECG over the phone if one has not yet been obtained.

When You Arrive Assess the patient's mental status. Review the full vital sign flow sheet, including blood oxygenation level, and any vital signs prior to admission, to assess the baseline heart rate for reference. Review whether the patient is currently receiving epidural anesthesia.

History

Ask the patient whether she is having any associated symptoms including chest pain, dyspnea, headache, or vision changes. Review whether the patient has a history of a low resting heart rate. Many healthy, young individuals (particularly those who pursue exercise and physical conditioning) have slow resting heart rates. Also review her medical history for any neurological or cardiovascular disease, or obstructive sleep apnea (which is more common in obese patients).

Physical Examination

Confirm the patient's heart rate on exam, and assess the regularity of the rhythm. In an immediately postoperative patient, ensure that she is normothermic (>36°C or 96.8°F). The physical exam should be targeted to any other complaints, including neurological symptoms, abdominal pain or chest pain.

Diagnosis

An ECG should be obtained. In patients with chest pain and/or ECG changes suggestive of ischemia including ST segment changes, serum troponins should be obtained as well as cardiology consultation.

In patients with bradyarrhythmias, such as heart block, a cardiology consult should be considered. In the example of patients with bradyarrhythmias such as second- or third-degree atrioventricular block with hemodynamic instability, emergency pacing (either transcutaneous or a temporary pacemaker wire) may be required [31].

Management

Postoperatively, if the patient is in sinus rhythm, hemodynamically stable, asymptomatic, and the heart rate is above 40 beats per minute, close monitoring is an appropriate intervention, ideally with transcutaneous pacing pads and atropine available in the event that the patient becomes symptomatic [1]. If the patient is hypotensive or has mental status changes, attach cutaneous pacing pads while mobilizing medical personnel and initiating a symptomatic bradycardia ACLS protocol. A multidisciplinary emergent team may administer medications such as atropine to increase the patient's heart rate [31].

Asymptomatic Hypertension

Hypertensive Urgency Elevated blood pressure, generally defined as above 180/120 mmHg (either systolic or diastolic threshold) in an asymptomatic patient. Blood pressure correction can be attained more gradually, as the risk of morbidity associated with severe range blood pressures in the absence of end-organ dysfunction is low [29, 32–35].

Hypertensive Emergency Severely elevated blood pressure in a patient with evidence of end-organ compromise, including pulmonary edema, acute coronary syndrome, acute renal failure, encephalopathy, or stroke [33, 36].

Differential Diagnosis [1, 36]

Preexisting hypertension
Postoperative hypervolemia
Poorly controlled pain
Hypoxemia
Withdrawal (alcohol, sedatives, opiates)
Nausea and vomiting
Bladder distention
Anxiety or delirium
Shivering
Blood pressure cuff too small
Pregnancy-related (see Chap. 12)

When You Get the Call Ask for a full set of vital signs, and ask whether the patient's pain is controlled.

When You Arrive Assess the patient for signs of pain, agitation or mental status changes. Review the full vital signs flow sheet, and review outpatient records for the patient's baseline blood pressure, which can provide insight into the degree of control of chronic hypertension. Repeat the blood pressure measurement and confirm that an appropriately sized cuff is being used; the arm circumference should fall within 80 % of the cuff length [32]. Blood pressure measurement manually should also be performed for verification of the elevated blood pressure, particularly for patients with arrhythmias (as automated measurements may be less accurate in these patients). Review the operative report and record, including intraoperative fluid resuscitation and blood loss.

History

Ask the patient about associated symptoms, namely, headache, vision changes, chest pain, dyspnea, and/or mental status changes. Inquire whether the patient has a history of elevated blood pressures; if the patient is taking antihypertensives at home, inquire whether she is taking her medications as prescribed and when she last took the medication. Review the rest of the patient's medical history, including cardiac and renal disease. Review the patient's other medications, as oral contraceptive pills, steroids, cyclosporine, tacrolimus, erythropoietin, tricyclic antidepressants, monoamine oxidase inhibitors, nonsteroidal anti-inflammatory drugs, nasal decongestants, and dietary supplements may contribute to elevated blood pressures [32, 34]. Alcohol intake and illicit drug use (cocaine, amphetamines) can also cause elevated blood pressures [34].

Physical Examination

Confirm that the patient has IV access. The physical exam can be tailored to the patient's symptoms. Assess alertness and orientation, and assess for visual, motor, or sensory defects. In patients with severe hypertension, a fundoscopic examination can be performed, assessing for retinal hemorrhage or papilledema. The cardiopulmonary exam should identify signs of heart failure, including rales or an S3 heart sound [32].

Diagnosis

A diagnostic workup should be tailored to a patient's symptoms. Please see Chap. 15, High-Acuity Postoperative and Inpatient Issues, for the diagnosis and management of acute chest pain, altered mental status, and hypoxemia. There are no clear recommendations regarding routine labs to obtain in an asymptomatic patient with severe hypertension; a basic metabolic panel to establish renal function may be helpful. A newly elevated creatinine or a urinalysis showing new

Table 14.2 Parenteral medications for the management of hypertensive emergency

Medication	Dose	Time to onset (min)
Hydralazine	10–20 mg IV every 4–6 h	20
Labetalol	20 mg IV, with repeat doses of 20–80 mg IV every 10 min up to 300 mg per day	5–10
Enalapril	1.25 mg IV over 5 min, every 6 h. Dose can be increased by 1.25 mg every 12 h to a maximum of 5 mg every 6 h	15–30
Esmolol	500 μg/kg IV over 1 min, followed by an infusion at 25–50 μg/kg/min. The dose can be increased by 25 μg/kg/min every 10–20 min to maximum of 300 μg/kg/min	1–2

From (1) Shayne and Pitts [32]. (2) Johnson and Nguyen [37]. (3) Haas and Marik [38]

hematuria suggests renal damage, indicative of a true hypertensive emergency. Finally, a urine screen for drugs of abuse, including cocaine or amphetamines, may identify the likely cause of acute hypertension in some patients [32].

Management

In caring for patients with acute hypertension and symptoms or clinical evidence of acute cardiac ischemia, neurologic morbidity or renal insufficiency, subspeciality teams (cardiology, neurology, and nephrology, respectively) should be urgently contacted, as blood pressure targets vary [32].

Hypertensive emergency is treated with IV medications, as blood pressure should be reduced from the severe range within 1–2 h (Table 14.2) [32]. When subspeciality teams, such

Table 14.3 Oral medications for the management of hypertensive urgency

Medication	Dose	Time to onset (min)	Duration (h)
Labetalol	200–400 mg PO, repeated every 2–3 h	20–120	8–12
Captopril	6.25–25 mg PO, uptitrated every 8 h	15–60	4–6
Clonidine	0.2 mg PO followed by 0.05–0.1 mg every hour if necessary with maximum total dose of 0.7 mg	30–60 (max effect at 2–4 h)	6–10
Hydralazine	10–75 mg PO every 6 h	20–30	Up to 8

From (1) Kessler and Joudeh [39]. (2) Hebert and Vidt [40]

as cardiology, neurology, or nephrology, are involved in the patient's care, these providers should be consulted when making medication choices [29]. In addition to the list below, nitroprusside and nitroglycerin IV infusions can also be used, but are better managed by clinicians with experience with these, including cardiologists and intensivists [37].

Hydralazine should be used with caution in patients with increased intracranial pressure, myocardial ischemia, or aortic dissection and may cause reflex tachycardia [29, 37]. Beta-blockers (labetalol, esmolol) should be used with caution in patients with heart block, bradycardia, acute heart failure, and bronchoconstrictive disease [27, 37]. Enalapril should be used with caution in patients with renal insufficiency, hyperkalemia, or hypovolemia; patient responses to enalapril are variable, and the peak response may not be seen for up to 4 h [29, 32, 38]. Enalapril is contraindicated in pregnancy.

Hypertensive urgency can often be treated with oral medications, as the preferred time to reduction in blood pressure is 24–72 h (Table 14.3) [39, 40]. These oral medications can be redosed as listed below, but care should be

taken not to administer excessive doses leading to hypotension.

Labetalol should be used with caution in patients with heart block, bradycardia, acute heart failure, and bronchoconstrictive disease [27, 32, 37]. Hydralazine should be used with caution in patients with increased intracranial pressure, myocardial ischemia, or aortic dissection and may cause reflex tachycardia [29, 37]. Clonidine should be used with caution in patients with heart failure or heart block; side effects include sedation and orthostatic hypotension [32]. Captopril should be avoided in pregnancy and in patients with renal artery stenosis [32, 41].

Nausea and Emesis

Definitions

Ileus Abnormal motility of the gastrointestinal tract, which is not due to a mechanical obstruction. An ileus is multifactorial, caused by inflammation, electrolyte derangements, and changes in neurologic or receptor-mediated function, particularly in the postoperative period [42]. Opioids, in particular, are implicated in the pathogenesis of ileus [43]. The incidence of ileus varies by type of surgery and, for instance, occurs in up to 24 % of patients undergoing colectomy [44]. Patients may complain of nausea, vomiting, and distention and may report delayed passage of flatus and stool.

Bowel Obstruction Mechanical impediment to normal gastrointestinal peristalsis, most commonly affecting the small bowel. Small bowel obstruction occurs after 0.53 % of benign gynecologic surgeries [45]. Patients commonly present with abdominal distention and pain, nausea, and vomiting 2–8 days after surgery, and report absence of flatus or stool [46]. Risk factors for bowel obstruction postoperatively include intraoperative lysis of adhesions and/or concomitant bowel surgery, blood transfusion, and cystotomy [47]. Obstructions may occur 5 years or more after abdominal surgery, due to adhesions [48].

Differential Diagnosis

Ileus
Bowel obstruction due to malignancy or prior pelvic adhesions
Bowel perforation or injury
Urinary tract injury (specifically urinary ascites causing ileus)
Cardiac ischemia
Medication effect (including anesthetics or chemotherapy)
Thyrotoxicosis
Diabetic ketoacidosis
Hepatic, pancreatic, or biliary disease (such as hepatitis and pancreatitis)
Urinary tract infection
Gastroparesis
Viral gastroenteritis
Pain (such as from ovarian torsion)

When You Get the Call Ask for a full set of vital signs and obtain an ECG in patients with risk factors for coronary artery disease.

When You Arrive Review the full vital signs flow sheet, including whether the patient is febrile, tachycardic, hypotensive, or tachypneic. Assess the patient's appearance for signs of pain or distress. Review the patient's current medications, including current chemotherapy and recent opiate administration, both of which may produce nausea. If the patient is postoperative, review the operative report for the extent of dissection and whether any bowel injury or resection occurred. Of note, cardiac ischemia also commonly manifests as nausea and should be considered with a high index of suspicion in those with risk factors for coronary artery disease.

History

Ask the patient to describe any associated symptoms, including quality and distribution of any new or worsening pelvic pain. Ask the patient if she is having flatus or diarrhea. Assess for chest pain or "pressure." Assess whether the jaw or arm is involved in the syndrome, suggestive of an acute coronary syndrome. Diabetic patients with cardiac ischemia often present silently or atypically and do not manifest classical chest pain; abdominal pain or nausea are possible presentations. Review from the medical record and with the patient any medical history, including malignancy, cardiac disease, diabetes, gastroparesis, thyroid dysfunction, and inflammatory bowel disease. Even if the patient has not recently had surgery, review her prior surgical history, as prior abdominal surgeries may increase the risk of adhesions and bowel obstruction.

Physical Examination

Assess the patient's alertness and orientation and whether she is in distress. Perform a focused cardiovascular exam for new heart sounds or paradoxical splitting. Examine the patient's abdomen, noting distention and bowel sounds. Absent or hypoactive bowel sounds may be noted in patients with ileus or obstruction, while high pitched bowel sounds may be associated with small bowel obstruction. Note the presence of peritoneal signs—including rebound (pain when abdominal pressure is quickly withdrawn), involuntary abdominal guarding, or shake tenderness (pain when shifting the patient's abdomen or bed)—which may indicate the presence of intra-abdominal inflammation, infection or bleeding.

Diagnosis

In patients with emesis, check a complete metabolic panel to assess for electrolyte and metabolic derangements that should be corrected; diabetic ketoacidosis will also be

detected with a metabolic panel. In a patient with hypotension, tachycardia, fever, or acute pain on exam, obtain a complete blood count, complete metabolic panel and lactate; causes of elevated lactate include, but are not limited to, sepsis and bowel ischemia [49]. A urinalysis may also be helpful, particularly in patients with a Foley catheter in place (or who had one recently), to assess for infection. Serum troponins may be sent for assessment of patients with possible coronary ischemia. Please see Chap. 15, High-Acuity Postoperative and Inpatient Issues, for more information on the diagnosis of acute coronary syndromes.

Please see Chap. 16, Complications of Minimally Invasive Gynecologic Surgery, for the diagnosis of ileus, bowel obstruction, and bowel and urinary tract injuries. For reference, the latter complications are commonly associated with abdominal pain and signs of systemic illness (such as fever and/or sepsis), in the days following surgery, though presentation may be delayed 1-2 weeks.

Management

If the patient is still in the Post-Anesthesia Care Unit (PACU), involve the anesthesia team in treatment of her postoperative nausea and emesis.

Administer antiemetics, which include ondansetron (4–8 mg IV or PO every 8 h), metoclopramide (10 mg IV or PO every 6 h), and/or prochlorperazine (10 mg IV or PO every 6 h, or 25 mg PR every 12 h). For patients receiving chemotherapy, an NK1 receptor antagonist such as aprepitant is often prescribed, in addition to ondansetron and dexamethasone (4 mg IV, IM or PO every 6 h) [50]. Lorazepam (0.5–2.5 mg IV, IM, or PO every 8–12 h) and antihistamines, including diphenhydramine (25–50 mg IM, IV, or PO every 6 h) or promethazine (12.5–25 mg IM, IV, PO, or PR every 4–6 h), may be helpful additions to an antiemetic regimen [51]. Electrolyte abnormalities should be corrected, and volume lost in emesis should be replaced with isotonic IV fluids. Thyrotoxicosis, acute coronary syndromes, and diabetic keto-

acidosis also require immediate intervention, which is beyond the scope of this chapter.

Please see Chap. 16, Complications of Minimally Invasive Gynecologic Surgery, for the management of ileus, bowel obstruction, and bowel and urinary tract injury.

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Chapter 15
High-Acuity Postoperative and Inpatient Issues

Paula C. Brady and J. Sawalla Guseh

Hypoxemia

Definitions

Hypoxemia Low oxygen saturation in the blood, usually defined as peripheral capillary oxygen saturation (SpO_2) of 90 % or less [1].

Atelectasis Collapse of alveoli, occurring in up to 90 % of surgical patients [2]. Atelectasis is theorized to serve as a nidus for infection. While sometimes associated with hypoxemia, atelectasis has also commonly been associated with low-grade postoperative fevers, though data for this association are sparse [3].

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Acute Respiratory Distress Syndrome (ARDS) Alveolar injury leading to inflammation and respiratory failure, which usually occurs within 1 week of the inciting clinical insult [4]. Conditions associated with ARDS include but are not limited to pneumonia, aspiration of gastric contents, sepsis, drug overdose, and acute pancreatitis [5]. The mortality rate of ARDS approaches 40 % [6].

Pulmonary Embolism (PE) Embolization of a thrombus, usually from the lower extremities or pelvic vasculature, to the pulmonary arteries. Risk factors include age over 40 years, obesity, smoking, immobility, malignancy, acute medical illness, diabetes, cardiac disease, chronic pulmonary disease, prior venous thrombosis, pregnancy or the postpartum period, or inherited or acquired thrombophilias (including factor V Leiden mutation, prothrombin gene mutation, and antiphospholipid antibody syndrome) [7]. This is a potentially life-threatening complication, with a mortality rate up to 2.3 %, with increased risk of death reported in patients over 80 years and with a history of malignancy or chronic cardiac or pulmonary disease, a heart rate above 110 beats per minute, or arterial oxygen saturation less than 90 % [8, 9].

Pulmonary Edema Accumulation of fluid in the pulmonary alveoli. Causes of pulmonary edema are cardiogenic, due to elevated pulmonary capillary wedge pressure resulting from left-sided heart failure, or noncardiogenic, due to endothelial damage such as in patients with pneumonia, sepsis, or ARDS [10, 11]. Risk factors for pulmonary edema include renal artery stenosis as well as the risk factors for acute decompensated heart failure, such as hypertension, coronary artery disease, diastolic dysfunction, and valvular disease [12, 13]. Acute decompensated heart failure, and thereby cardiogenic pulmonary edema, may be precipitated by medication nonadherence, acute coronary syndromes, uncorrected hypertension, cardiac arrhythmia, pericarditis, aortic dissection, pulmonary embolus, increased salt intake, diabetes, and thyroid dysfunction [14]. Patients with pulmonary edema often complain of dyspnea, cough, and tachypnea.

Transfusion-Associated Circulatory Overload (TACO) Clinically significant fluid overload occurring shortly after transfusion of blood products in up to 8 % of patients [15]. Patients report dyspnea and may have hypertension, tachypnea, and/or tachycardia. TACO is more common in patients with a positive fluid balance, receiving a large volume or rapid infusion of blood products, advanced age, and preexisting left ventricular dysfunction or renal dysfunction [16, 17]. The risk of TACO may be reduced with preemptive administration of intravenous furosemide (20–40 milligrams (mg) once) in between units of blood products or after transfusion [18].

Transfusion-Related Acute Lung Injury (TRALI) A clinical syndrome of acute-onset hypoxemia and noncardiogenic pulmonary edema occurring during or immediately after the transfusion of blood products [19]. The leading cause of transfusion-related deaths, TRALI occurs in at least 1 in 5,000 transfusions of blood products [19]. Risk factors include but are not limited to sepsis, aspiration of gastric contents, multiple transfusions, disseminated intravascular coagulation, current smoking, liver surgery, and chronic alcohol abuse [20]. Patients complain of dyspnea and are hypoxemic. They are also often tachypneic, febrile, tachycardic, hypertensive, or hypotensive.

Anaphylaxis A life-threatening allergic reaction, estimated to occur in 1.7 % of people in their lifetimes [21].

Differential Diagnosis [22, 23]

Sepsis
Acute respiratory distress syndrome (ARDS)
Pulmonary embolism (PE)
Pulmonary edema
Transfusion-associated circulatory overload (TACO)
Transfusion-related lung injury (TRALI)
Pneumonia
Pleural effusion

(continued)

(continued)

Pneumothorax
Atelectasis
Asthma
Chronic obstructive pulmonary disease (COPD)
Acute chest syndrome due to sickle cell disease
Acute coronary syndrome (ACS)
Arrhythmia
Heart failure
Cardiac tamponade
Anaphylaxis
Obstructive sleep apnea (OSA)
Hypoventilation due to oversedation, neuromuscular disorders, and pain

When You Get the Call Ask for a full set of vital signs including pulse oximetry. If the patient is hemodynamically unstable or reported to be somnolent, call for respiratory support staff and additional personnel while en route.

When You Arrive In patients receiving a transfusion, stop the transfusion, and confirm the blood product and patient identifiers to ensure an error has not occurred. Place the pulse oximeter on the patient's other hand, a foot, or earlobe to confirm the hypoxemia. Assess whether the patient is tachypneic or appears distressed or lethargic; a patient with significant dyspnea may assume the "tripod" position, which is a hunched position with the arms (often with hands on knees) supporting the torso [24]. You may see the patient using accessory muscles of respiration. If the patient is in distress, hemodynamically unstable, or nonresponsive to verbal stimuli, mobilize additional medical personnel and respiratory support staff. If the patient is stable, ask her to take a few slow, deep breaths to assess whether her oxygenation improves; mild atelectatic or hypoventilatory hypoxemia often improves. Review the full vital sign flow sheet including the patient's fluid balance. Note whether the hypoxemia occurs when she is sleeping, characteristic of obesity and/or obstructive sleep apnea.

History

Ask the patient whether she is having chest pain, shortness of breath, dyspnea, cough, or hemoptysis; review whether she is experiencing orthopnea (inability to lie flat due to dyspnea), paroxysmal nocturnal dyspnea (waking from sleep with dyspnea), decreased exercise tolerance, or any other new symptoms. Ask if her symptoms are acute or gradual in onset and whether she has had these symptoms previously. Inquire whether she has a cough productive of sputum, and ask her to describe the sputum, whether clear, purulent (concerning for pneumonia or COPD exacerbation), or frothy (consistent with pulmonary edema).

Review whether the patient is currently receiving a transfusion, or completed one in the last 6 h. Obtain a full past medical history, including sleep apnea, heart failure, hypertension, coronary artery disease, cardiac valvular disease, cardiac arrhythmia, chronic obstructive pulmonary disease, asthma, malignancy, sickle cell anemia, or a history of thromboembolism. Ask whether the patient smokes, for how long, and if she quit, how recently. Review whether the patient is receiving thromboprophylaxis. If the patient is postoperative, review whether she received thromboprophylaxis (such as sequential compression boots or heparin) at the time of surgery.

Physical

Assess the patient's mental status, agitation, use of accessory muscles for breathing, and her ability to speak in full sentences. Perform a cardiac exam, noting tachycardia, arrhythmia, and muffled or extra heart sounds. On pulmonary exam, note the presence of decreased breath sounds, particularly at one or both lung bases, crackles, stridor, or wheezing. Assess the patient's lower extremities for signs of fluid overload (edema) or deep vein thrombosis, particularly asymmetrical lower extremity edema or calf pain.

Diagnosis

Sepsis should be among the leading diagnoses in patients with fever, hypotension, tachycardia, and/or altered mental status. Please see Chap. 1, Acute Pelvic Pain, for the diagnosis and management of sepsis.

In approaching the patient with hypoxemia, the diagnostic algorithm depends in part on the patient's degree of distress. In patients with an elevated respiratory rate who appear fatigued or lethargic, or have other vital sign abnormalities, an arterial blood gas while breathing room air, a troponin I or T, complete blood count, and complete metabolic panel should be obtained. In patients with a history of heart failure or evidence of fluid overload, consider adding a brain natriuretic peptide (BNP); acute heart failure is unlikely with a BNP less than 100 picograms per milliliter (pg/mL) [25]. Of note, BNP can be impacted by comorbid conditions. In particular, it is often low in patients with high BMI and therefore the value should be integrated into a full clinical assessment.

In all patients, an electrocardiogram (ECG) should be obtained, which may reveal an arrhythmia or changes suggestive of ischemia, particularly ST segment changes or T wave inversions [26, 27]. If any abnormalities are noted, compare the ECG to a prior one. Of note, ST segment deviation may be noted in nonischemic disease, including acute pericarditis, left ventricular hypertrophy (LVH), left bundle branch block (LBBB), and cardiomyopathies [28]. In patients with ECG changes, or any patient with concerning chest pain, a troponin I or T should be drawn; three serial levels every 8 h are usually collected in high-risk patients [27].

A chest radiograph is of high clinical utility in a patient with hypoxemia, particularity a patient with crackles (concerning for pulmonary edema) or decreased breath sounds on lung exam (suggestive of pneumonia, pleural effusion, or pneumothorax), a productive cough (particularly in conjunction with fever), or evidence of fluid overload. Chest

radiographs can reveal opacities or infiltrates suggestive of pneumonia, ARDS, acute chest syndrome, pleural effusion, atelectasis and pulmonary edema; a chest radiograph may also show pneumothorax, COPD and cardiomegaly. A chest CT can be considered in clinically ill patients with chest radiograph findings that are indeterminate, such as diffuse consolidations that could be consistent with pneumonia, pulmonary edema, atelectasis, or the acute respiratory distress syndrome.

In patients with tachycardia and hypoxemia, and/or risk factors for thromboembolism (malignancy, obesity, immobility, recent surgery), a D-dimer can be obtained, though a D-dimer level may be falsely elevated in pregnant, postoperative, or elderly patients [29–31]. For patients in whom the leading clinical diagnosis is pulmonary embolism, particularly those with significant tachycardia or hypoxemia, ordering a chest CT with IV contrast may be a prudent first step, instead of waiting for a D-dimer result.

Management

Administration of oxygen by nasal cannula or face mask is an acceptable first step while diagnostic tests are pending and further resources are mobilized [32]. The exception is patients with COPD, whose normal partial pressure of oxygen is 60–65 millimeters of mercury (mmHg), corresponding to an oxygen saturation of 90–92 %; a higher oxygen level may result in worsening hypercapnia in patients with COPD [33]. Patients with altered mental status, hemodynamic instability, severe hypoxemia, or failure to respond to less invasive measures may require noninvasive positive pressure ventilation in the form of continuous positive airway pressure (CPAP), bilevel positive airway pressure (BPAP), or intubation, as directed by critical care providers.

Acute coronary syndromes are discussed in the following section “Chest pain.”

Acute Chest Syndrome

Acute chest syndrome is diagnosed in patients with sickle cell anemia, with a new infiltrate in at least one lung segment, a temperature over 38.5 °C, and evidence of respiratory distress, including tachypnea, hypoxemia, wheezing, and cough [34].

Patients with acute chest syndrome require pain control, supplemental oxygen, and usually simple or exchange transfusion [34]. Patients may benefit from bronchodilators—particularly in patients with wheezing—folic acid supplementation, and broad-spectrum antibiotics.

Anaphylaxis

Criteria for the diagnosis of anaphylaxis include acute onset (over minutes to hours) of symptoms involving the skin and/or mucosa, including hives, pruritus, or edema, with either respiratory compromise (such as dyspnea, wheezing, or hypoxemia) or evidence of hypoperfusion, such as hypotension or syncope [35]. Patients may also develop abdominal cramping or vomiting. Hypotension in isolation after exposure to a known allergen is an alternative diagnostic criterion of anaphylaxis.

Any current medication or blood product infusions at the time of a suspected anaphylactic reaction should be stopped. Additional medical personnel and respiratory support staff should be called. If the patient was receiving a blood transfusion when her symptoms began, confirm patient and blood product identifiers, and contact the blood bank. Anaphylaxis should be treated with epinephrine intramuscularly (0.01 mg per kilogram (kg), for a maximum dose 0.5 mg every 5–15 min) [35]. Albuterol or racemic nebulized epinephrine may be used as an adjunct to IM epinephrine in patients with bronchospasm; patients should also receive an antihistamine, such as diphenhydramine (25–50 mg IV). Intravenous steroids are also commonly used, such as methylprednisolone 1.0–2.0 mg/kg every 6 h. Patients should also receive high-flow oxygen and aggressive fluid resuscitation and be positioned supine with elevated legs if possible. Vasopressors may be needed for refractory hypotension.

ARDS

In patients with ARDS, chest radiographs reveal bilateral opacities not attributable to effusions, pneumothorax or lung nodules, and pulmonary edema not explained by fluid overload or cardiac failure (Fig. 15.1) [36]. In patients with ARDS, the ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO_2/FiO_2) is expected to be less than 300 mmHg; this ratio will be lower in more severe disease [36].

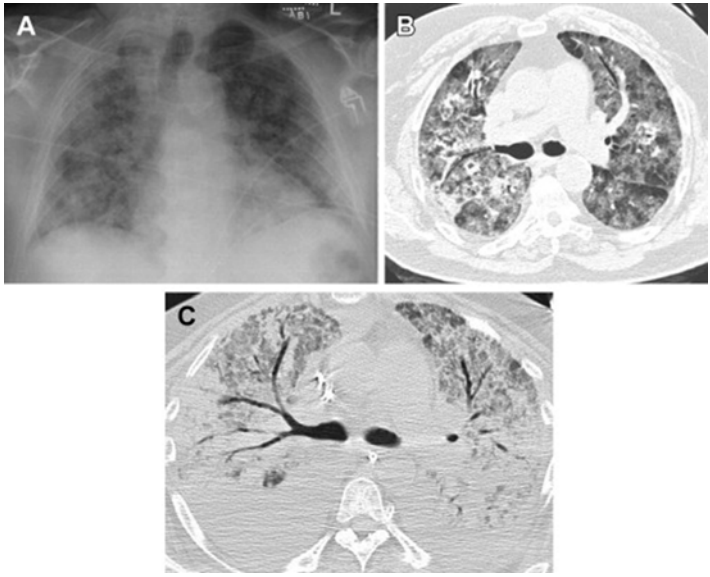

Fig. 15.1 Acute respiratory distress syndrome (ARDS). (**a**) AP chest radiograph shows low lung volumes and diffuse bilateral pulmonary opacities. (**b**) Axial CT image in the same patient shows ground-glass and consolidative opacities without pleural effusions. (**c**) Axial CT image from another patient shows dense bilateral consolidation with air bronchograms and diffuse ground-glass opacity (Reprinted from Bentz and Primack [11], with permission from Elsevier)

Patients with suspected ARDS require care by a multidisciplinary team, most often in an intensive care unit, and many patients require mechanical ventilation. Underlying infections must be treated aggressively [5]. Adequate intravascular volume should be provided, though excessive fluid administration may cause or exacerbate pulmonary edema [5].

Asthma

In patients with a history of asthma reporting shortness of breath and symptoms consistent with prior asthma exacerbations, a forced expiratory volume in 1 s (FEV1) or peak expiratory flow (PEF) should be measured. A mild exacerbation is indicated by values >70 % of predicted, while values less than 40 % of predicted constitute a severe exacerbation; predicted FEV1 and PEF by age, height, and ethnicity are available at the website for the Centers for Disease Control and Prevention [37, 38]. Inability to speak in complete sentences, agitation or distress, use of accessory muscles, and an oxygen saturation less than 90 % are consistent with an asthma exacerbation [24].

Supplemental oxygen should be administered, with a goal oxygen saturation of 95 % or more [37]. Short-acting beta-agonists, particularly albuterol, may be administered by an inhaler or nebulizer, depending on the patient's degree of distress. Addition of ipratropium bromide to an albuterol nebulizer is beneficial, particularly in severe exacerbations; a 3 mL nebulized solution, consisting of 0.5 mg of ipratropium bromide and 2.5 mg of albuterol, can be administered every 20 min for 3 doses, then as needed [37]. In patients with worsening distress, hypoxemia, and concern for impending respiratory arrest, the use of intravenous systemic steroids has an important role (e.g. IV methylprednisone 40–80 mg every 6–12 h) [37].

COPD

In patients with exacerbations of COPD, supplemental oxygen can be administered and titrated to an oxygen saturation of

90–92 %; bilevel noninvasive positive pressure ventilation may be required [33]. Ipratropium bromide and albuterol inhalers can be administered every 4–6 h. In patients with worsened dyspnea or increased volume or purulence of sputum, antibiotics are often administered for a 10-day course, including trimethoprim–sulfamethoxazole, doxycycline, or amoxicillin [39]. As in patients with asthma, worsening distress, hypoxemia, and concern for impending respiratory arrest, the use of intravenous systemic steroids has an important role (e.g. IV methylprednisone 40–80 mg every 6–12 h).

Hypoventilation

Pain-related hypoventilation is typically the result of inadequate tidal volumes due to shallow breathing, in patients for whom taking deep breaths exacerbates pain. In patients with hypoventilation due to pain, provide adequate pain control. Conversely, narcotic-related hypoventilation is principally due to suppression of medullary centers resulting in a low respiratory rate. In patients with hypoventilation potentially due to excessive administration of narcotics, doses and/or frequency of the medication should be decreased. In severe or refractory hypoxemia attributed to narcotics consider administering intravenous naloxone. Start with 0.4 mg, which can be increased to 2 mg if there is no response; doses can be repeated every 2-3 min, up to a total dose of 10 mg [39]. Naloxone drips may be used in patients who received a longer acting narcotic, and in whom repeated administration of IV naloxone has proven incompletely effective. In this setting, be sure to remove fentanyl patches. If altered mental status, lethargy, or stupor is contributing to a patient's hypoventilation, see section "Altered mental status" below.

OSA

Obstructive sleep apnea is characterized by intermittent airway occlusion during sleep; patients commonly become hypoxemic and hypercarbic while sleeping. For patient with

OSA admitted to the hospital, CPAP should be ordered at the patient's home settings. Patients with OSA should be closely monitored while receiving opiates or sedatives as these may unmask the obesity hypoventilation syndrome [41].

Pleural Effusion

In gynecology patients, pleural effusions will most commonly be identified in patients with ovarian hyperstimulation syndrome (OHSS) or malignancy. Pleural effusions are associated with a blunting of the costophrenic angles on chest radiograph (Fig. 15.2) [11]. A chest CT scan may be helpful in distinguishing pleural effusions from parenchymal disease or atelectasis [11]. An empyema (purulent pleural effusion) may be suspected when the pleura is thickened and enhanced around the pleural fluid.

In patients with hypoxemia or dyspnea attributed to a pleural effusion, thoracentesis should be considered, and can be performed at the bedside by appropriately trained providers or by interventional radiology [42]. Patients with OHSS may also have respiratory distress due to compression

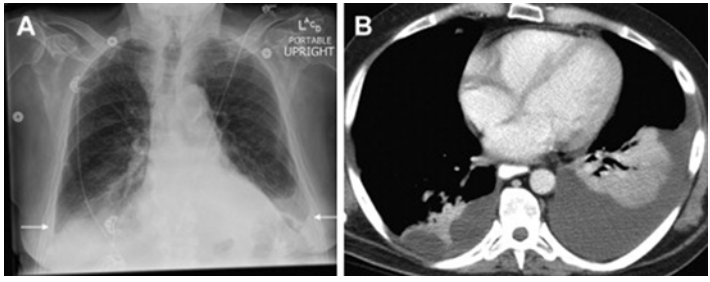

Fig. 15.2 Pleural effusion. (**a**) AP chest radiograph shows blunting of the costophrenic angles and a small amount of fluid tracking up the pleural space laterally (*arrows*), indicating bilateral pleural effusions. (**b**) Axial CT image confirms moderate left and small right pleural effusions, with adjacent atelectasis (Reprinted from Bentz and Primack [11], with permission from Elsevier)

from abdominal ascites, which may require concomitant drainage [43]. In patients with recurrent symptomatic malignant effusion, indwelling catheters can be placed, or pleurodesis can be performed [44, 45].

Pneumonia

Risk factors for hospital-acquired pneumonia include intubation, age greater than 70 years, a depressed level of consciousness, thoracic or upper abdominal surgery, and chronic lung disease [46]. Patients may be febrile or report cough with or without sputum production, dyspnea, and/or pleuritic chest pain. On physical examination, patients may have decreased breath sounds in a focal area or other abnormalities on auscultation [47]. Chest radiograph is a widely available, rapid test for confirmation.

For the management of patients with septic physiology attributed to pneumonia, please see Chap. 1, Acute Pelvic Pain, for more information on the diagnosis and management of sepsis. In stable patients diagnosed with pneumonia, risk factors for multidrug-resistant pathogens include antibiotic exposure within the last 90 days, current hospitalization of 5 days or more, hospitalization of 2 days or more in the past 90 days, immunosuppression, and residence in a nursing home or extended care facility [48]. Patients who do not meet these criteria can be treated with ceftriaxone (2 g IV daily), fluoroquinolones such as levofloxacin (750 mg IV or PO daily), ampicillin–sulbactam (3 g IV every 6 h), or ertapenem (1 g IV daily). Patients with risk factors for multidrug resistance require broad-spectrum coverage: an antipseudomonal cephalosporin (cefepime 1–2 g IV every 8–12 h or ceftazidime 2 g IV every 8 h) or an antipseudomonal carbapenem (imipenem 500 mg IV every 6 h or meropenem 1 g every 8 h) or piperacillin–tazobactam (4.5 g every 6 h), **plus** linezolid (600 mg IV every 12 h) or vancomycin (12 mg/kg IV every 12 h) [48]. The original American Thoracic Society (ATS) and Infectious Diseases Society of America (IDSA) guidelines propose double coverage with an aminoglycoside such as gentamicin

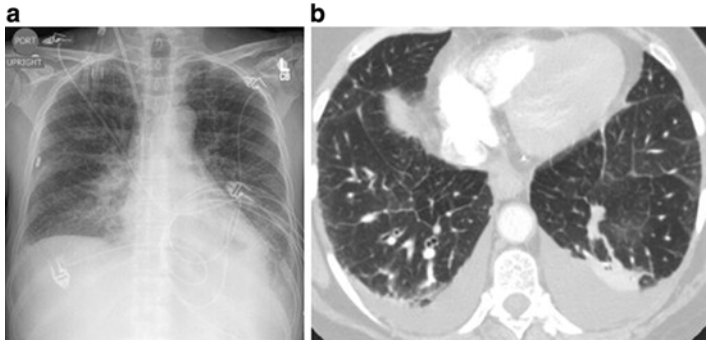

Fig. 15.3 Pulmonary edema. (**a**) AP chest radiograph shows pulmonary vascular indistinctness, diffuse opacification, and septal thickening. Blunting of the costophrenic angles indicates bilateral pleural effusions. (**b**) Axial CT image through the lower lobes, demonstrating interlobular septal thickening, ground-glass opacities, and small bilateral pleural effusions (Reprinted from Bentz and Primack [11], with permission from Elsevier)

or a fluoroquinolone such as levofloxacin or ciprofloxacin, which may add to the toxicity of the regimen, but can be considered in patients with cultures showing gram-negative bacilli or risk factors for resistant gram negative organisms [49].

Pulmonary Edema

Pulmonary edema can be visualized on chest radiograph as diffuse interstitial opacities, which may coalesce into consolidations; the periphery is often spared in cardiogenic pulmonary edema (Fig. 15.3) [13].

The underlying cause of the pulmonary edema should be considered, as treatment varies according to etiology. A brain natriuretic peptide (BNP) can be collected in patients with risk factors or signs of heart failure, as heart failure is unlikely with a BNP less than 100 pg/mL; a cutoff of 200 pg/mL has been suggested in patients with an estimated glomerular filtration rate less than 60 mL per minute [13, 50]. If not already

ordered, an ECG should be obtained in patients complaining of chest pain, shortness of breath, or with risk factors for myocardial infarction—age greater than 65 years in women, prior coronary artery disease, current smoking, diabetes, hypertension, hyperlipidemia, obesity, and family history of coronary artery disease [51]. In addition to an ECG, patients with an extra heart sound on cardiac exam, elevated jugular venous pressure, a history of heart failure, or risk factors for heart failure—including known diastolic dysfunction, coronary artery disease, hypertension, or valvular dysfunction—may need an echocardiogram to assess for left ventricular dysfunction or valvular dysfunction [12, 13].

In patients with pulmonary edema or TACO, supplemental oxygen should be administered; noninvasive positive pressure ventilation may be required to maintain adequate oxygenation. Treatment is primarily with diuretics; intravenous furosemide is commonly used, administered at a dose 20–40 mg in patients not routinely taking this medication [14, 52]. Diuretic therapy can result in intravascular fluid depletion and hypotension; diuretics may not work as well in patients with impaired renal function. Patients started on loop or thiazide diuretics should have daily electrolytes checked while in the hospital, as low serum potassium and magnesium may result [14].

If cardiogenic pulmonary edema is suspected, consultation with internal medicine or cardiology should be considered. Angiotensin-converting enzyme (ACE) inhibitors, beta blockers, and diuretics are often used in the chronic management of heart failure [14]. However, in the acute setting, beta-blockers should be avoided as the reduction in contractility may lead to clinical deterioration.

Pulmonary Embolism

Patients with pulmonary embolism are commonly tachycardic, hypoxemic, and/or tachypneic. ECG may sometimes reveal findings suggestive of pulmonary embolism, including

tachycardia, T wave inversions in leads V1–V3, and right bundle branch block, which is associated with greater mortality [53, 54]. The classic S1Q3T3 (or McGinn–White) pattern—an exaggerated S wave in lead I, a Q wave, and inverted T wave in lead III (Fig. 15.4)—has poor sensitivity, but is highly specific for the diagnosis of pulmonary embolism [55, 56].

If a D-dimer has been obtained, PE is unlikely below a level of 500 nanograms (ng) per mL, potentially obviating the need for chest CT with IV contrast [29, 30]. Patients may also be stratified according to Wells' criteria, shown in Table 15.1. A total of less than 2 points is low risk, with an associated rate of PE of 2.0 %. A score of 2–6 points is considered moderate risk, with a rate of PE of 18.8 %, while a score of greater than 6 points is considered high risk, with a rate of PE of 50 %. In patients with a positive D-dimer (above 500 ng/mL), moderate to high risk of PE by Wells' criteria, or who raise strong clinical suspicion for PE, a chest CT with IV contrast, with a protocol specific to the detection of PE, should be ordered.

Patients with pulmonary embolism require prompt anticoagulation. For patients with hemodynamic instability, shock or severe hypoxemia, an unfractionated heparin IV infusion should be started, in a weight-based algorithm guided by activated partial thromboplastin time. Clinical specialties comfortable with the management of acute PE (cardiology, vascular medicine, and pulmonary intensivists) should be consulted, and can evaluate for the potential use of thrombolytic therapy with streptokinase, urokinase, or recombinant tissue plasminogen activator, catheter-directed lysis or surgical embolectomy [58].

Hemodynamically stable patients with pulmonary embolism at low risk for bleeding and with normal renal function should be started on subcutaneous low molecular weight heparin, such as enoxaparin (1 mg/kg subcutaneously twice daily or 1.5 mg/kg subcutaneously once daily) or fondaparinux [59, 60]. In patients without cancer, warfarin can begin in 5 days, titrated to a target international normalized ratio (INR) of 2–3; warfarin should be continued for 3 months if the PE was considered provoked, by surgery or a medical illness, while warfarin should be continued for more than 3 months if

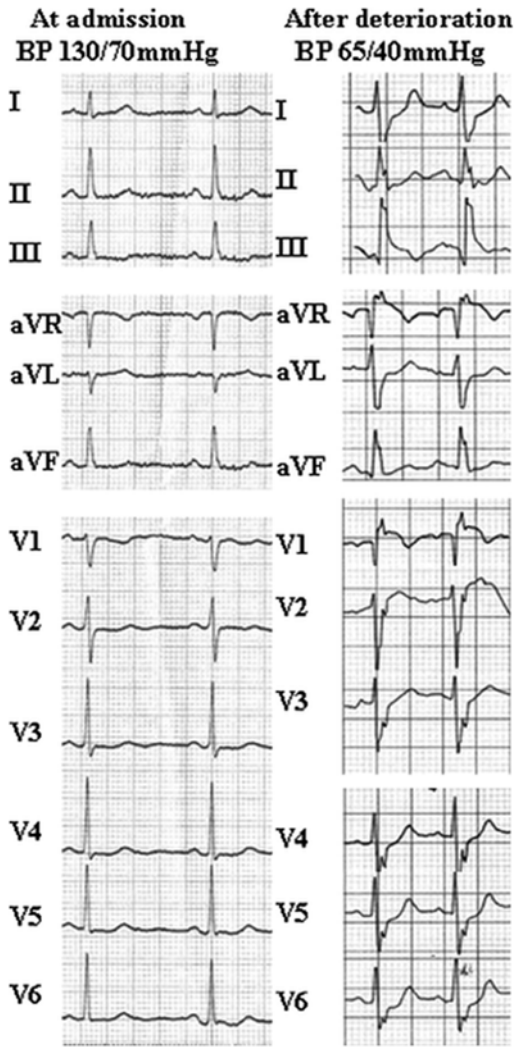

FIG. 15.4 The ECG showing S1Q3T3 in a patient with pulmonary embolism. The admission ECG (*left*) was normal. The ECG after deterioration (*right*) shows sinus tachycardia and S1Q3T3 (Reprinted from Zhan et al. [55], with permission of John Wiley & Sons, Inc)

Table 15.1 Wells' criteria for the prediction of pulmonary embolism (PE)

Clinical data	Points
Clinical symptoms concerning for deep vein thrombosis (DVT), particularly lower extremity swelling or pain	3
Clinical suspicion of PE as the leading diagnosis	3
Heart rate of greater than 100 beats per minute	1.5
Immobilization or surgery within the past month	1.5
History of a prior DVT or PE	1.5
Hemoptysis	1
Malignancy (treated currently or within the past 6 months or palliative)	1

From Wells et al. [57]

the PE was unprovoked. Those with malignancy should be continued on low molecular weight heparin as opposed to warfarin, for the duration of the active malignancy. Patients with renal dysfunction (creatinine clearance less than 30 mL/min) should be treated with unfractionated heparin. Although not discussed in detail here, an emerging role for non-vitamin K oral anticoagulants has been established and can be considered in treating patients with PE (e.g. rivaroxaban, dabigatran, edoxaban, apixaban).

TRALI

TRALI is suspected in patients with no preexisting lung injury and with new-onset respiratory distress during or within 6 h of transfusion of plasma-containing blood products [21]. Diagnostic criteria include acute onset of symptoms, with an oxygen saturation of less than 90 %, pulmonary artery wedge pressure of less than 18 mmHg (when available), and a chest radiograph with bilateral infiltrates [61].

Any transfusion should be stopped and the blood bank notified. In patients with TRALI, administer additional oxygen, which may be sufficient in mild illness [62]. Patients with significant or refractory hypoxemia may require mechanical

ventilation or even extracorporeal membrane oxygenation; respiratory support should be called to the patient's bedside and consultation emergently requested with an intensivist.

Chest Pain

Definitions

Acute Coronary Syndromes (ACSs) Syndromes of myocardial ischemia include unstable angina, non-ST segment elevation myocardial infarction (NSTEMI), and ST segment elevation myocardial infarction (STEMI) [27]. These syndromes are attributed to atherosclerotic plaque formation in the coronary arteries, which may rupture and/or thrombose [63]. Risk factors include age greater than 65 years in women, prior coronary artery disease, current smoking, diabetes, hypertension, hyperlipidemia, obesity, and family history of coronary artery disease [51].

Acute Aortic Syndrome A clinical syndrome encompassing classical aortic dissection as well as variant forms including penetrating atherosclerotic ulcer and intramural hematoma [64]. Risk factors include hypertension, dyslipidemia, cardiac valvular disease, smoking, illicit drug use, connective tissue disorders such as Marfan syndrome, autoimmune diseases such as giant cell or Takayasu arteritis, syphilis, tuberculosis, and cardiac surgery [65].

Pericarditis and Cardiac Tamponade Inflammation of the pericardium, the fibrous sac surrounding the heart, resulting in chest pain and ECG changes. Pericarditis can occur due to a variety of causes, including but not limited to viral and bacterial infections, sepsis, autoimmune or rheumatologic diseases, acute coronary syndromes, renal insufficiency, diabetes, malignancy, paraneoplastic disease, and following cardiac surgery or trauma [66]. Pericarditis can rarely result in constriction of the pericardium, which is usually chronic, eventually leading to

hemodynamic compromise. Pericardial effusions may develop, which may consist of transudate, exudate, purulence, or blood; 60 % of pericardial effusions are due to known medical conditions [67]. In patients with pericardial effusions, compression of the atria or ventricles may develop, called cardiac tamponade, which is a potentially life-threatening condition requiring immediate intervention.

Differential Diagnosis [56, 68]

Pulmonary embolism
Acute coronary syndrome
Angina
Acute aortic syndrome
Pericarditis
Myocarditis
Pneumonia
Pneumothorax
Pleural effusion
Asthma
Acute chest syndrome
Costochondritis
Gastroesophageal reflux (GERD)
Biliary colic
Mastalgia (breast pain)
Shoulder pain (including referred diaphragmatic irritation postoperatively)
Psychogenic/anxiety

When You Get the Call Ask for a complete set of vital signs and a 12-lead ECG.

When You Arrive Review the full vital signs flow sheet. If the patient is tachypneic, tachycardic, hypoxemic, or otherwise hemodynamically unstable, consider calling for additional

medical support for resuscitation. If the patient describes tearing chest pain, obtain blood pressures in both upper extremities and prepare for urgent aortic dissection protocol imaging [69].

History

Ask the patient when her pain started; review the distribution, quality, and radiation of her pain, any exacerbating (such as deep breaths) or alleviating factors, and whether she has had this pain before. Review whether certain actions or events preceded the pain, including ambulation/exertion, vomiting, eating, or feelings of anxiety. Review associated symptoms of dyspnea, palpitations, diaphoresis, pre-syncope or syncope, cough, nausea, or vomiting. If the patient is postoperative, review the details of her surgery, including surgical approach (vaginal, laparotomy, or laparoscopy), duration, thromboembolism prophylaxis, and intraoperative fluid resuscitation.

Review her past medical history, including prior cardiac disease, arrhythmias, hyperlipidemia, pulmonary disease, gastroesophageal reflux disease, costochondritis, arthritis, rheumatologic disease, sickle cell anemia, and risk factors for hypercoagulability (including recent surgery, obesity, or active malignancy). Review the patient's medications, including current prophylaxis against thromboembolism.

Physical Exam

Perform a targeted physical exam, first observing the patient's degree of distress and mental status. In patients with altered mental status or complaining of headache, neck pain, or blurry vision, perform a neurologic exam. Assess whether the patient's chest pain is reproducible by palpation of the chest, particularly the costochondral joints. Perform a cardiac exam, noting tachycardia, arrhythmia, muffled or extra heart sounds, or a pericardial rub. On pulmonary exam, note the presence of decreased breath sounds, particularly at one or both lung bases, crackles, stridor, or wheezing. Assess the patient's

pulses in bilateral upper and lower extremities. Assess the patient's fluid status, including edema in the extremities, and check for signs of deep vein thrombosis, particularly asymmetrical lower extremity edema or calf pain.

Diagnosis

In an acutely ill patient, particularly one with mental status changes or hemodynamic instability, a complete blood count and comprehensive metabolic panel should be collected; a lactate level should be obtained in patients with signs of sepsis. An arterial blood gas should be obtained in any patient with altered mental status, hypoxemia, or other evidence of hemodynamic instability. A troponin I or T should be collected in any patient with possible acute coronary syndrome. A D-dimer may be of utility in ruling out acute pulmonary embolism or acute aortic syndrome, though a D-dimer level may be falsely elevated in pregnant, postoperative, or elderly patients [29–31].

An ECG should be obtained in all patients with chest pain or pressure. If any abnormalities are noted, compare the most recent ECG to a prior one. ECG changes consistent with an acute coronary syndrome include ST segment changes, T wave inversions, pathologic Q waves, and/or a new left bundle branch block [70]. An ECG may also reveal an arrhythmia or changes associated with pulmonary embolism (Fig. 15.4).

In patients with "tearing" or sharp chest pain (usually maximal at onset), the diagnosis of an acute aortic syndrome should be considered. If an absent carotid or extremity pulse and/or a blood pressure differential between the upper extremities is found, the diagnosis of acute aortic syndrome should be assumed. For confirmation, the most rapidly available test of the following should be ordered for the diagnosis of aortic dissection: transesophageal echocardiogram, chest CT, or cardiac MRI [71].

In patients with chest pain and fever, productive cough, other pulmonary symptoms or positive pulmonary exam findings (particularly decreased breath sounds or crackles), or clinical evidence of fluid overload, a chest radiograph

should be obtained, which may reveal such pathology as pneumonia, pneumothorax, pulmonary effusion, pulmonary edema, cardiomegaly, mediastinal or aortic widening, and acute chest syndrome.

In patients with tachycardia and/or hypoxemia in addition to their chest pain, pulmonary embolism should be considered. Please see the preceding section, "Hypoxemia," for further information on the diagnosis and management of pulmonary embolism.

Management

Please see the preceding section, "Hypoxemia," for the management of pulmonary edema, pulmonary embolism, pneumonia, asthma, and acute chest syndrome.

Acute Coronary Syndrome

Reported symptoms most suggestive of an acute coronary syndrome are exertional chest pain, with radiation to one or both arms [72]. Chest pressure, nausea, and diaphoresis are moderately predictive, while pleuritic, positional, sharp, and reproducible pains are least consistent with an acute coronary syndrome.

Diagnosis of an acute myocardial infarction requires elevated troponin cTn (troponin I or troponin T) above the 99th percentile upper reference limit, with symptoms of ischemia or characteristic ECG changes (Fig. 15.5, Table 15.2) [70].

Of note, ST segment deviations may be noted in nonischemic disease, including acute pericarditis, left ventricular hypertrophy (LVH), left bundle branch block (LBBB), and stress cardiomyopathies [28].

In patients with clinical symptoms or ECG suggestive of an acute coronary syndrome, cardiology must be contacted emergently for further assessment and management. In patients with ECG changes and symptoms consistent with an acute coronary syndrome, cardiology can be contacted before a troponin level is resulted, in order to limit time to possible

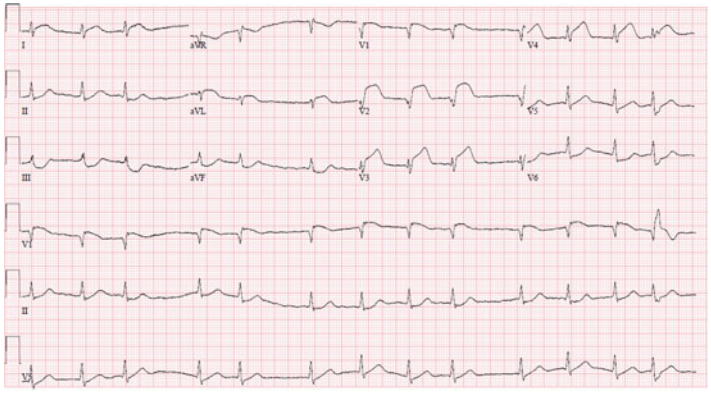

Fig. 15.5 ST elevation myocardial infarction (STEMI). The ECG demonstrates ST segment elevation in an anteroseptal (*V1–V4*) and high lateral distribution (*avL*) with inferior (*III*, *avF*) reciprocal ST segment depressions. These findings are consistent with the diagnosis of acute myocardial infarction. The patient's underlying rhythm is atrial fibrillation

percutaneous intervention. ECGs should be obtained every 15 min, and the patient should be given a full-dose aspirin that should be chewed to promote rapid absorption. If the patient is a candidate for percutaneous coronary intervention, weight-based heparin should be initiated immediately. While awaiting potential mobilization for percutaneous intervention, the patient's risk for bleeding should be assessed, including a bleeding diathesis, active bleeding, recent surgery, or surgery planned for the near future. These elements help to define the patient's suitability for dual antiplatelet therapy which is required during and after intervention.

Acute Aortic Syndrome

Sudden tearing chest pain that migrates from the chest to the lower back, particularly associated with neurologic deficits, a blood pressure difference of 20 mmHg or more between the upper extremities, and an absent carotid or extremity pulse are very strongly associated with acute aortic syndrome [69]. These findings are rarely all seen together.

Table 15.2 Electrocardiogram (ECG) findings concerning for acute coronary syndrome

ECG findings	Comment
ST segment elevations in two contiguous leads	Elevation >0.1 millivolts (mV), except in V2 or V3, where elevations should be >0.15 mV in women. Shown in Fig. 15.5
ST segment depression >0.05 mV in two contiguous leads	ST depressions can also result from nonischemic causes
T wave inversion in two contiguous leads with prominent R wave or R/S ratio of greater than 1	
New left bundle branch block	
Pathologic Q waves	

Thygesen et al. [70]

A D-dimer less than 500 ng/mL decreases the likelihood of an acute aortic syndrome [73]. Transesophageal echocardiogram, chest CT, and cardiac MRI are equally useful in diagnosing aortic dissection, though MRI requires the longest examination time, which limits clinicians' ability to closely monitor an unstable patient (Fig. 15.6) [74]. Chest radiograph and ECG are insufficient to diagnose or exclude an aortic dissection, though mediastinal widening may be noted on chest radiograph [69, 74].

Aortic dissections are classified as Type A, involving just the aortic arch, and Type B, occurring below the brachiocephalic vessels [75]. Cardiothoracic surgery (Type A) or vascular surgery (Type B) should be emergently consulted in the event of a positive radiographic finding of aortic dissection.

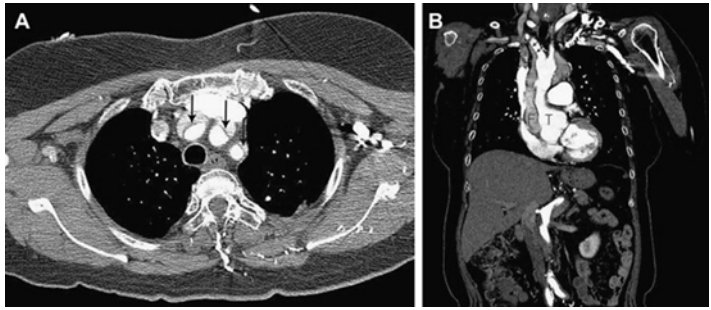

Fig. 15.6 Stanford type A aortic dissection by contrast-enhanced CT. (**a**) Intimomedial flap (*arrows*) is noted in brachiocephalic, left common carotid, and left subclavian artery at the level of left brachiocephalic vein. (**b**) Intimomedial flap (*arrows*) extending into brachiocephalic artery is noted on coronal image. The contrast enhancement in the true lumen (*T*) is higher than that of false lumen (*F*) (Reprinted from Yoo et al. [74], with permission from Elsevier)

Pericarditis and Cardiac Tamponade

Patients may be febrile, with chest pain, cough, and/or orthopnea [66]. On exam, patients may have a pericardial friction rub; patients with tamponade usually demonstrate an exaggerated pulsus paradoxus, which is a decline in systolic blood pressure of 10 mmHg or more with inspiration [66]. Tamponade in the absence of two or more signs of inflammation (pain, fever, pericardial friction rub on exam, or diffuse ST segment elevations) is more likely to due to a malignant effusion [66]. Patients with tamponade develop cardiogenic shock, evidenced by tachycardia, hypotension, and/or altered mental status.

Blood work may reveal leukocytosis, elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), and potentially elevated troponin if the patient has myopericarditis. The ECG in pericarditis may reveal diffuse ST segment elevations and T wave inversions, often in a non-vascular

distribution [76]. In contrast, the ECG in tamponade may reveal only low ECG voltage, and sometimes electrical alternans. Chest radiograph may show an enlarged, globular cardiac silhouette [77]. An echocardiogram may reveal an effusion; in patients with large effusions resulting in tamponade, echocardiogram will reveal the diastolic collapse of atrial or ventricular walls [66].

Pericarditis in stable patients can be treated with nonsteroidal anti-inflammatory drugs in addition to colchicine (0.5 mg PO twice per day); corticosteroids may be used for patients with pericardial disease attributed to autoimmune or rheumatologic conditions or uremia [66]. Steroids are not first-line therapy for pericarditis as they are associated with an increased rate of recurrent pericarditis. Large effusions resulting in hemodynamic changes or tamponade require drainage [66].

GERD

In patients with a history of gastroesophageal reflux, retrosternal burning pain, and/or an acidic taste in the mouth, a trial of an antacid—proton pump inhibitors or H2-receptor antagonists—may be helpful [78]. GERD should be a diagnosis of exclusion in patients with chest pain.

Musculoskeletal

Patients with reproducible chest or breast pain, in the absence of other clinically significant findings or vital sign changes, can be treated with analgesia; heating pads may also improve symptoms. Patients with primarily shoulder pain after surgery, particularly laparoscopy, may be symptomatic from diaphragmatic irritation by pneumoperitoneum or fluid. This is a diagnosis of exclusion [79].

Hypotension

Definition

Hypotension Definitions include a systolic blood pressure (SBP) decline of 20 % or more from a patient's baseline for 15 min or more or an SBP below 90 mmHg [80, 81]. While hypotension may be due to a variety of causes, when it is due to hemorrhage, up to 40 % of a patient's blood volume has already been lost by the time hypotension begins; this often marks the onset of decompensated hypovolemic shock [82].

Differential Diagnosis [83–85]

Hypovolemia, including hemorrhage
Sepsis
Cardiac dysfunction, including myocardial infarction, tamponade, heart failure, pulmonary embolus, arrhythmia
Anaphylaxis
Medication effect: antihypertensives, antipsychotics, anxiolytics, diuretics, nitrates, and opioids
Orthostasis
Vasovagal

When You Get the Call Ask for a full set of vital signs and a repeat blood pressure measurement, preferably manually if possible. Ask whether any events instigated the hypotension, such as standing quickly.

When You Arrive Assess the patient's distress and mental status. Confirm the patient's blood pressure, with a manual cuff if possible. In hypotensive patients who are febrile, hypoxemic, and tachycardic or have altered mental status, call for additional medical personnel, particularly if the patient may require triage to an intensive care unit.

Confirm that the patient has IV access; place a second IV in patients with hypotension and altered mental status, clinical evidence of bleeding, or other evidence of hemodynamic instability. Review the patient's known allergies, and compare with any new recent exposures that may have instigated anaphylaxis. Review the full vital sign flow sheet, including assessing for fever and adequate urine output (0.3–0.5 mL/kg per hour) [84]. Review any available blood pressure measurements prior to admission to establish her baseline blood pressure.

History

Review whether the patient is symptomatic from her hypotension, including headache, dizziness, pre-syncope, palpitations, chest pain, and shortness of breath. Ask the patient for her baseline blood pressure, whether low, normal, or high. Review the patient's past medical history, including known thrombophilia, bleeding diatheses, or cardiac disease including heart failure, hypertension, coronary artery disease, cardiac valvular disease, or cardiac arrhythmia. Review whether the patient was taking glucocorticoids prior to admission, which may place her at risk of adrenal insufficiency in the setting of surgery or acute illness.

Review the patient's current medications including epidural anesthesia and any recent medication or dosage changes. Review the patient's recent hemoglobin values, noting any downtrend. Assess whether she has had emesis or diarrhea, resulting in hypovolemia. If the patient is recently postoperative, review the operative report, including extent of surgical dissection, intravascular resuscitation, and blood loss. Of note, many surgical patients are already hypovolemic preoperatively due to fasting and an oral mechanical bowel preparation, and intraoperative blood and insensible fluid losses may have been inadequately replaced.

Physical Examination

Perform a focused physical examination, including a mental status assessment, cardiopulmonary exam, and abdominal exam for evidence of distension, rebound, or guarding. Examine recent surgical incisions for deformity (suggestive of dehiscence, hernia or hematoma), drainage or bleeding. Examine the abdomen and flanks for ecchymosis (the latter suggestive of retroperitoneal bleeding). Assess for vaginal hemorrhage. Examine the extremities for evidence of deep vein thrombosis, also noting whether the extremities are cool and clammy (suggestive of shock).

Diagnosis

Any patients with acute hypotension should have a complete blood count and basic metabolic panel; an ECG should be obtained, particularly in any patient with a cardiac history or symptoms of chest pain or dyspnea. Obtain coagulation studies (prothrombin time (PTT), activated partial thromboplastin time (aPTT) and fibrinogen) in patients receiving therapeutic anticoagulation or with clinical findings suggestive of hemorrhage. A lactate level should be obtained in patients with signs of sepsis or exam findings concerning for an acute intra-abdominal process. An arterial blood gas should be obtained in any patient with altered mental status, hypoxemia, or other evidence of hemodynamic instability [84].

Regarding patients who are acutely hypotensive in the hours after surgery—usually occurring in the postanesthesia care unit—inform the anesthesiology service. In addition to lab work, assess for vaginal bleeding and consider a focused assessment with sonography for trauma (FAST) scan for the rapid assessment of hemoperitoneum if ultrasound is readily available [86]. Assess for intraoperative exposures that may cause anaphylaxis, including medications, latex, and adhesives [84]. Consider chest x-ray if lung exam suggests decreased breath sounds and/or possible pneumothorax. The ECG remains critical in this setting to evaluate for arrhythmias that are poorly tolerated.

In patients with fever, obtain blood cultures, urine cultures, and sputum or wound cultures as applicable and a lactate level. A chest radiograph may be helpful, particularly in hypoxemic patients and postoperative patients who may have aspiration pneumonia. Please see Chap. 1, Acute Pelvic Pain, for more information on the diagnosis and management of sepsis.

In a postoperative patient, or an oncology patient receiving bevacizumab (conferring an increased risk of spontaneous bowel perforation), who also have a fever or otherwise concerning abdominal exam, consider an emergency abdominal CT scan to assess for abscess, bowel leakage, urinary tract injury, or hemorrhage [87]. Postoperative hemorrhage is likely to present in the hours after surgery, while abscess and occult gastrointestinal or urinary tract injuries commonly present days later. Please see Chap. 16, Complications of Minimally Invasive Gynecologic Surgery, for the diagnosis and management of visceral injury.

Management

In acutely ill patients, particularly those with fever, tachycardia, or altered mental status, call for additional medical personnel for support, particularly if the patient may require triage to an intensive care unit.

In patients with **sepsis**, expeditious resuscitation, including antibiotic initiation within 1 h of the diagnosis of sepsis, is vital to improved patient survival. Please see Chap. 1, Acute Pelvic Pain, for the management of sepsis. Essentially, identification of the suspected source of infection is crucial, either by clinical history, examination, or imaging. Antibiotic selection should be tailored to the suspected source and recent antibiotic exposure. Please refer to Chap. 16, Complications of Minimally Invasive Gynecologic Surgery, for antibiotic recommendations for specific infectious sources. In patients with sepsis from an unknown source, a broad-spectrum regimen can include vancomycin (15 mg/kg IV every 12 h in patients with normal renal function) and piperacillin–tazobactam (3.375–4.5 g IV every 6 h); alternatives to piperacillin–tazobactam include cefepime (2 g IV every 8 h) and ceftazidime (2 g IV every 8 h) [88].

Please see the preceding section "Hypoxemia" for the diagnosis and management of **pulmonary embolism** and **anaphylaxis. Acute coronary syndromes** are discussed in section "Chest pain." Please see Chap. 14, Common Postoperative and Inpatient Issues, section "Tachycardia" for the diagnosis and management of **atrial fibrillation**, the most common arrhythmia in postoperative or acutely ill patients.

Patients taking glucocorticoids chronically often require additional glucocorticoid supplementation—"stress dose steroids"—in the setting of acute illness or surgery [89]. Patients without this supplementation may develop **adrenal insufficiency**, resulting in hypotension and/or hyponatremia [89]. Patients taking more than 5 mg of prednisone or the equivalent per day for more than 3 weeks require stress dose steroids [89, 90]. For minor surgeries or illness (such as mild febrile illness), hydrocortisone (25 mg IV once) or methylprednisolone (5 mg IV once) is recommended, in addition to the patient's maintenance steroids [89]. Patients undergoing moderate surgeries or illness (such as hemicolectomy or pneumonia) can be treated with hydrocortisone (50–75 mg IV) or methylprednisolone (10–15 mg IV) on the day of the procedure, tapered over 1–2 days. Patients undergoing major surgery or severely ill (such as a Whipple procedure or pancreatitis) should be treated with hydrocortisone (100–150 mg IV) or methylprednisolone (20–30 mg IV) on the day of the procedure, tapered over 1–2 days. Finally, critically ill patients, with sepsis or septic shock, should receive hydrocortisone (50–100 mg IV every 6–8 h) and fludrocortisone (50 micrograms (μg) per day) until the shock is resolved, then tapered over a week.

Subacute relative hypotension in an otherwise stable patient is often due to hypovolemia and can usually be remedied with a fluid challenge, by infusing a 500-1,000 mL normal saline bolus over 15–20 min [91]. Fluid should be administered judiciously in older patients with cardiac, pulmonary or renal disease, due to the risk of fluid overload. In acutely ill patients, time should not be wasted with a trial of IV hydration alone.

Older and/or recently postoperative patients may also have **orthostatic hypotension**. If the patient is symptomatic or has vital sign changes with movement, check orthostatic vital signs by measuring blood pressure and pulse while the patient is lying down then standing [92]. A positive finding is a decrease in systolic blood pressure by at least 20 mmHg or diastolic blood pressure by at least 10 mmHg within 3 min of standing, usually accompanied by compensatory tachycardia. Conditions associated with orthostasis are hypovolemia—such as due to hemorrhage, dehydration from vomiting/diarrhea, or inadequate resuscitation in the operating room—deconditioning, and medications such as diuretics and narcotics. Orthostasis in the absence of more acute pathology is a diagnosis of exclusion. Until fully resuscitated, patients with orthostasis should be accompanied when standing up and may ultimately benefit from physical therapy consult depending on their functional capacity.

Finally, even in the absence of an allergic reaction, medications may contribute to relative hypotension in otherwise hemodynamically stable, well-appearing patients; consider decreasing the dose and/or frequency of narcotics. In surgical patients, epidural medication infusions can produce hypotension, and decreasing the analgesic infusion rate may be of utility in correcting hypotension [93].

Altered Mental Status

Definitions

Delirium An acute alteration in attention, awareness, and cognition, which often fluctuates [94]. Delirium is common in older people admitted to the hospital or residing in long-term care facilities; delirium occurs in 15–53 % of older adults after surgery [94]. Risk factors for delirium include major surgery, anesthesia, chronic illness, age greater than 65 years, dementia, and cognitive or vision impairment [95, 96]. Delirium confers an increased risk of mortality [95].

Alcohol Withdrawal Symptoms precipitated by alcohol cessation include anxiety, tachycardia, tachypnea, hypertension, pyrexia, and hand tremors [97]. Patients with severe withdrawal (delirium tremens) may have vomiting, hallucinations, agitation, and generalized tonic–clonic seizures [97]. After alcohol cessation, symptoms may begin within 8 h, peak in 72 h, and begin to resolve by 5–7 days [98].

Thrombotic thrombocytopenic purpura (TTP) A rare thrombotic microangiopathy, either familial or more commonly acquired, which results in a syndrome of thrombocytopenia, microangiopathic hemolytic anemia, neurologic abnormalities, renal failure, and fever [99, 100].

Differential Diagnosis [101]

Sepsis
Infection (urinary tract infection, pneumonia, bacteremia, meningitis)
Stroke
Seizure (postictal)
Hypertensive encephalopathy
Withdrawal (alcohol, sedatives)
Hypoxia
Hypoperfusion of the brain, including hypotension and cardiac arrhythmia
Medication effect (sedatives, narcotics, anticholinergics, barbiturates, dopamine agonists, serotonin syndrome)
Metabolic (electrolytes, renal failure, uremia, thyrotoxicosis, hyper-/hypoglycemia)
Thiamine deficiency
Urinary retention
Thrombotic thrombocytopenic purpura (TTP)
Dementia
Delirium
Psychiatric illness

When You Get the Call Ask for a full set of vital signs, including temperature and oxygenation.

When You Arrive Review the full vital signs flow sheet. Ensure that the patient has IV access. Assess the patient's degree of alertness and agitation. Stupor—meaning the patient is not arousable to verbal stimuli—or coma constitutes a medical emergency, and additional help should be called.

History

The extent of history taking may be limited by the acuity of the patient's illness or obtained while resuscitation maneuvers have begun. The patient may not be able to provide a history of her symptoms; collateral history from nurses and family is helpful. Ascertain the onset of symptoms (sudden or progressive) and whether the patient complained, or is complaining, of any symptoms such as abdominal pain, chest pain, shortness of breath, and severe headache. Determine whether the patient had any baseline cognitive or sensory impairments, which would predispose to delirium or affect the current assessment.

Review the patient's current medications including narcotics, sedatives, benzodiazepines, digoxin, and lithium. Review her full patient medical history, including seizure disorders, prior strokes or thromboembolic disease, risk factors for thromboembolism (including hereditary thrombophilias, obesity, immobility, recent surgery, or active malignancy), thrombotic thrombocytopenic purpura, renal insufficiency, liver disease, thyroid dysfunction, diabetes, dementia, psychiatric illness, or alcohol abuse.

Physical

Assess the patient's alertness and orientation. Assess for meningeal signs (including pain with flexion of the neck),

asterixis, and involuntary movements. Perform a full neurologic exam. Ophthalmoplegia can also be seen in patients with increased intracranial pressure or Wernicke encephalopathy (thiamine deficiency); the latter may also demonstrate ataxia [40]. The remainder of the physical exam should be directed to the patient's complaints. All postoperative patients should have an abdominal exam to assess for distention, pain, ecchymosis, and intact incisions.

Diagnosis

In any patient who becomes lethargic or somnolent, obtain a complete blood count with differential, complete metabolic panel (electrolytes including calcium, a creatinine level, and liver function tests), and an ECG. Obtain a lactate dehydrogenase (LDH) and ADAMTS 13 in patients with a history of TTP. If hemorrhage—vaginal or intra-abdominal—is suspected, coagulation studies, and a blood type and antibody screen should be collected. A finger-stick and arterial blood gas should be obtained in any patient with lethargy or somnolence. A toxicology screen can be obtained in new admissions or patients suspected of bringing illicit substances into the hospital. A urinalysis should also be obtained, as urinary tract infection can instigate delirium, particularly in the elderly. An emergent head CT should be ordered for any patients with focal neurologic findings or concern for stroke. In patients suspected of having had a seizure, urgent neurology consultation should be requested; these patients may require electroencephalograms. Please see Chap. 1, Acute Pelvic Pain, for the diagnosis and management of sepsis.

Differentiating delirium from dementia is an important step. Delirium is rapid onset and fluctuating; patients have inattention, altered consciousness, and disturbances of the sleep–wake cycle and may have disorganized thinking and hallucinations [40]. Dementia is gradual in onset, typically in a stably progressive course over months to years. Inattention, altered consciousness, disordered thinking, hallucinations, and sleep–wake

cycle disturbances are not usually present in patients with dementia. To meet the criteria for delirium, a patient's symptoms must wax and wane, with evidence of inattention—commonly tested by asking patients to count backward from 20 or recite the days of the week backward [102]. In addition, patients should demonstrate either disorganized thinking or altered consciousness, which can span lethargy to agitation [103].

Management

In an acutely somnolent patient who may not "protect the airway," optimally position the patient with extended neck and chin thrust if necessary. Altered mental status may result from hypoxemia; please see the preceding section "Hypoxemia" for the differential diagnosis and management of causal conditions. For the management of severe elevations in blood pressure or cardiac arrhythmias which may contribute to altered mental status, please see Chap. 14, Common Postoperative and Inpatient Issues, sections "Asymptomatic hypertension" and "Tachycardia," respectively, for more information. Please see Chap. 1, Acute Pelvic Pain, for the management of sepsis.

Metabolic derangements should be corrected. In patients with **hypoglycemia**, administer an ampule (50 mL) of a dextrose 50 % solution (D50) intravenously or 2 mg glucagon intramuscularly [40]. In malnourished patients or those with alcohol abuse, consider administering 100 mg of thiamine IV before administering glucose, as **Wernicke encephalopathy** (an acute, potentially life-threatening encephalopathy resulting from thiamine deficiency) can be precipitated or exacerbated by glucose administration.

In patients with new thrombocytopenia and an elevated LDH, **TTP** is a strong possibility and hematology should be consulted. Clinically, the presence of thrombocytopenia, schistocytes (fragmented erythrocytes) on a blood smear, and an elevated LDH, suggestive of hemolysis, are sufficient for diagnosis [100]. Acquired TTP, which is more common than familial TTP and generally presents in adolescents and adults, requires

emergent plasma exchange, which is overseen by hematology. Pregnancy is a known risk factor for the TTP syndrome. TTP is a medical emergency and a high index of clinical suspicion should remain in any patient with altered mental status and thrombocytopenia.

In patients receiving narcotics, particularly postoperative patients who may be receiving large doses of narcotics, consider the diagnosis of **narcotic excess**, managed by administering intravenous naloxone. Start with 0.4 mg, which can be increased to 2 mg if there is no response; doses can be repeated every 2–3 min, up to a total dose of 10 mg [40]. In this setting, be sure to remove fentanyl patches.

Signs and symptoms of **alcohol withdrawal** are commonly assessed using the Clinical Institute Withdrawal Assessment of Alcohol Scale (CIWA-Ar) [104, 105]. The score is based on a patient's symptoms of sweating, anxiety, agitation, tremor, auditory, visual or tactile disturbances, nausea, headache, or clouded sensorium [105]. Scores lower than 8 are generally mild. Patients with scores above 8–10 can receive chlordiazepoxide (50–100 mg), diazepam (10–20 mg), or lorazepam (2–4 mg), with reassessment hourly for improvement or need for more medication [106]. Patients with scores above 15 are at risk of delirium tremens and require close observation, sometimes in an intensive care unit [105]. The nutritional (such as thiamine) and intravascular volume deficits of patients in alcohol withdrawal must also be carefully repleted.

Medications contributing to altered mental status should be decreased or discontinued. Patients with **delirium** should be reoriented; a normal sleep cycle should be facilitated, adequate hydration and nutrition should be ensured, and early mobilization should be encouraged [95]. In patients with acute agitation who may be a danger to themselves, medication treatment options exist (Table 15.3). Haloperidol should be avoided in patients in substance withdrawal, hepatic insufficiency, Parkinson disease, or neuroleptic malignant syndrome [94]. Obtain baseline ECGs in hospitalized patients receiving these or other QT-prolonging medications, and repeat ECGs in patients receiving escalating doses; the QTc should be less than 500 msec [107].

Table 15.3 Medical management of delirium

Medication	Dose	Side effects
Haloperidol	0.5–1.0 mg PO twice per day with additional doses every 4 h as needed 0.5–1.0 mg IM or IV every 60 min as needed Maximum dose: 20 mg in 24 h	Extrapyramidal effects, prolonged QT, and torsades de pointes
Atypical antipsychotics	Olanzapine: 2.5–5.0 mg PO daily. Maximum dose of 20 mg in 24 h Quetiapine: 25 mg PO twice daily Risperidone: 0.5 mg PO twice daily	Extrapyramidal effects, prolonged QT and torsades de pointes, cerebrovascular accident, anticholinergic effects, hypotension Increased morality rate among elderly with dementia
Lorazepam	0.5–1.0 mg PO every 4 h	Oversedation, paradoxical excitation, worsened delirium
Trazodone	25–150 mg PO at bedtime	Oversedation or worsened delirium

From (1) Kalish et al. [94]. (2) Inouye [96]

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Chapter 16
Complications of Minimally Invasive Gynecologic Surgery

Paula C. Brady and Sarah L. Cohen

Definitions

Laparoscopy

Laparoscopy is a surgical approach in which the abdomen is insufflated with CO_2 and the procedure is completed using instruments inserted through small incisions in the abdomen (Fig. 16.1). Ports, usually 5–12 mm in diameter, are placed into the abdominal incisions to allow for insertion and removal of instruments, and the CO_2 gas source is connected to one of these ports to maintain abdominal insufflation. The surgery is visualized using a laparoscope, which is a telescopic lens 5–10 mm in diameter. At the conclusion of the surgery, the patient will have just a few small incisions on the abdomen. A patient who undergoes a total laparoscopic hysterectomy (meaning the cervix was removed with the uterus) will have an incision at the top of the

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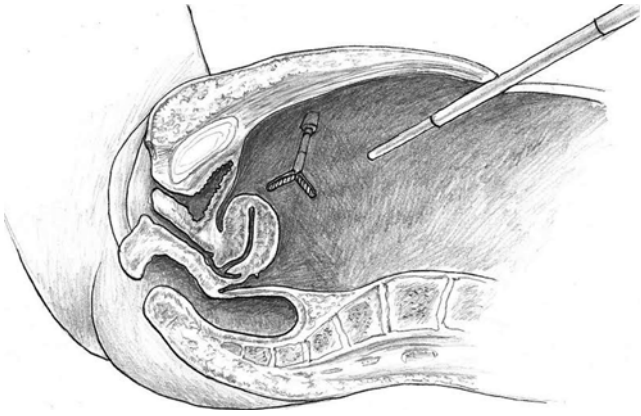

FIG. 16.1 Pelvic laparoscopy

vagina, called the **vaginal cuff**. If a patient has a supracervical hysterectomy (meaning the cervix is left in situ), a myomectomy (removal of fibroids), or removal of a large adnexal mass, one of the abdominal port sites may be enlarged (usually up to 3–5 cm) to accommodate the transabdominal removal of this tissue.

Robot-Assisted Laparoscopy

Robot-assisted laparoscopy involves similar core principles as conventional laparoscopy, with the assistance of a computerized system for enhanced visualization and manipulation of specialized laparoscopic instruments. The advantages of robotic surgery include three-dimensional visualization, articulated robotic arms with additional degrees of freedom, and improved ergonomics for the surgeon [1].

Hysteroscopy

Hysteroscopy is visualization of the endometrial cavity through distention of the uterus with fluid. Using a hysteroscope, fibroids, polyps, intrauterine septa, or adhesions can be removed. Distention media include electrolyte-poor fluids such as glycine 1.5 %, sorbitol 3 %, and mannitol 5 %—with risk of electrolyte abnormalities in the setting of excessive fluid absorption—and

isotonic fluids such as normal saline or lactated Ringer's solution [2]. Due to concerns of excessive intravascular absorption of the distention medium, a procedure should be stopped in the setting of fluid deficits of 1000–1500 mL of an electrolyte-poor solution or 2500 mL of an isotonic solution [2].

Differential Diagnosis by Primary Complaint

Fever

Superficial surgical site infection
Vaginal cuff cellulitis
Pelvic hematoma or abscess
Endomyometritis
Cystitis
Pyelonephritis
Clostridium difficile colitis
Toxic shock syndrome
Necrotizing fasciitis
Septic pelvic thrombophlebitis
Ovarian vein thrombosis
Deep vein thrombosis (DVT)
Pulmonary embolism (PE)
Pneumonia
Medication effect (drug fever)
Urinary tract or bowel injury
Retained foreign body
Alcohol withdrawal
Transfusion reaction

The differential diagnosis for fever varies with the interval from surgery. Fevers in the first 24 h after surgery are commonly noninfectious, due to inflammation or medication reactions. Infectious complications of surgery usually present 48 h or more after surgery. Pneumonia (particularly aspiration) and urinary tract infections may present as early as 2–3

days postoperatively, while the presentation of surgical site infections, vaginal cuff complications and pelvic abscesses commonly may be delayed by 5 or more days postoperatively. Bowel and urinary tract injuries typically present in the days following surgery, but may be delayed by 1–2 weeks. Thromboembolism may occur at any point.

Pain

Inadequate analgesic medication
Superficial surgical site infection
Endomyometritis
Vaginal cuff cellulitis
Pelvic hematoma or abscess
Necrotizing fasciitis
Cystitis
Pyelonephritis
Ovarian vein thrombosis
Vaginal cuff dehiscence
Uterine perforation
Bowel injury
Bowel obstruction
Urinary tract injury
Urinary retention
Port site hernia or hematoma
Persistent pneumoperitoneum
Nerve entrapment
Musculoskeletal pain

Nausea/Vomiting

Bowel obstruction or injury
Ileus
Port site herniation
Urinary tract infection
Urinary ascites (urinary tract injury)
Medication effects (including anesthetics and narcotics)
Nonsurgery related (e.g., viral gastroenteritis)

When You Get the Call Ask for a full set of the most recent vital signs. If the patient's complaint is pain, consider requesting that pain medications are temporarily withheld, if possible, to allow for an accurate physical examination.

When You Arrive Review the patient's vital signs to assess for hypotension, tachycardia, or hypoxia. Clarify the date of the patient's surgery, as certain complications may be expected at specific intervals from surgery. Review the operative report, including the extent of dissection, complications, administration of perioperative antibiotics, and use of mechanical or chemical thromboprophylaxis. Also review for any implants—such as clips and mesh—or hemostatic agents, which may affect interpretation of imaging. Hemostatic agents, such as oxidized regenerated cellulose (Surgicel®, Ethicon, Somerville, NJ) and gelatin bioabsorbable sponges (Gelfoam®, Pfizer, New York, NY, and Surgifoam®, Ethicon, Somerville, NJ), may appear as an abscess on imaging, in the absence of infection [3–5]. If hysteroscopy was performed, note the distention medium and fluid deficit.

History

Review with the patient when her primary symptoms began and any associated symptoms, including but not limited to fever, abdominal distention, nausea, vomiting, or diarrhea. If the patient is presenting with vaginal bleeding, discharge or abdominal pain, review her activities at the time of symptom onset, including heavy lifting or intercourse. Sudden onset of pain after bearing down or intercourse may raise concern for vaginal cuff dehiscence in patients who have had a total hysterectomy.

Review her full medical history, including any chronic diseases such as diabetes, a history of venous thromboembolism, whether she smokes, and menopausal status. Make note of

any current medications, including anticoagulant therapy, and whether this medication was withheld surrounding surgery. Review her prior surgical history, as prior surgeries may increase the risk of adhesions and intraoperative injury to other organs.

Physical Examination

In the setting of fever, the patient should have a head-to-toe assessment, including examination of the respiratory tract for signs of pneumonia, the abdomen for signs of peritonitis and port site hernia or infection, and the lower extremities for evidence of thrombus.

For patients with pain and/or fever after a total hysterectomy, a bimanual exam should be performed to confirm that the vaginal cuff is intact and to assess for tenderness or a fullness of the vaginal cuff concerning for abscess or hematoma, as well as pelvic tenderness or pain. On sterile speculum exam, note any sources of bleeding and whether the vaginal cuff is intact; assess for erythema, induration, or vaginal discharge, and culture any purulent vaginal discharge.

Diagnosis

Fever

Postoperatively, a temperature of 100.4 °F (38 °C) on two occasions more than 4 h apart or a single temperature of 101 °F (38.5 °C) constitutes a fever [6]. Patients with significant complications, such as pelvic abscess or bowel injury, may present with septic physiology, which must be identified and addressed quickly [7]. The diagnostic criteria of sepsis are shown in Table 16.1; for further management of sepsis, please see Chap. 1., Acute Pelvic Pain [8, 9].

Table 16.1 Clinical criteria of sepsis and severe sepsis

Sepsis	Severe sepsis
Suspected source plus 2 or more: 1. Temperature >38.3 °C (101 °F) or <36 °C (96.8 °F) 2. Heart rate >90 beats per minute 3. Tachypnea (>20 breaths/min) 4. WBC >12,000 μ/L or <4000 μ/L or normal with >10 % immature (band) forms	Sepsis plus one or more: 1. Systolic blood pressure < 90 mmHg or decrease from baseline by 40 mm Hg 2. Elevated lactate (>1 mmol/L; >4 particularly concerning, sign of organ hypoperfusion) 3. Acute lung injury: PaO_2/FIO_2 <250 (in the absence of pneumonia) or <200 (with pneumonia) 4. Acute oliguria: <0.5 mL/kg/h despite fluid resuscitation 5. Creatinine >2 mg/dL 6. INR >1.5 7. Platelets <100,000/uL 8. Bilirubin >2 mg/dL

Criteria from Fischerova [8]; Dellinger et al. [9]

Risk factors for postoperative infection include advanced age, immunosuppression, diabetes, smoking, obesity, operative time greater than 3 h, use of a razor for hair removal at the surgical site, and lack of prophylactic antibiotics [10]. The wound classification also affects risk of infection, with the risk increases progressively along the classes up to 27 % or more with dirty wounds (Table 16.2) [11–14].

Laboratory testing should include a complete blood count with a differential and urinalysis. Patients with possible sepsis (including high fever and hemodynamic changes) should also have electrolytes, creatinine, liver function tests, coagulation studies (prothrombin time and activated partial thromboplastin time) and a lactate checked. In patients with a fever of

Table 16.2 Surgical wound classification

Class I/*clean*: An uninfected operative wound in which no inflammation is encountered and the respiratory, alimentary, genital, or urinary tract is not entered. In addition, clean wounds are primarily closed and, if necessary, drained with closed drainage. Operative incisional wounds that follow nonpenetrating (blunt) trauma should be included in this category if they meet the criteria
Class II/*clean-contaminated*: An operative wound in which the respiratory, alimentary, genital, or urinary tracts are entered under controlled conditions and without unusual contamination. Specifically, operations involving the biliary tract, appendix, vagina, and oropharynx are included in this category, provided no evidence of infection or major break in technique is encountered
Class III/*contaminated*: Open, fresh, accidental wounds. In addition, operations with major breaks in sterile technique (e.g., open cardiac massage) or gross spillage from the gastrointestinal tract and incisions in which acute, nonpurulent inflammation is encountered are included in this category
Class IV/*dirty-infected*: Old traumatic wounds with retained devitalized tissue and those that involve existing clinical infection or perforated viscera. This definition suggests that the organisms causing postoperative infection were present in the operative field before the operation

Adapted from Mangram et al. [12], with permission from Elsevier and the Association for Professionals in Infection Control and Epidemiology, Inc.

38.5 °C (101 °F) or more, obtain blood cultures in addition to a urine culture, cultures of any purulent wound exudate, or a vaginal culture. Obtain imaging as indicated by the history and physical exam, including chest radiograph, pelvic ultrasound, or abdominal CT scan. Abdominal CT scans are particularly helpful in identifying pelvic hematomas or abscesses but can also identify other sources of fever, including bowel injuries and urinary tract injuries. Oral and intravenous CT contrast should be given whenever possible.

Pain

Patients presenting with significant pain postoperatively should have a complete blood count to assess for leukocytosis and anemia. A basic metabolic panel may be obtained to assess for electrolyte derangements and creatinine elevation, particularly in the setting of nausea/vomiting. A urinalysis may reveal urinary tract infection. Abdominal imaging should be obtained, targeted to the suspected source of pain. If the differential diagnosis remains broad, an abdominal CT scan with oral and IV contrast can be helpful, revealing urinary or gastrointestinal tract injuries or obstructions, pelvic fluid collections (hematoma, abscess, or urinary ascites), or thromboses in pelvic vessels.

Management

The most common complications of laparoscopy are shown in Table 16.3, presented in the order they are discussed in the text.

Infection

Superficial Surgical Site Infection

Laparoscopy is associated with a reduced risk of surgical site infection as compared to laparotomy (0–2 % versus 6.5 %, respectively) [15]. Worsening pain at an incision, accompanied by warmth, erythema, or induration, is suggestive of a surgical site infection [7, 11]. If examination or imaging suggests the presence of a fluid collection under the skin—seroma, hematoma, or abscess—or purulent fluid is expressed from the incision, a wound should be opened, irrigated, and managed with wet-to-dry dressings [7, 16]. The fascia should be probed with a sterile cotton swab to ensure no dehiscence has occurred.

Table 16.3 Complications of gynecologic laparoscopic surgery

Complication	Incidence
Surgical site infection	1 %
Vaginal cuff cellulitis	1.5 %
Pelvic abscess	0.8 %
Urinary tract infection	13 %
Pneumonia	1.6 %
Venous thromboembolism	1 %
Ureteral injury	0.8–1.7 %
Bladder injury	1.6–2.9 %
Urinary retention	7–15 %
Bowel injury	0.03–0.39 %
Small bowel obstruction	0.53 %
Ileus	0.2 %
Vaginal cuff dehiscence	0.31 %
Port site herniation	3.1 % (12 mm ports), 0.57 % (10 mm ports)
Port site hematoma	0.5 %
Nerve injury	2 %
Subcutaneous emphysema	2.3 %

References for these values are provided in the text. The high end of each range reflects complication rates of laparoscopic hysterectomy, while the low end represents other gynecologic laparoscopy

Opening an infected wound can be sufficient management; however, if surrounding erythema is observed, or fever and/or leukocytosis are documented, antibiotics should be given. For mild symptoms, cephalexin (500 milligrams (mg) PO every 6 h) or trimethoprim-sulfamethoxazole double strength (160–800 mg PO every 12 h) can be used [17]. The latter provides coverage for methicillin-resistant *Staphylococcus aureus*, as does clindamycin (300–450 mg PO every 6 h) [18].

Vaginal Cuff Cellulitis

Vaginal cuff cellulitis occurs following 1.5 % of hysterectomies [19]. Patients with untreated preoperative vaginal infections, including bacterial vaginosis and *Trichomonas vaginalis*, are at increased risk of developing postoperative cuff cellulitis [20]. Patients usually present 5–10 days after surgery with fever, pelvic or low back pain, the feeling of pelvic fullness, and/or vaginal discharge [6]. Patients will have tenderness localized to the vaginal cuff, which may be erythematous and indurated or have purulent discharge [21]. Any discharge should be cultured in order to direct antibiotic therapy [22].

Hemodynamically stable patients with mild symptoms and no evidence of cuff abscess may be treated with oral antibiotics, including amoxicillin–clavulanate (875–125 mg PO every 12 h) alone, or metronidazole (500 mg PO every 8 h) with either a fluoroquinolone such as ciprofloxacin (500 mg PO every 12 h) or trimethoprim-sulfamethoxazole double strength (160–800 mg PO every 12 h) [21–23]. If a patient's symptoms do not improve in 24–48 h, assessment should be initiated for other sources of infection, including imaging to assess for pelvic abscesses.

In patients with any hemodynamic derangements, severe pain, inability to tolerate oral antibiotics, or evidence of pelvic abscess, intravenous antibiotics should be initiated. If an abscess is present, consideration of surgical drainage should be undertaken per discussion below. Options for parenteral antibiotics include penicillins with beta-lactamase inhibitors, such as ampicillin–sulbactam (3 g IV every 6 h) or piperacillin-tazobactam (3375 g IV every 6 h), or a later-generation cephalosporin such as cefotetan (2 g IV every 12 h) [23]. If a patient does not improve, or is acutely ill, broader-spectrum antibiotics should be started, such as clindamycin (900 mg IV every 8 h) plus ampicillin (2 g IV every 6 h) plus gentamicin (2 mg per kilogram (kg) IV, then 1.5 mg/kg every 8 h *or* 5 mg/kg ideal body weight every 24 h). Metronidazole (500 mg IV every 8 h) is an alternative to clindamycin in this regimen. An alternative regimen is levofloxacin (500 mg IV every 24 h) and metronidazole (500 mg IV every 8 h).

Pelvic Abscess

Pelvic abscesses, including tubo-ovarian abscesses, occur in 0.8 % of patients who have undergone gynecologic surgery [24]. Patients present 10–14 days after surgery with fever, pelvic pain or fullness [6, 16]. Infections are typically polymicrobial and often include anaerobes [6]. Pelvic fluid collections may be imaged using ultrasonography, CT, or MRI. The presence of internal gas bubbles and a capsule or ring-enhancing lesion are suggestive of abscess [25]. Of note, some degree of fluid or even hematoma in the pelvis after hysterectomy is commonly detected on imaging; this alone does not indicate that a complication has occurred [7]. Additionally, if a hemostatic agent was utilized during the initial surgical procedure—such as oxidized regenerated cellulose (Surgicel®, Ethicon, Somerville, NJ) and gelatin bioabsorbable sponges (Gelfoam®, Pfizer, New York, NY, and Surgifoam®, Ethicon, Somerville, NJ)—it may appear on postoperative imaging as a complex fluid collection located in the hemostatic bed.

Patients with fever and a pelvic abscess by imaging should be treated with IV broad-spectrum antibiotics until afebrile for 24–48 h. Extrapolating from studies of tubo-ovarian abscesses, 8 cm is the upper limit of abscess size that may be treated with IV antibiotics without drainage, although many clinicians would pursue drainage at a smaller abscess size or when initial antibiotic therapy fails to produce clinical improvement [26]. Similar to severe vaginal cuff cellulitis, presumptive regimens include clindamycin (900 mg IV every 8 h) or metronidazole (500 mg IV every 8 h) plus gentamicin (2 mg/kg IV, then 1.5 mg/kg every 8 h *or* 5 mg/kg ideal body weight every 24 h), with or without ampicillin (2 g IV every 6 h) [21, 23]. Other broad-spectrum regimens include (1) piperacillin-tazobactam (3375 g IV every 6 h), (2) ceftriaxone (2 g IV every 24 h) plus metronidazole (500 mg IV every 8 h) or clindamycin (900 mg IV every 8 h), or (3) a carbapenem, such as meropenem (1 g IV every 8 h) [21, 27].

If patients do not initially improve, abscess drainage should be pursued. Persistent fevers and leukocytosis, worsening pain, and increase in abscess size by imaging constitute failure of IV antibiotics alone, often due to poor perfusion of the abscess, preventing adequate antibiotic penetration [21]. Development of septic physiology is also an indication for intervention, either surgical or by interventional radiology. Patients with ruptured abscesses may develop septic shock and require emergent surgical intervention. Drainage of pelvic abscesses in sufficiently stable patients is most commonly performed percutaneously (transabdominally or transgluteally) by interventional radiology with CT guidance. Abscesses in the posterior cul-de-sac could potentially be accessed transvaginally. Alternatively, surgical drainage and washout of the abscess can be pursued; surgical treatment of a pelvic abscess can be a complex and morbid procedure, potentially requiring removal of involved gynecologic organs [23].

After the patient is afebrile for 24–48 h, she should be transitioned to oral antibiotics, for 7–10 days as dictated by wound culture results. Oral options include metronidazole (500 mg every 8 h) and trimethoprim-sulfamethoxazole (160–800 mg every 12 h), or amoxicillin–clavulanate (875–125 mg every 12 h alone) [21].

Endomyometritis

Endomyometritis is a polymicrobial infection of the endometrial lining or uterine muscle that can occur after any uterine instrumentation, including hysteroscopy or curettage. Risk of endomyometritis is less than 1 % following hysteroscopy [28, 29]. Patients present with vague abdominal pain and irregular spotting or bleeding. On physical examination, patients have uterine tenderness and may have cervical motion tenderness. Options for treatment include (1) amoxicillin–clavulanate (875–125 mg PO every 12 h), or (2) amoxicillin (500 mg PO every 8 h) and metronidazole (500 mg PO every 8 h) [30]. Please see Chap. 12, Obstetrics in the Emergency Room, for discussion of group A streptococcus endomyometritis, a severe, potentially lethal infection.

Toxic Shock Syndrome (TSS)

A syndrome initially recognized most commonly in menstruating women with *Staphylococcus aureus* infections and associated with tampon use, TSS is now diagnosed most often in nonmenstruating women and can also be caused by *Streptococcus pyogenes* (group A streptococcus, or GAS) or *Clostridium sordellii* [31–33]. TSS can occur postoperatively, usually developing 2 days after surgery; it has been reported following hysterectomy, as well as after cone biopsy, IUD insertion, endometrial biopsy, and medical abortion [31, 34–37]. TSS also occurs in postpartum women.

General diagnostic criteria of toxic shock syndrome include fever of at least 38.9 °C (102 °F), hypotension (defined as a systolic blood pressure of 90 mm Hg or less in patients over 16 years of age), erythroderma (a diffuse blanching rash resembling a sunburn), desquamation occurring 1–2 weeks after the initial rash, and dysfunction of three or more organ systems, including vomiting or diarrhea, severe myalgias or elevated creatine phosphokinase, elevated creatinine or pyuria without urinary tract infection, liver function testing twice the upper limit of normal, platelets of 100,000/μL or less, mucous membrane hyperemia, and mental status changes [38]. Cultures should be negative for Rocky Mountain spotted fever, leptospirosis, or measles, which can have overlapping features. Criteria specific to GAS TSS include cultures (blood, cerebrospinal fluid, tissue or surgical wound) positive for GAS and hypotension, with evidence of dysfunction in two organ systems, including creatinine greater than 2 mg per deciliter (dL) (or twice the baseline value), platelets of 100,000/μL or abnormal coagulation factors or fibrinogen, liver function testing twice the baseline or upper limit of normal, acute respiratory distress syndrome, erythroderma, or soft tissue necrosis [39]. Patients with toxic shock syndrome commonly also have 15,000 or more white blood cells per μL with 10 % or more bands present on differential.

Treatment is supportive, involving aggressive fluid resuscitations to address hypotension and correction of coagulopathy; patients usually require admission to an intensive care

unit and coordination with infectious disease specialists. Any necrotizing wounds should be debrided, which may include hysterectomy if the uterus is the suspected source of infection [40].

Management also includes antibiotics; clindamycin (900 mg IV every 8 h) is indicated for all TSS as it inhibits toxin production [35]. Patients with GAS or clostridial TSS should also receive penicillin G (4 million units IV every 4 h). Treatment for TSS associated with methicillin-sensitive *Staphylococcus aureus* requires the addition of oxacillin (2 g IV every 4 h), while methicillin-resistant *Staphylococcus aureus* requires vancomycin (15–20 mg/kg IV every 8–12 h) or linezolid (600 mg IV every 12 h) [41, 42]. Intravenous immunoglobulin may be considered as well.

Necrotizing Fasciitis

This rare wound complication is often caused by either *Streptococcus pyogenes* (group A streptococcus) or infection with one or more anaerobic species. Risk factors include chronic disease such as diabetes or renal insufficiency, immunosuppression, malnutrition, obesity, and age over 60 years [43]. Initial physical findings may resemble cellulitis, but bullae and skin necrosis may develop, with rapid progression of erythema and edema. Patients may develop creptius (subcutaneous gas) [44]. On physical exam, patients will often have fever and exquisite pain out of proportion to their exam findings. A white blood cell count above 25,000/μL is suggestive of necrotizing fasciitis [43]. Patients may also have elevated glucose (above 180 mg/dL), creatinine (above 1.6 mg/dL), and C-reaction protein (above 4 mg/L), as well as elevated lactate and creatine kinase (600 U/L or greater) [43, 44]. Imaging can be helpful in diagnosing necrotizing fasciitis; depending on the type of surgery performed and the patient's symptoms, ultrasound, CT, or MRI may reveal infectious collections, thickened fascia or subcutaneous air [45]. Definitive diagnosis can only be made following surgery by histopathologic analysis.

Once the diagnosis is suspected, general surgery and infectious disease consultations should be obtained. Expeditious surgical debridement of infected tissue is vital in the management of necrotizing fasciitis. Affected tissues may appear gray and necrotic and can be bluntly dissected with ease; purulence resembling "dishwater" may also be present [44]. Cultures should be obtained to tailor antibiotic treatment.

Broad-spectrum antibiotics should also be initiated as soon as necrotizing fasciitis is suspected; possible regimens include vancomycin (15–20 mg/kg IV every 8–12 h) or linezolid (600 mg IV every 12 h) plus a carbapenem (such as meropenem 1 g IV every 8 h) or piperacillin-tazobactam (3375 g IV every 6 h) [17, 42]. Once confirmed by wound or blood cultures, streptococcal or clostridial necrotizing fasciitis should be treated with penicillin (2–4 million units IV every 4–6 h) and clindamycin (900 mg IV every 8 h). Mixed bacterial infections can be managed with (1) cefotaxime (2 g IV every 6 h) plus metronidazole or clindamycin, (2) piperacillin-tazobactam plus vancomycin, or (3) monotherapy with a carbapenem in the doses described above [17]. During the patient's hospitalization, frequent physical exams and serial white blood cell counts should be performed to assess clinical progress. Serial debridements are often necessary.

Urinary Tract Infections

Cystitis, commonly called a urinary tract infection (UTI), occurs in up to 13 % of patients following gynecologic surgery [46]. Signs and symptoms include low-grade fever, frequency, urgency, and dysuria. On exam, patients may have suprapubic pain or tenderness of the anterior abdominal wall [7]. Urinalysis may show leukocyte esterase (a sign that leukocytes are present), nitrites (a sign that bacteria are present), and, on microscopic analysis, pyuria (10 leukocytes/mL) and/or bacteriuria [47]. Urine cultures should be obtained before starting any antibiotics if possible.

Antibiotic options include trimethoprim-sulfamethoxazole (160–800 mg PO every 12 h for 3 days), ciprofloxacin (250 mg PO every 12 h for 3 days), and nitrofurantoin monohydrate (100 mg PO every 12 h for 7 days); nitrofurantoin is bacteriostatic and may be less effective against some infections [47]. Alternatives with less efficacy that are also acceptable include fosfomycin trometamol (3 g PO one dose), amoxicillin–clavulanate, cefaclor, or cefpodoxime proxetil for 3–7 days. Antibiotic selection should be adjusted according to urine culture results.

Patients with infection of the upper urologic tract, also called pyelonephritis, will present with fevers and flank pain in addition to the symptoms of a UTI. In patients with severe flank pain, renal calculus should be ruled out with imaging such as CT scan or renal ultrasound. Hemodynamically stable, nongravid patients with mild symptoms may be treated as outpatients with fluoroquinolones, either levofloxacin (750 mg PO once per day for 5 days) or ciprofloxacin (500 mg PO twice daily, or extended release 1000 mg PO once daily, for 7 days) [48, 49]. Alternatively, trimethoprim-sulfamethoxazole (160–800 mg PO every 12 h for 14 days) may be used. In patients with septic physiology and inability to tolerate oral antibiotics or in cases in which resistance to fluoroquinolones is suspected, inpatient management with parenteral antibiotics may be indicated. Options include ceftriaxone (1–2 g IV daily), or, for severe infection, piperacillin-tazobactam (3375 g IV every 6 h), or meropenem (500 mg IV every 8 h) [42, 49, 50]. Severely ill patients, or those whose symptoms have not improved in 48 h, may require CT scan to assess for abscess or other complicating factors.

Pneumonia

Pneumonia occurs postoperatively in approximately 1.6 % of patients following gynecologic surgery [51]. Patients may present with fever, dyspnea, and cough productive of sputum. Patients will have decreased breath sounds on physical exam

and may have hypoxia. Diagnosis is made by chest radiograph; sputum cultures can be sent to direct antibiotic selection.

Risk factors for multidrug-resistant pathogens include antibiotic exposure within the last 90 days, current hospitalization of 5 days or more, hospitalization of 2 days or more in the past 90 days, immunosuppression, home wound care, and residence in a nursing home or extended care facility [52]. Patients who do not meet these criteria can be treated with ceftriaxone (2 g IV daily), fluoroquinolones such as levofloxacin (750 mg IV or PO daily), ampicillin–sulbactam (3 g IV every 6 h), or ertapenem (1 g IV daily). Patients with risk factors for multidrug resistance require broad-spectrum antibiotics: an antipseudomonal cephalosporin (cefepime 1–2 g IV every 8–12 h or ceftazidime 2 g IV every 8 h), an antipseudomonal carbapenem (imipenem 500 mg IV every 6 h or meropenem 1 g every 8 h), or piperacillin-tazobactam (4.5 g every 6 h). In patients with suspected or confirmed methicillin-resistant *Staphylococcus aureus*, risk factors for MRSA or in areas with high incidence, add linezolid (600 mg IV every 12 h), or vancomycin (12 mg/kg IV every 12 h) [52]. The original American Thoracic Society (ATS) and Infectious Diseases Society of America (IDSA) guidelines propose double coverage with an aminoglycoside such as gentamicin or a fluoroquinolone such as levofloxacin or ciprofloxacin, which may add to the toxicity of the regimen but can be considered in patients with cultures showing gram-negative bacilli [53]. Consider discussion with the hospital's infectious disease staff, as local pathogen and resistance profiles vary. Antibiotics should be adjusted according to sputum and blood culture results.

Thrombotic

Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE)

The incidence of venous thromboembolism after laparoscopic hysterectomy is 1 % [54]. Various risk assessment scores exist to quantify a patient's risk of perioperative

venous thromboembolism (VTE), such as the Caprini Risk Assessment Model [55, 56]. Low risk factors (conferring one point each in this scoring system) include age 41–60 years, minor surgery, body mass index greater than 25 kg/m^2, swollen legs, varicose veins, pregnancy or postpartum state, history of recurrent abortion, oral contraceptives or hormone replacement, sepsis within the last month, significant pulmonary disease (such as pneumonia in the last month), acute myocardial infarction, congestive heart failure, inflammatory bowel disease, and immobilization. Moderate risk factors (conferring two points each) include age 61–74 years, major open surgery or laparoscopic surgery (longer than 45 min), malignancy, and central venous access. Factors associated with highest risk, each conferring 3 points, include age greater than 75 years, a family history of VTE, thrombophilias (particularly factor V Leiden, prothrombin 20210A gene mutation, and antiphospholipid antibodies), and heparin-induced thrombocytopenia. Stroke and spinal cord injury in the past month each confer 5 points. Patients with no risk factors have a VTE risk of 0.5 %, while those with 1–2 points have a risk of 1.5 %; patients with 3–4 points have a VTE risk of 3 %, and those with 5 points or more have a risk of 6 % [57].

Patients with DVT may present with unilateral lower extremity pain, erythema, and edema. Tenderness in the distribution of deep veins of the leg, or a calf swollen to 3 cm greater in diameter than the contralateral side, 10 cm below the tibial tuberosity, is particularly concerning for DVT [58]. Duplex Doppler venous ultrasonography is the definitive method of diagnosis [7].

PE is a highly morbid surgical complication; in a review of venous thromboembolism after hysterectomy, the mortality rate of postoperative PE was 0.91 % [59]. Increased risk of death from PE is associated with age over 80 years, chronic cardiopulmonary disease, and arterial oxygen saturation less than 90 % [60]. Patients with pulmonary embolism may complain of dyspnea, chest pain, cough, or hemoptysis. Patients with PE may present with hypoxia, tachypnea, and tachycardia. D-dimer is artificially elevated in the postoperative setting and may be less useful as a triage test [61]. Patients' risk

Table 16.4 Wells criteria for prediction of pulmonary embolism (PE)

Clinical data	Points
Clinical symptoms concerning for deep vein thrombosis (DVT), particularly lower extremity swelling or pain	3
Clinical suspicion of PE as the leading diagnosis	3
Heart rate of greater than 100 beats per minute	1.5
Immobilization or surgery within the past month	1.5
History of a prior DVT or PE	1.5
Hemoptysis	1
Malignancy (treated currently or within the past 6 months, or palliative)	1

Wells et al. [62]

for pulmonary embolism may be stratified according to Wells Criteria, shown in Table 16.4 [62].

A total of less than 2 points is low risk; in this category, 2 % of patients are diagnosed with PE. Moderate risk is defined as a score of 2–6 points, with a rate of PE of 18.8 %, while a score of greater than 6 points is considered high risk, with a rate of PE of 50 %. Patients with moderate to high risk of PE by Wells Criteria, or otherwise high risk or clinically concerning for PE, should undergo a chest CT with IV contrast, with a protocol specific to the detection of PE [7].

Patients with deep vein thrombosis or pulmonary embolism require anticoagulation. In patients with hemodynamic instability, shock, or severe hypoxemia attributed to pulmonary embolism, an unfractionated heparin IV infusion should be started, in a weight-based algorithm guided by activated partial thromboplastin time. An intensivist and/or vascular medicine specialist should be consulted immediately, for possible thrombolytic therapy and/or surgical or catheter embolectomy [63].

In hemodynamically stable patients, PE and DVT may be treated with unfractionated heparin IV, in a weight-based algorithm guided by activated partial thromboplastin time, or low molecular weight heparin, such as enoxaparin (1 mg/kg

subcutaneously twice daily or 1.5 mg/kg subcutaneously once daily), which are equally effective [64]. Patients with renal dysfunction (creatinine clearance less than 30 ml/min) should be treated with unfractionated heparin. Hemodynamically stable patients without significant symptoms, chronic medical illness, or high risk for bleeding, and who are reliable for follow-up, can be treated as outpatients with subcutaneous low molecular weight heparin and eventually transitioned to warfarin if appropriate [65]. These patients should be managed along with a hematologist and anticoagulation clinic.

Septic Pelvic Thrombophlebitis (SPT)

Inflammation of the pelvic vessels may occur in the postpartum or postoperative setting, with thrombus and bacterial infection [66]. SPT is often a diagnosis of exclusion, in patients who are persistently febrile for 3 days despite broad-spectrum antibiotics and negative diagnostic workup for pelvic abscess [27, 67]. The pelvic vasculature can be imaged by CT or MRI; however, absence of a thrombus by imaging does not rule out the condition.

Patients should be treated with antibiotics; the duration of treatment is not standardized, but many are treated until 48 h afebrile. Treatment with ertapenem, a beta-lactam/beta-lactamase inhibitor such as piperacillin-tazobactam, or a combination of ampicillin, gentamicin, and clindamycin, has been described [67]. Though somewhat controversial, anticoagulation is commonly used in the treatment of SPT, with either therapeutic intravenous heparin or enoxaparin (1 mg/kg subcutaneously every 12 h) [67–69]. The duration of anticoagulation is not clearly defined; in patients without documented thrombosis, anticoagulation may be stopped after 48 h if symptoms have improved [70].

Ovarian Vein Thrombosis

Ovarian vein thrombosis is similar to SPT in risk factors and presenting symptoms; the two can coexist, though ovarian vein

thrombus may also be detected in isolation. A thrombus in the ovarian vein is a rare cause of pelvic pain and fever in women postoperatively, occurring most commonly in the right ovarian vein [71]. Patients commonly present with unilateral pain and may have fever; as with SPT, pain and fever refractory to optimal antibiotics should raise concern for this diagnosis. Ovarian vein thrombi are detected most commonly in postpartum women, with an estimated incidence of 0.15–0.18 %, but can also be found in women with recent pelvic surgery, malignancy, pelvic infection, or other hypercoagulable state [71].

CT scan is currently considered the diagnostic modality of choice, though the diagnosis can also be made by MRI or pelvic ultrasound with Doppler [72]. If untreated, ovarian vein thrombosis can result in pulmonary embolism or sepsis. No clear guidelines for management of ovarian vein thrombosis exist; 3–6 months of anticoagulation is often suggested in reviews, and use of antibiotics is controversial [72, 73].

Urinary Tract Injuries

Risk factors for injuries to the urinary system at the time of laparoscopy include malignancy, adhesions from endometriosis, pelvic inflammatory disease or prior surgery, presence of pelvic masses distorting the anatomy, prior pelvic radiation, or congenital anomalies of the urinary tract [74, 75]. Injury to the urinary system during hysteroscopy is very rare (0.1 %) but could occur at the time of uterine perforation, particularly with electrosurgical devices [2, 29].

Reported rates of urologic injuries during gynecologic surgery are highest during laparoscopic hysterectomies, as compared to vaginal or abdominal hysterectomies. Pelvic reconstructive surgeries are associated with higher risk, though injuries have also been reported during oophorectomy, lymphadenectomy, laparoscopic sterilization, and surgeries for endometriosis [46, 76–78]. Bladder injuries occur more commonly than ureteral injuries; in a large meta-analysis, bladder and ureteral injuries occurred in 1.6–2.9 %

and 0.8–1.7 % of cases, respectively [79]. In this series, laparoscopic hysterectomies (with or without bilateral salpingo-oophorectomy) accounted for the upper end of each range, as compared to other gynecologic procedures. Intraoperative cystoscopy has been shown to aid in identification of these injuries at the time of surgery, but despite cystoscopy, 12–15 % of urinary tract injuries may be identified only postoperatively [80].

Ureteral Injury

During surgery, ureteral injuries occur most often at the pelvic brim or near the cardinal ligament [81]. Preoperative stent placement may be used to aid in intraoperative ureteral identification in cases of distorted anatomy [82]. The ureter may be impacted by crush injuries, ligation, transection, perforation, or thermal injury; these injuries can result in strictures, urinomas, or fistulas to the vagina or skin [81, 83]. Particularly in the case of thermal injury, ureteral damage may not be recognized at the time of initial surgery and may lead to delayed necrosis or progressive obstruction [74]. Ureteral injuries are most commonly recognized within 30 days of surgery [83].

Patients with ureteral injury will present with flank pain, fever, hematuria, abdominal distention, or ileus, particularly if urinary ascites is present [74, 81]. If only one ureter is injured, creatinine may only be transiently and mildly elevated. Women with unilateral ureteral obstruction have been shown to have a mean serum creatinine elevation of 0.8 mg/dL postoperatively [84]. Patients also often have a leukocytosis and elevated C-reactive protein, a marker of inflammation [77].

A renal ultrasound is a low-cost imaging modality without radiation exposure that will reveal hydronephrosis, absent ureteric jets, and peritoneal fluid in the presence of a ureteral injury [83]. It can be considered first-line imaging in patients with poor renal function, contrast allergy, or pregnancy. An abdominopelvic CT with IV contrast or a CT urogram may

show a contrast medium leak, noncontiguous ureter, hydroureter, and abnormal ureteric enhancement [83]. The most invasive test is cystoscopy with a retrograde intravenous pyelogram, with the advantage that a ureteral injury can be stented concomitantly [74, 83].

If ureteral injury is suspected, urology should be consulted. Patients may require proximal diversion with percutaneous nephrostomy tubes, placement of a ureteral stent, or either immediate or interval operative repair [85, 86].

Bladder Injury

The bladder may be injured on entry to the abdomen in laparoscopic surgery with the Veress needle or trocars; more commonly, the bladder is injured by thermal damage, incision, or trauma during surgery [75]. The dome of the bladder is most commonly injured, particularly in patients who have a history of prior cesarean section; the incidence of bladder injury during laparoscopic hysterectomy rises to 21 % in patients with three prior cesarean sections [75, 87]. The presenting symptoms of bladder injury include abdominal pain, oliguria, hematuria, elevated creatinine, and urinary ascites causing ileus and leakage of urine from incisions, namely, the vaginal cuff in patients who underwent hysterectomy [75, 88, 89]. Fistula formation involving the bladder is a delayed complication of unrecognized bladder injury.

Bladder injuries are optimally diagnosed with cystoscopy to directly visualize any transmural sutures or disruptions. Retrograde or CT cystography is an alternative, involving retrograde instillation of contrast into the bladder followed by radiograph or CT, which may miss small defects [25]. An abdominopelvic CT with IV contrast may also show contrast extravasation [16].

A small (<2 cm) or puncture lesion of the extraperitoneal bladder may be managed with bladder rest and prolonged catheter drainage [89]. Larger full-thickness extraperitoneal bladder wall defects, and any intraperitoneal bladder wall injuries, are best repaired surgically. Full-thickness injury to the bladder

dome is generally repaired in two layers, with polydioxanone or Vicryl sutures, and a catheter should be left in place for at least 7 days [85]. Injury to the bladder trigone requires more extensive assessment and surgical expertise in order to assess injury to the ureters, and ureteral stents may be required [7].

Urinary Retention

Urinary retention is relatively common after gynecologic surgery and occurs following 7–15 % of hysterectomies and 4 % of general surgical procedures [90, 91]. Risk factors for urinary retention also include age over 50 years and urine volume of greater than 270 mL upon arrival to the postoperative recovery unit [92]. Postoperative urinary retention is associated with a higher risk of urinary tract infection; pain and medication effects can also contribute [93, 94]. Patients may report pain and may have tachycardia and suprapubic fullness on examination. For diagnosis, a bedside bladder scan may be performed, or the bladder may be catheterized. A bladder capacity of 600 mL without the urge to void and a postvoid residual of greater than 100–150 mL are diagnostic of postoperative voiding dysfunction [93, 94]. The patient may also report an urge without the ability to void.

For patients with urinary retention, Foley catheter replacement for 24–72 h or intermittent catheterization, ideally 4–5 times per day, are equally effective [91, 95]. Patients can be taught to self-catheterize as needed. Prophylactic antibiotics are not necessary for either indwelling catheter or intermittent self-catheterization.

Gastrointestinal Tract Injury

Bowel Injury

The incidence of bowel injuries during gynecologic laparoscopy ranges from 0.03 % for minor laparoscopies to 0.39 % for laparoscopic hysterectomy, with injury occurring most

commonly to the small bowel, followed by the large bowel and stomach [46, 96–98]. Bowel injuries may occur on initial entry into the abdomen, with the Veress needle or trocars, or during adhesiolysis [7, 16]. Alternatively, thermal damage may be inflicted with energy devices or, less commonly, intestinal vascular supply may be compromised during dissection, leading to organ necrosis. Up to 41 % of injuries are not recognized at the time of surgery and patients often become symptomatic within 2 weeks of surgery [98]. Bowel injuries are exceedingly rare at the time of hysteroscopy but could occur with a uterine perforation, particularly if the uterus was perforated with a sharp instrument or with an activated energy device [29].

Patients with bowel injuries will commonly present with fever, nausea, vomiting, and abdominal distention. On examination, patients may be febrile, with hemodynamic changes suggestive of sepsis or septic shock (Table 16.1). Due to spillage of bowel contents, patients may develop peritoneal signs. A complete blood count and complete metabolic panel should be obtained to assess for leukocytosis and electrolyte or metabolic derangements. In acutely ill patients, a serum lactate should also be sent, which has high sensitivity for bowel ischemia; lactate may also be elevated in patients with bowel spillage or bowel obstruction [99]. An abdominal radiograph is not particularly helpful in this setting, as some degree of intra-abdominal free air is expected in the acute postoperative phase. Diagnosis is optimally made using abdominal and pelvic CT with oral contrast, which can reveal contrast extravasation [7, 25].

Patients with iatrogenic bowel injuries should be started on broad-spectrum antibiotics, primarily targeting anaerobes and gram-negative aerobes; one possible regimen is piperacillin-tazobactam (4.5 g IV every 8 h) [100]. Expeditious surgical exploration is most often performed by laparotomy, though laparoscopic exploration and repair have also been reported. Small injuries may be oversewn, though bowel resection may be required for areas of necrosis or thermal injury; bowel diversion, by ileostomy or colostomy, is performed in approximately 11 % of cases [101]. Bowel injury is

associated with the highest mortality rate of all complications of gynecologic laparoscopy; mortality is reported in 1 in 31 patients with delayed diagnosis of bowel injury [98, 102].

Ileus and Bowel Obstruction

Diminished bowel function postoperatively can be attributed to ileus—a decrease in intestinal motor activity—or mechanical bowel obstruction. With both conditions, patients may present with nausea, vomiting, or abdominal pain or distention; patients often report an absence of flatus or bowel movements [103].

A complete blood count should be obtained, as leukocytosis may suggest the presence of a complication such as bowel injury or obstruction. In patients presenting with nausea and vomiting, a complete metabolic panel should be obtained to assess for electrolyte or metabolic derangements. Abdominal radiographs and abdominal CT scans with oral contrast can be used to clarify the diagnosis; abdominal CTs have superior sensitivity and specificity for the diagnoses of ileus or bowel obstruction and may reveal bowel or urinary tract injuries contributing to the patient's presentation [104, 105, 110].

In patients with **postoperative ileus** imaged by abdominal CT, oral contrast will pass through the entire digestive tract, and the colon will contain air and fluid [104]. Postoperative ileus is usually a self-limited condition, occurring after 0.2 % of laparoscopic hysterectomies, which resolves in 3–5 days with bowel rest, and decompression with nasogastric tubes is not recommended [106–108]. A postoperative ileus that is persistent despite bowel rest, intravenous hydration, and electrolyte repletion is concerning for bowel obstruction.

Small bowel obstruction occurs after 0.53 % of benign gynecologic surgeries [109]. Patients present with abdominal distention, nausea, and vomiting 2–8 days after surgery [110]. Risk factors for bowel obstruction postoperatively include intraoperative lysis of adhesions and/or concomitant bowel surgery, blood transfusion, and cystotomy [111]. On abdominal CT scan, a transition point may be identifiable, with

proximally dilated small bowel and distally collapsed bowel, with no oral contrast beyond this point [104]. A demonstrative CT scan is shown in Chap. 18, Gynecologic Oncology. Initial management with nasogastric tube, antiemetics, and intravenous fluids is advised, though 13–50 % of patients with bowel obstructions after surgery for benign gynecologic disease fail medical management and require a second surgery for bowel obstruction due to adhesions, herniation, or injury [104, 110]. **A "closed-loop" obstruction**, or obstruction of a segment of bowel at both ends (sometimes by bowel torsion or incarceration), may appear as a "C" on CT scan with mesenteric vessels converging. This can quickly progress to ischemia and perforation, and usually requires urgent surgical management. For diagnosis and management of large bowel obstruction, please see Chap. 18: Gynecologic Oncology.

Vaginal Cuff Dehiscence

Vaginal cuff dehiscence occurs in 0.31 % of hysterectomies and is more common following laparoscopic hysterectomy (0.64 %) as compared to vaginal (0.13 %) or abdominal hysterectomy (0.2 %) [112]. Evisceration occurs in 35–67 % of cases [113, 114]. Risk factors for vaginal cuff dehiscence include postoperative intercourse, obesity, smoking, malnutrition, immunosuppression, prior pelvic radiation, diabetes, corticosteroid use, and menopausal status [115]. Patients can present with cuff dehiscence at any point after hysterectomy, but dehiscence is most common in the first weeks to months [114, 116]. Patients present with vaginal bleeding or discharge, sometimes occurring after intercourse or Valsalva; patients may also report a vaginal bulge due to bowel evisceration [7].

Vaginal cuff dehiscence, with or without evisceration, is diagnosed clinically. The vaginal cuff disruption is palpable on bimanual exam, and speculum exam reveals the dehiscence and/or evisceration; the cuff should also be carefully inspected for evidence of cellulitis or abscess [117]. If an evisceration is diagnosed, any protruding peritoneal contents should be wrapped with a moist towel while expeditiously proceeding to the operating room. A comprehensive meta-

bolic panel and complete blood count should be obtained in all patients with suspected or confirmed vaginal cuff dehiscence, as leukocytosis may suggest peritonitis or bowel ischemia. A CT scan can be obtained in stable patients without evisceration, and with presentations suspicious for pelvic abscess or bowel injury [7].

Patients with vaginal dehiscence require prophylactic broad-spectrum antibiotics, as the peritoneal cavity is exposed to the vaginal flora, and surgical repair [7]. Vaginal cuff dehiscence without evisceration or evidence of peritonitis can be repaired vaginally; patients with abdominal tenderness, leukocytosis, concerning findings on CT scan, or evisceration are best served with an abdominal approach, by either laparoscopy or laparotomy, to allow for visual inspection for bowel injury or pelvic abscess [117, 118]. Regardless of approach, the vaginal cuff edges should be gently debrided and closed with a delayed absorbable suture such as 0-polydioxanone [117].

Abdominal Wall Complications

For diagnosis and management of fascial dehiscence, which is rare following minimally invasive gynecologic surgery, please see Chap. 18, Gynecologic Oncology.

Port Site Hernia

The risk of port site herniation is related to port diameter; the fascia of ports greater than 8 mm should be closed as risk of herniation is higher with larger ports [119, 120]. The incidence of port site hernia is 3.1 % at 12 mm ports and 0.57 % at 10 mm ports [121]. However, up to 12 % of port site herniations occur through 5 mm ports [122].

Patients present, on average, 9 days postoperatively, though they may present a month or more after surgery [120]. Port site herniations usually contain fat or small bowel, though omentum and large bowel may be involved. Patients may present with abdominal pain and symptoms of bowel

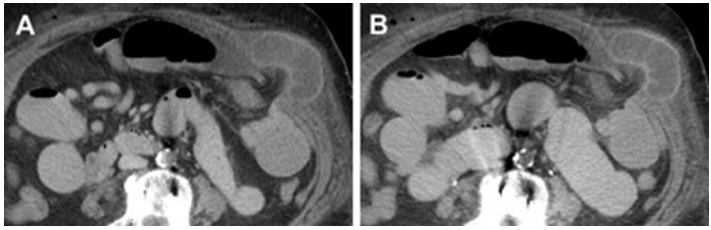

Fig. 16.2 Port site hernia. The herniated loop of bowel is persistently enhanced on the delayed phase image (**b**) as compared to the portal venous phase image (**a**). The patient required resection of a small segment of bowel secondary to ischemia (Reprinted from Santillan [138], with permission from Elsevier)

obstruction, including distention, nausea and vomiting, or port site protrusion [120, 123]. Diagnosis may be made by CT scan or ultrasound of the port site (Fig. 16.2) [120]. Repair may be by laparotomy, by laparoscopy, or through the port site, depending on clinician judgment and the acuity of the patient's presentation [119].

Abdominal Wall Hematoma

The incidence of abdominal wall bleeding is 0.5 %, usually due to injury of the inferior epigastric vessels [124]. Vascular injuries to the abdominal wall are often identified intraoperatively, but hematomas may develop within hours of arriving in the postoperative recovery unit, or after 2–3 days [125]. Signs of an abdominal wall hematoma include pain, ecchymosis, and bleeding from an incision. In patients who are still in the post-anesthesia recovery unit, outline the ecchymosis to allow for ongoing comparison. A rapidly expanding hematoma, acutely declining hemoglobin or hemodynamic instability should prompt aggressive resuscitation and operative management. In patients who are hemodynamically stable with stable hemoglobin, without signs of hematoma expansion or infection, management is supportive while awaiting spontaneous hematoma resolution.

Nerve Injuries

Fewer than 2 % of women develop neuropathies after laparoscopic surgery, and most resolve spontaneously or with addition of physical therapy [126]. Nerve injuries may be due to patient positioning leading to nerve compression or direct nerve injury during dissection. Nerve injuries can occur after hysteroscopy as well, though are less likely as the duration of the positioning is shorter with hysteroscopy than laparoscopy. Postoperative nerve injuries are usually diagnosed clinically, and motor neuropathies require the early involvement of physical therapists to ensure proper resolution [7].

Motor and Sensory Nerves

Femoral nerve injury leads to deficits in hip flexion and adduction and knee extension, with impaired sensation over the anterior and medial thigh and medial calf, and loss of the patellar reflex. This injury occurs in patients positioned with excessive hip flexion or external rotation or excessive stretch placed on the nerve; rarely, this injury may result from retroperitoneal hematoma, or, in open surgery, by deep, lateral retractor placement [7]. Injury to the **obturator nerve** leads to weakened adduction of the hip and loss of sensation over the medial thigh. Obturator nerve injury occurs most commonly during lymph node dissection or paravaginal defect repair [127]. Obturator nerve transection at the time of surgery should be immediately repaired with microsurgical technique. Injuries to the **sciatic nerve**, which innervates the posterior thigh and indirectly the lower leg and foot, are rare in gynecologic surgery; sciatic nerve injury may occur due to deep stitches placed in the setting of sudden hemorrhage or due to knee hyperextension with the hip flexed [127]. The **peroneal nerve** is a branch of the sciatic nerve specifically responsible for ankle flexion and sensation over the calf and dorsal foot and can be injured by excessive pressure on the lateral knee against stirrups in the dorsal lithotomy position [7]. Patients with an injury to the peroneal nerve may report foot drop.

Sensory Nerves

Injury of the **lateral femoral cutaneous nerve** results in numbness or pain over the lateral thigh, following excessive or prolonged hip flexion or external rotation [127]. **Genitofemoral nerve** injury results in paresthesias or numbness of the ipsilateral mons and inguinal area and is most often caused by direct injury at the time of external iliac lymphadenectomy or, in open surgery, by deep retractor placement over the psoas [7]. **Iliohypogastric** and **ilioinguinal nerve** injuries lead to neuropathic pain over the anterior abdominal wall, mons, and/or medial thigh [7]. These nerves are most commonly injured in gynecologic surgery at the lateral edges of Pfannenstiel incisions but can be injured at laparoscopy with placement of lateral ports or incorporation into fascial closures [7, 127]. Local nerve blocks can be both diagnostic and therapeutic for ilioinguinal or iliohypogastric nerve injury [128]. Local injections of anesthetics (2–10 mL of either 1 % lidocaine or 0.5 % bupivacaine), with or without corticosteroids (such as 40 mg of triamcinolone), can greatly improve cutaneous nerve pain in the abdominal wall [129, 130]. Lidoderm patches may also be helpful [128]. Persistent pain attributed to entrapment of these nerves may be relieved with surgical resection of the entrapped nerve [127, 128].

Complications of Pneumoperitoneum

Subcutaneous emphysema, or CO_2 trapped in the subcutaneous tissues, occurs in 2.3 % of patients following laparoscopy [131]. The subcutaneous tissues can be insufflated at the time of Veress needle placement, or via leakage from the intraperitoneal cavity or CO_2 flow through incompletely inserted trocars. Risk factors include age over 65 years, operative time over 200 min, and higher number of ports [131]. Subcutaneous emphysema results in palpable subcutaneous air (crepitus) and generally resolves in 1–2 days as the gas is absorbed and metabolized [132]. Massive subcutaneous

emphysema may result in hypercarbia as the CO_2 is reabsorbed and may rarely result in pneumothorax or pneumomediastinum [133]. Postoperative patients with significant subcutaneous emphysema and hypoxia, tachypnea, or tachycardia should have a chest radiograph to assess for pneumothorax or pneumomediastinum and an arterial blood gas to assess for hypercarbia [133].

Patients commonly report shoulder pain after laparoscopy, attributed to diaphragmatic irrigation by intraperitoneal CO_2, stretch, or pressure due to the Trendelenburg position, and which resolves with time [119]. Persistent pneumoperitoneum, which may result in abdominal discomfort and distention and shoulder pain, is more common in thinner women and can persist for over 3 weeks [134].

Complications of Hysteroscopy

The most common complications of hysteroscopy are shown in Table 16.5.

Fluid Extravasation

Hysteroscopic fluid, instilled in the uterus to produce distention and allow for visualization, is generally chosen for its electrolyte content; normal saline, which contains electrolytes, is the preferred choice given its safety profile, as compared to an electrolyte-free fluid such as 1.5 % glycine [135].

Table 16.5 Complications of hysteroscopy

Complication	**Incidence**
Endomyometritis	0.85 %
Fluid overload	0.2 %
Uterine perforation	0.12 % (diagnostic), 0.76 % (operative)

References for these values are provided in the text

Use of monopolar instruments requires electrolyte-free fluid, while bipolar instruments can be used in a solution with electrolytes [135].

Fluid overload, resulting from absorption of the hysteroscopic distention medium during hysteroscopy, is reported in 0.06–0.2 % of cases [29, 136]. Assessment of the patient's vital signs and respiratory function should be performed once 500 mL of a hypotonic solution has extravasated, and the procedure should be stopped once 1000 mL of fluid has been absorbed [135]. When isotonic solution is used for uterine distention, the procedure should be stopped once 2500 mL of solution has extravasated [135].

Complications of fluid extravasation are more likely at lower absorbed volumes in patients with medical comorbidities, particularly cardiac and pulmonary disease. Patients with fluid overload during hysteroscopy, particularly those with medical comorbidities, may develop complications such as pulmonary edema.

In patients with large absorbed volumes and/or significant comorbidities, a sodium level should be checked intraoperatively. Hyponatremia is more common with the use of electrolyte-poor, hypotonic solutions such as glycine; normal saline is isotonic to serum and less likely to cause hyponatremia [135]. Patients may report mild symptoms such as nausea with serum sodium declines of 5–10 millimole per liter (mmol/L), while levels below 120 mmol/L are severe and potentially life threatening [137]. Patients with symptomatic hyponatremia may present with confusion, nausea, and seizure; severe neurologic complications include cerebral edema and death [2].

Patients with fluid overload or mild hyponatremia can be managed with loop diuretics; hypertonic saline is also used in the treatment of hyponatremia. Patients with symptomatic hyponatremia, particularly those 48 h or more after surgery, may require admission to intensive care for correction, which, if corrected too quickly, risks further neurologic complications [137].

Uterine Perforation

Uterine perforation is estimated to occur in 0.12 % of diagnostic hysteroscopies and 0.76 % of operative hysteroscopies [136]. Adhesiolysis is associated with the highest complication rate, as compared to hysteroscopic myomectomy or polypectomy. Diagnostic laparoscopy for the detection of visceral injuries is required when perforation occurs with sharp or electrosurgical instruments. Hemostatic uterine perforations do not require repair. Uterine perforation occurring with blunt instrument (such as a dilator) is often managed expectantly but may rarely result in significant hemorrhage (0.03 %), requiring laparoscopy or laparotomy and, in extreme cases, hysterectomy [29, 136].

Postoperatively, patients with uterine perforation may report pain, bleeding, fever, or symptoms suggestive of urinary or bowel tract injuries. Diagnostic assessment should focus on the patient's symptoms, and management is dictated by the presence of hemorrhage, infection, and/or visceral injury.

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Chapter 17
Induced Abortion

Paula C. Brady and Katherine D. Pocius

Background

In the United States, 1.1 million induced abortions occur annually [1]. While both medical and surgical abortions are safe, overall low-risk interventions, with a complication and mortality rate significantly less than term delivery, 2 % of patients present within 6 weeks of their abortions with abortion-related complaints [2, 3]. Providers should be able to differentiate normal postabortion findings from significant or potentially life-threatening complications, which include hemorrhage, sepsis, and visceral injury.

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Definitions

First Trimester Medical Abortion

The most commonly used regimen of medication abortion is a combination of mifepristone, an antiprogestin, and misoprostol, a prostaglandin analogue. The FDA-approved regimen consists of mifepristone 600 mg orally followed by misoprostol 400 μg orally 48 h later and is approved up to 49 days of gestation with up to 92 % efficacy [4]. The more commonly used, evidence-based regimen includes mifepristone 200 mg orally followed by misoprostol 800 μg administered buccally, sublingually, or vaginally 24–48 h later [5, 6]. This regimen is commonly provided up to 63 days gestation and is 95–99 % effective [5]. This regimen is now being extended up to 70 days gestation with an efficacy above 92 % [7]. Most women are eligible for medication abortion. Contraindications are few but include anemia (often defined as hemoglobin <9.5 or 10 g/dL), high clinical suspicion for ectopic pregnancy, current use of an intrauterine device (IUD), long-term corticosteroid use, adrenal insufficiency, coagulopathy or anticoagulant therapy, severe liver, renal, pulmonary or cardiovascular disease, uncontrolled hypertension and inability to follow-up [4, 5]. Asthma is not a contraindication to medical abortion.

As compared to surgical abortion, patients undergoing medical abortion are more likely to present to the emergency room for assessment within 6 weeks of their abortion [2]. These patients report higher rates of pain, nausea, vomiting, and diarrhea than patients undergoing surgical abortion, while no difference has been reported in infectious complications [8, 9]. Of note, misoprostol can be associated with fevers of greater than 38 °C (100.4 °F) in 40 % of women without other signs of infection, particularly in the first 24 h, though patients should still be assessed for infection [10]. As the uterus is not instrumented, infectious complications are low. Rare cases of sepsis due to *Clostridium sordellii* have been reported, noted to occur most often in patients who received vaginal misoprostol [11]. These findings have led to an

increase in buccal administration of misoprostol and routine use of prophylactic antibiotics with medical abortions, with reduction in severe infections [12].

During a medical abortion, patients routinely report bleeding heavier than a period. A patient report of soaking two maxi pads per hour for 2 h is often used as an estimate of excessive bleeding [13]. Patients have higher blood loss with medical abortion as compared to surgical abortion, with a mean hemoglobin decline of 0.7 g/dL; the amount of blood loss is directly correlated to duration of the gestation [14, 15]. Transfusion is very rarely required. Patients will commonly bleed or spot for 2 weeks, though spotting may continue for 30 days [4].

Women who undergo medication abortion should have routine follow-up to confirm abortion completion within 2 weeks. This follow-up typically includes either an ultrasound or repeat serum hCG, though other novel methods are currently being investigated. The absence of a gestational sac is evidence of a successful medical abortion [16]. Within the first week, a majority of patients will still have a thick endometrial lining with heterogenous material; these ultrasound findings are not an indication for surgical intervention [16]. Doppler flow may still be present without retained products of conception [17]. Ultrasound findings correlate poorly to patients' bleeding symptoms; a patient's report of symptoms should be used to guide decision-making regarding subsequent evacuation [18]. Alternatively, serum hCG can be used for follow-up, with an 80 % decline in serum hCG by day 7–14 from baseline indicating success [19]. Women who report little or no bleeding or ongoing pregnancy symptoms should be evaluated sooner given concern for ongoing pregnancy.

Second Trimester Medical Abortion

The majority of second trimester abortions are performed surgically. Second trimester medical abortions are performed through a variety of agents, including prostaglandin analogues such as misoprostol, mifepristone, oxytocin, and osmotic dilators, with success rates up to 91 % [4]. Rates of retained placenta, up to 8 %, are higher in second trimester medical

abortions than surgical ones [20]. Rates of infection, hemorrhage, and cervical laceration are low (1–2 %) and similar to second trimester surgical abortion [21]. While medical abortions at any gestational age are associated with more bleeding than surgical abortions, clinically significant hemorrhage is rare, and only 0.1 % of patients require transfusion [22].

First Trimester Surgical Abortion

Surgical abortion is a highly effective and safe method of pregnancy termination, with a complication rate of less than 1 % [23]. The success rate of first trimester surgical abortion is even higher than medical abortion, approximately 99 % [5]. Surgical abortions are generally performed with local anesthesia injected paracervically. Procedural sedation or general anesthesia may also be used.

Immediate complications after first trimester surgical abortion include bleeding or uterine perforation. Other complications, such as infection or delayed bleeding, can occur in the weeks following the procedure [23–25]. Hemorrhage after a surgical abortion can result from atony (loss of uterine contractile tone which normally serves to compress blood vessels and limit blood loss), retained products of conception, uterine perforation, cervical laceration, or, rarely, abnormal placentation. Most risk factors for cervical laceration, perforation, and atony are derived from studies of second trimester surgical abortions, with risk factors including prior cesarean sections, gestational age above 20 weeks, and nulliparity [26]. Absence of intraoperative ultrasound use is associated with retained products of conception after first trimester surgical abortions, which can present with postoperative hemorrhage or infection [27]. Abnormally adherent placental tissue that has invaded the myometrium, called a placenta accreta, is a very rare cause of hemorrhage following first trimester surgical abortion [28].

Hemorrhage may also result from coagulopathy—either preexisting (due to a congenital hematologic abnormality such as von Willebrand disease or use of anticoagulant medications) or acquired, most commonly disseminated intravascular coagulation (DIC), which is a coagulation and fibrinolysis

cascade leading to both diffuse thrombi and hemorrhage. Patients may develop DIC in the setting of with fetal demise (more often in the second trimester) prior to the procedure, or DIC may develop due to significant hemorrhage [29, 30]. Very rarely (3/100,000), DIC may result from an amniotic fluid embolism, which is a catastrophic complication in pregnancy with a very high associated mortality rate [31, 32].

Second Trimester Surgical Abortion

Unlike first trimester surgical procedures, which can generally be performed with mechanical cervical dilation alone, second trimester surgical abortions generally require additional cervical preparation with either osmotic dilators or prostaglandin analogues. Cervical preparation is generally initiated about 24 h prior to an abortion, but the timing can range from 2 to 48 h prior to surgical procedure [5]. After adequate cervical dilation is attained, the amniotic fluid, fetus, and placenta are removed. Most of these procedures can be performed in the outpatient setting [26].

The overall rate of complications from second trimester surgical abortions is low, approximately 1 % [29]. The range of possible complications is similar to first trimester surgical abortions, including uterine perforation or other uterine or cervical lacerations or trauma, post-procedural infection, and anesthesia complications. Hemorrhage occurs more commonly in second trimester surgical abortions than in first trimester surgical abortions, attributed to trauma to the gynecologic organs, atony, abnormal placentation, or DIC [26, 34]. The rates of hemorrhage and DIC are higher following second trimester surgical abortion in patients with two or more cesarean sections and 20 weeks of gestation or more [33]. Cervical laceration occurs in up to 3 % of second trimester abortions; risk factors include nulliparity, mechanical dilation, lack of sufficient dilation, and advanced gestational age [4, 33, 35]. Abnormal placentation is also a cause of hemorrhage after second trimester surgical abortion; the rate of placenta accreta, in which the placenta invades into the myometrium, is currently 0.3 % and rising due to the increasing rate of cesarean sections [36]. The

risk of abnormally adherent placenta is increased with each successive cesarean section, particularly in conjunction with a placenta previa (a placenta overlying the cervical os) [37].

After surgical abortion at any gestational age, a very rare cause of prolonged bleeding or delayed hemorrhage is a vascular malformation, which is thought to be induced by uterine curettage. The optimal imaging is ultrasound with color Doppler flow or angiography [38, 39]. Repeat instrumentation in the setting of a vascular malformation may lead to profuse hemorrhage; uterine vascular malformations are most often managed with embolization or hysterectomy, though spontaneous resolution has also been reported [39].

Differential Diagnosis

Pain

Infection
Hematometra
Uterine perforation/visceral injury
Ectopic pregnancy
Normal postabortion cramping

Vaginal Bleeding

Retained products of conception
Uterine perforation
Cervical laceration
Atony
Abnormal placentation
Coagulopathy (inherited, anticoagulant medication, DIC)

Vascular malformation
Menses (3–6 weeks after abortion)
Normally progressing medical abortion
Normal postabortion bleeding/spotting

Fever

Endometritis
Infected retained products of conception
Pyometra
Pulmonary embolism
Prostaglandin analogue effects
Anesthesia complication, including aspiration/pneumonia, medication reaction
Non-abortion related

When You Get the Call Ask for a set of vital signs. Ensure that basic labs (including a complete metabolic panel, complete blood count, coagulation factors, and a blood type) have been ordered in patients with reported heavy bleeding or vital sign abnormalities, and ensure that at least one peripheral IV has been placed.

When You Arrive Review the patient's vital signs in detail to assess for tachycardia or hypotension, and assess the patient's general appearance for signs of distress, including altered mental status, extreme pain, or obvious ongoing hemorrhage.

Recognition of sepsis and hemorrhage is vital to limiting morbidity and mortality; diagnostic criteria of sepsis are shown in Table 17.1, and the stages of hemorrhagic shock are shown in Table 17.2. Tachycardia, hypotension, tachypnea, and/or altered mental status may be associated with sepsis or hemorrhage [40–42]. Resuscitation of patients with severe sepsis or hemorrhage should begin in parallel with the exam and further investigation (see Management).

Table 17.1 Clinical criteria of sepsis and severe sepsis

Sepsis	Severe sepsis
Suspected source plus 2 or more: 1. Temperature >38.3 °C (101 °F) or <36 °C (96.8 °F) 2. Heart rate >90 beats per minute 3. Tachypnea (>20 breaths/min) 4. WBC >12,000 μ/L or <4,000 μ/L or normal with >10 % immature (band) forms	Sepsis plus one or more: 1. Systolic blood pressure <90 mmHg or decrease from baseline by 40 mmHg 2. Elevated lactate (>1 mmol/L; >4 particularly concerning, sign of organ hypoperfusion) 3. Acute lung injury: PaO_2/FiO_2 <250 (in the absence of pneumonia) or <200 (with pneumonia) 4. Acute oliguria: <0.5 mL/kg/h despite fluid resuscitation 5. Creatinine >2 mg/dL 6. INR >1.5 7. Platelets <100,000/uL 8. Bilirubin >2 mg/dL

Criteria from Fischerova [40]; Dellinger et al. [41]

History

The method and date of abortion should be reviewed, in addition to the patient's gestational age at the time of the abortion, and any factors complicating the pregnancy (such as placenta previa, which, in conjunction with a prior cesarean section, increases her risk for abnormally adherent placental tissue) [37]. Review whether an intrauterine pregnancy was ever definitively confirmed—by ultrasound, gross assessment of intrauterine contents at the time of surgical abortion, or on pathologic analysis—and if not, the patient is theoretically at risk of an ectopic pregnancy.

Table 17.2 Stages of hemorrhagic shock

Class I: blood volume lost <15 %	**Class II:** blood volume lost 15–30 %
Heart rate <100 beats per minute	Heart rate >100 beats per minute
Blood pressure normal	Blood pressure normal
Respiratory rate 14–20 breaths/min	Respiratory rate 20–30 breaths/min
Urine output >30 mL/h	Urine output 20–30 mL/h
Mental status normal	Mental status mildly anxious
Class III: blood volume lost 30–40 %	**Class IV:** blood volume lost >40 %
Heart rate >120 beats per minute	Heart rate >140 beats per minute
Blood pressure decreased	Blood pressure decreased
Respiratory rate 30–40 breaths/min	Respiratory rate >35 breaths/min
Urine output 5–15 mL/h	Urine output negligible
Mental status anxious/confused	Mental status confused/ lethargic
Often marks the onset of decompensated hypovolemic shock	

Committee on Trauma [41]

If the patient has been transferred to the emergency room from another care setting, either a surgical abortion center or other outpatient care center, review the interventions that have already been performed and medications already administered. Complications of surgical procedures should be reviewed from the medical record and/or with the patient or transferring clinician.

The use of prophylactic antibiotics with the abortion should be reviewed, including asking the patient whether she took prescribed antibiotics. Review whether the patient was prescribed contraception or whether indwelling contraception—such as an intrauterine device or progestin implant—was placed at the time of abortion, which may affect bleeding patterns and risk of a new pregnancy.

Review with the patient the time course of her presenting complaint and any associated symptoms, including nausea, vomiting, diarrhea, and purulent or foul-smelling vaginal discharge. Review whether she has been sexually active and how soon after her abortion.

The patient's full medical history should be reviewed, including sexually transmitted infections, thrombophilia or prior thromboembolism, bleeding disorders, prior episodes of bleeding after procedures or use of anticoagulant medications. In patients with bleeding, be sure to elicit a history of asthma and hypertension, which are contraindications to certain uterotonic medications. Review her surgical history, including prior abortions and cesarean sections.

Physical Examination

The physical exam is a key component of the assessment of women with possible postabortion complications. On abdominal examination, note the presence of peritoneal signs, including rebound (pain with abdominal pressure is quickly withdrawn) or involuntary guarding, which may indicate intra-abdominal infection, trauma, or hemorrhage.

On bimanual exam, assess for cervical motion or adnexal tenderness, and note the uterine size and tenderness [43]. Soon after medical or surgical abortions, patients are expected to have some degree of uterine and cervical tenderness, but providers should have a low threshold to treat a possible pelvic infection following abortion due to the reproductive sequelae. A large globular or boggy uterus may suggest hematometra or atony.

On speculum exam, make note of the amount of vaginal bleeding; if vaginal hemorrhage is present, use wall suction to assist with visualization. Assess for cervical or vaginal lacerations. Make note of purulent discharge, whether the cervical os is open or closed and the presence of products of conception at the cervical os, which should be extracted and sent for pathologic confirmation. Of note, if tissue in the cervix cannot be easily extracted, do not try to remove it; this tissue could represent abnormally adherent placental tissue, and extraction could lead to severe hemorrhage.

Diagnosis

In patients with fever or otherwise concerning for infection, a complete blood count with a differential should be obtained to assess for leukocytosis and the presence of bands. Of note, fevers in the first 24 h after an abortion may be related to administration of prostaglandin analogues such as misoprostol, but infection must be ruled out regardless [10]. Cervical cultures for gonorrhea and chlamydia are generally helpful. In patients with temperatures over 101 °F, blood and urine cultures should be obtained.

In patients with signs of sepsis, order electrolytes, creatinine, liver function tests, a blood type and antibody screen, coagulation studies (prothrombin time (PT), activated partial thromboplastin time (aPTT) and fibrinogen), and a lactate level. Consider an arterial blood gas if the patient is in distress. If a patient is septic and hemodynamically unstable, with the uterus being the most likely source of infection, it may be necessary to proceed to the operating room for reevacuation and potentially other exploratory procedures, without imaging.

Patients with hemorrhage must have a complete blood count blood type and antibody screen ordered, coagulation studies (PT and PTT), and a fibrinogen level. Ultimately, however, hemorrhagic shock can be diagnosed clinically, shown in Table 17.2. Notably, tachycardia is the first sign of

hemorrhage, and hypotension may not appear until 30–40 % of a patient's blood volume has been lost [42]. In patients with severe hemorrhage, resuscitation should begin alongside diagnosis. Resuscitation is discussed under Management below.

Beta-Human Chorionic Gonadotropin (hCG)

Serum or urine hCG is often sent for patients presenting after abortions to the emergency room and can be hard to interpret. The time to hCG resolution is dependent on serum levels at the time of abortion and ranges from 3 to 5 weeks; hCG may be present in the blood for as long as 60 days following uterine evacuation [44]. On average, menses should return by 6 weeks after an abortion, unless patients are using contraception that may suppress ovulation [45]. Patients may have resumption of menstruation despite residual hCG in the blood, as high as 35 milli-international units per milliliter (mIU/mL) [46].

In patients presenting after their abortion with pain or bleeding and a positive serum hCG, the possibility of an ectopic pregnancy should be considered, particularly if an intrauterine pregnancy was never confirmed (by ultrasound, by gross assessment of intrauterine contents at the time of surgical abortion, or on pathologic analysis). Alternatively, a new pregnancy should be considered, depending on the interval from the first abortion.

Imaging

For an unstable patient who had a very recent surgical abortion, waiting for a formal ultrasound is not recommended; instead, a focused assessment with sonography for trauma (FAST) scan can be performed for the rapid assessment of hemoperitoneum, which may be the result of uterine perforation and vascular injury [47].

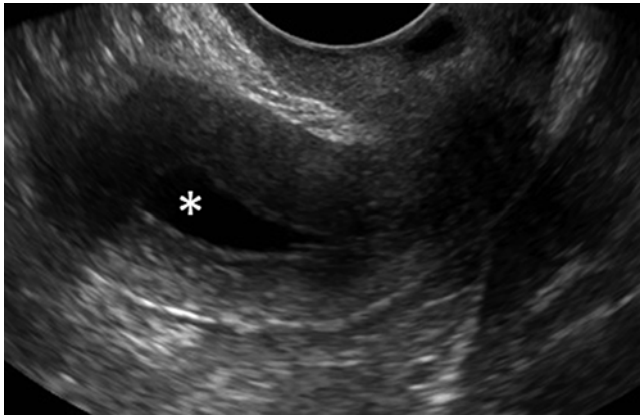

Fig. 17.1 Hematometra. Transvaginal ultrasound showing hematometra, indicated with an *asterisk* (*), and a thin endometrial lining

In a stable patient, pelvic ultrasound should be obtained to assess for hematometra—blood distending the uterus—retained products of conception and ongoing pregnancy (Fig. 17.1). Of note, ultrasounds have a false-positive rate of 34 % for retained products of conception, and Doppler flow may be present in the endometrial linings of patients who do not ultimately have retained productions of conception [17, 48]. Ultrasound might also show free fluid or complex free fluid in the pelvis if uterine perforation has occurred. If there is concern for uterine perforation, consider an upright abdominal radiograph to assess for intra-abdominal free air [43]. In patients with refractory pain not otherwise clarified by ultrasound, CT or MRI may diagnose perforations and incarceration of pelvic organs [49, 50].

Finally, any pregnant (or recently pregnant) patient is at increased risk of thromboembolism; tachycardia, hypoxia, and/or low-grade fever may also be presenting signs of pulmonary embolism. Please see Chap. 15 for the diagnosis and management of pulmonary embolism.

Management

Infection

In patients with signs of sepsis, resuscitation must begin immediately. In patients with potential evidence of infected retained products of conception or pyometra (purulence in the uterine cavity), surgical planning should also begin immediately, as delayed uterine evacuation places patients at risk of sepsis and death [51].

A patient should have two large-bore IVs and oxygen by high-flow facemask as needed. Antibiotics should be started within an hour of presentation. The patient should receive crystalloid resuscitation, with goals of a central venous pressure of 8–12 millimeters of mercury (mmHg), mean arterial pressure of at least 65 mmHg, urine output of greater than 0.5 mL/kg/h, superior vena cava oxygenation saturation or mixed venous oxygen saturation 70 % or 65 %, respectively, a normalized lactate level, and a hemoglobin level of 7–9 g/dL [41].

In patients with any evidence of septic physiology (see Diagnosis), intravenous broad-spectrum antibiotics are required. A common regimen is ampicillin (2–3 g IV every 6 h), clindamycin (900 mg IV every 8 h), and gentamicin (2 mg/kg IV one time, followed by 1.5 mg/kg IV every 8 h). Another option is ampicillin-sulbactam (3 g IV every 6 h) [52]. Tissue obtained from any uterine evacuation should be sent for culture to direct antibiotic selection [43].

For patients with mild endometritis, without evidence of retained products of conception or pyometra, management with oral antibiotics is reasonable, and recommendations are largely extrapolated from guidelines for postpartum endometritis. Options include amoxicillin-clavulanic acid alone (875 mg PO every 12 h) or amoxicillin (500 mg PO every 8 h) plus metronidazole (500 mg PO every 8 h) [53]. Clindamycin can also be given orally (600 mg every 6 h), and gentamicin can be given intramuscularly (4.5 g every 24 h), which is less convenient but feasible if no other options are available. Of note, chlamydia and gonorrhea is not addressed by this regimen, and testing for these bacteria should be sent [54].

Hemorrhage

Particularly in patients with hemodynamic changes or estimated blood loss of 500 mL or more, resuscitation efforts should immediately start, with crystalloid and packed red blood cells as necessary. For massive transfusion (>10 units of packed red cells), administer units of red blood cells, fresh frozen plasma, and platelets in 1:1:6 ratio (extrapolated from trauma literature) [55–57]. Resuscitation goals include a heart rate below 100 beats per minute, hemoglobin of at least 7 g/dL, platelets above 50,000 per μL, fibrinogen above 100 mg/dL, and an INR less than 1.5. Please see Chap. 13 for more information on resuscitation and blood products.

Management is directed to the suspected source of bleeding (Fig. 17.2). For superficial cervical lacerations, silver nitrate or ferric subsulfate (Monsel's) can be applied, followed by holding pressure with a sponge stick [26]. More significant lacerations may require repair with absorbable

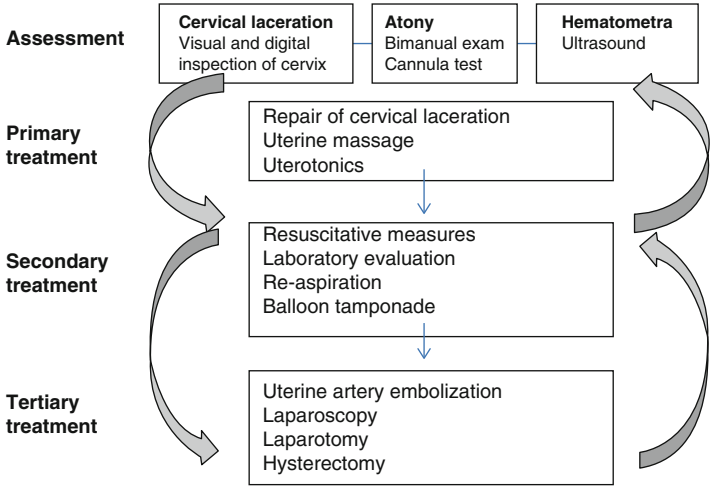

Fig. 17.2 Interventions for vaginal hemorrhage (Reprinted from Kerns and Steinauer [26], with permission from Elsevier and the Association of Reproductive Health Professionals and the Society of Family Planning)

Table 17.3 Uterotonic medications

Medication	Comment
Misoprostol 800–1000 μg PO, SL, PV or PR	Peak serum concentration of misoprostol is lower following rectal administration
Oxytocin 10 units IM or 10–40 units IV in 1 L of normal saline or lactated Ringer's	Not helpful in the first trimester
Methylergonovine maleate (Methergine®, Novartis, East Hanover, New Jersey) 0.2 mg IM every 2–4 h, or PO every 6–8 h	Contraindicated in patients with hypertension
Carboprost tromethamine (Hemabate®, Pfizer, New York, NY) 0.25 mg IM every 15–90 min, maximum 8 doses	Contraindicated in patients with asthma or suspected amniotic fluid embolism

From: O'Connell et al. [59]; American College of Obstetricians and Gynecologists [60]; Nygaard et al. [70]
PO oral, *SL* sublingual, *PV* vaginally, *PR* rectally, *IM* intramuscular

sutures. If bleeding continues after repair of any lacerations, uterine massage should be initiated, and uterotonics should be administered, shown in Table 17.3 [58–61]. If the patient has been transferred to the emergency room immediately following a surgical abortion, many of these interventions have likely already been performed by the clinicians performing the termination, and should be reviewed to avoid excessive medication administration.

If the patient is symptomatic and imaging suggests retained products of conception or hematometra, the patient requires reaspiration. If reaspiration is not indicated, or the bleeding continues despite reintervention, and/or atony is suspected, lower uterine segment tamponade can be established with a Foley catheter or Bakri® balloon (Cook Medical, Bloomington, IN), inflated with normal saline [33, 62, 63]. Foley catheter balloons can be inflated to double their usual volume as needed.

Bakri balloons, which can hold 500 mL, may be too large for the uterine cavity following an abortion; at most half the maximum volume is sufficient in the postabortion setting [26]. Patients should be closely observed after placement to assess for bleeding around the balloon or excessive bleeding through the central channel draining the uterus. Bedside ultrasound may also be helpful to assess whether the uterus is distended with blood around the balloon. If tamponade is curative, the balloon can stay in place for 12–24 h, with or without uterotonics and antibiotics [26].

For refractory bleeding, patients require additional interventions, including uterine artery embolization (UAE), laparoscopy, laparotomy, or rarely hysterectomy. UAE involves the cannulation of the femoral artery followed by catheter-guided delivery of embolic particles to the uterine arteries. Uterine artery embolization has been used with great success to treat postabortion atony, lacerations, and abnormal placentation (Fig. 17.3) [34]. It is a relatively low-risk and well-tolerated procedure, though can result in significant cramping; complications include groin puncture site hematoma, contrast allergy, or accidental embolization of vessels in the pelvis or leg [64]. UAE is not currently recommended in patients desiring future fertility, but may be required to avoid surgical intervention or hysterectomy.

If interventional radiology is not available, surgical intervention may be required. Uterine artery ligation and/or uterine compression (B-lynch) sutures are additional possible interventions for hemostasis at the time of surgery [26]. Hypogastric artery ligation, historically performed for postpartum hemorrhage, may be an option as well [65]. For refractory bleeding, hysterectomy may be required. In the United States, 1.4 in 10,000 abortions require hysterectomy [66].

Uterine Perforation

Patients may be referred to emergency rooms by their abortion providers due to suspicion that uterine perforation occurred during suction curettage or tissue extraction with

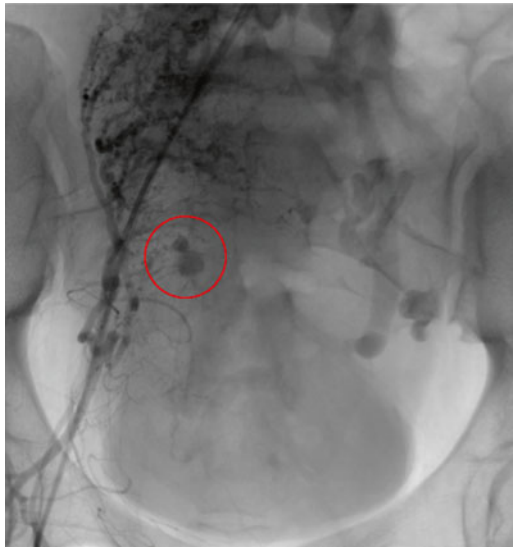

Fig. 17.3 Uterine artery embolism for postabortion hemorrhage. Following a late second trimester surgical abortion complicated by bleeding refractory to uterotonics and tamponade, angiography revealed a laceration of the right uterine artery (*circled*) which was successfully embolized

forceps; in these cases, surgical intervention is required. Abdominal exploration is not strictly required if perforation occurred using blunt instruments. In hemodynamically stable patients with a mechanism of perforation concerning for visceral injury, laparoscopy can be performed for assessment of the intra-abdominal cavity. A hemostatic uterine perforation detected at the time of laparoscopy does not require repair [67]. If perforation is confirmed, the bowel and other pelvic organs should be carefully inspected for damage. This may require general surgery or other advanced surgical consultation, particularly for laparoscopic procedures.

Hematometra

Patients with hematometra may present with vasovagal symptoms, including hypotension, bradycardia, and/or diaphoresis, as well as lower abdominal pain, vaginal bleeding, and nausea [68]. In patients presenting with symptomatic hematometra, even in the absence of hemorrhage or infection, prompt surgical evacuation is recommended. Administration of methylergonovine maleate (Methergine®, Novartis, East Hanover, New Jersey) may prevent reaccumulation, including orally (0.2 mg PO every 6–8 h) for a short interval afterward, though data are sparse [69].

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Chapter 18
Gynecologic Oncology

Emily M. Hinchcliff

Background

Ovarian Cancer

Primary ovarian malignancies occur in 1.3 % of women in their lifetimes [1]. Risk factors for epithelial ovarian cancer (the most common type) include advancing age, a family history of ovarian cancer, and genetic mutations conferring increased risk, including BRCA1 and BRCA2 [2]. Non-epithelial ovarian cancers include germ cell tumors, which often occur in young patients, and sex cord stromal tumors, which can present in any age group. Non-epithelial tumors are generally associated with a very favorable prognosis.

Cervical Cancer

Cervical cancer is diagnosed in 0.6% of women in their lifetimes and is the most common gynecologic cancer worldwide [1]. The majority are squamous cell carcinomas; risk factors

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are smoking, low socioeconomic status, immunosuppressive therapy, and infection with human papillomavirus (HPV), particularly strains 16 and 18 [3]. Cervical adenocarcinomas are less common but account for an increasing percentage of cervical cancers because they are less effectively diagnosed by Pap smears [4].

Uterine Cancer

By far the most common cancer of the uterus is endometrial cancer; in their lifetimes, 2.8 % of women will be diagnosed with endometrial cancer, the majority of which are adenocarcinomas [1, 5]. Risk factors for endometrial cancer include obesity, unopposed estrogen exposure—either through medications or anovulation—advanced age, and family history, particularly Lynch syndrome, an autosomal dominant syndrome that increases the risk of endometrial and colorectal cancers [5].

Vulvar Cancer

In their lifetimes, 0.3 % of women will be diagnosed with vulvar cancer [1]. In younger women, vulvar cancers are associated with HPV infection, vulvar intraepithelial neoplasia, and smoking, while these associations are not observed as frequently in postmenopausal women, in whom vulvar cancer is associated with vulvar inflammation and lichen sclerosis [6].

Vaginal Cancer

Vaginal cancer is an uncommon gynecologic cancer; approximately 4,000 cases are diagnosed per year [7]. The majority are squamous cell carcinomas, which are associated with the same risk factors as squamous cell carcinoma of the cervix [8].

Gestational Trophoblastic Disease

Gestational trophoblastic disease (GTD) is the abnormal proliferation of trophoblastic tissue, occurring in approximately 0.1 % of pregnancies (including live births, miscarriages, and ectopic pregnancies), most of which are hydatidiform moles [9]. Malignant forms of GTD include invasive mole, choriocarcinoma, placental site trophoblastic tumor, and epithelioid trophoblastic tumor. Risk factors include advanced maternal age and a history of gestational trophoblastic disease [10]. Please see Chap. 8, Spontaneous Abortions, for more information on molar pregnancy.

Radical Hysterectomy

Radical hysterectomy refers to the removal of the uterus, parametrium, and upper vagina en bloc, with or without salpingo-oophorectomy. The extent of dissection is determined by the indication for the more radical surgery, and similarly, complications and postoperative considerations depend on the extent of the initial surgery. Indications for radical hysterectomy include but are not limited to cervical cancer up to stage IIA, stage II endometrial cancer if feasible, upper vaginal carcinoma, and non-oncologic indications such as extensive pelvic adhesions.

Urinary retention is particularly common following radical hysterectomy; long-term postoperative urinary tract dysfunction is observed in 30–85 % of women following radical hysterectomy, likely due to disruption of sensory or motor pathways to the detrusor muscle or due to direct bladder injury [11]. Therefore, it is common (though debated) to leave a Foley catheter in place for bladder decompression for 2 weeks postoperatively. Please refer to Chap. 16, Complications of Minimally Invasive Gynecologic Surgery for more information on the diagnosis and management of postoperative urinary retention.

Trachelectomy

A trachelectomy entails the surgical removal of the cervix with preservation of the uterine body, generally performed for fertility preservation. Candidates for trachelectomy are usually less than 40 years of age, desiring future fertility with cervical cancer up to stage IB1 [12, 13]. An abdominal cerclage—a circumferential suture placed superior to the excision margin—is usually placed at the conclusion of the procedure, in preparation for pregnancy.

Overall, complication rates are similar between radical trachelectomy and radical hysterectomy, as are oncologic recurrence rates [14]. However, the remaining uterus and presence of cerclage can present distinct challenges postoperatively. Patients who have undergone trachelectomy can develop cervical stenosis, dysmenorrhea with or without hematometra, and vaginal discharge.

Ovarian Cancer Cytoreduction

The standard of care for staging and treatment of ovarian, fallopian tube, and peritoneal cancers includes total hysterectomy with bilateral salpingo-oophorectomy, omentectomy, cytology of the pelvic fluid and diaphragm, and resection of all gross disease. Removal of lymph nodes may be indicated for complete staging or if lymph nodes are grossly enlarged. Patients with extensive disease by imaging or who are poor surgical candidates may receive neoadjuvant chemotherapy—usually three cycles of a platinum and taxane-based chemotherapy regimen—prior to surgery [15, 16]. If possible, any obvious tumor implants are removed, known as **cytoreduction**. Complete cytoreduction (removal of any visible disease) is associated with the greatest survival advantage but may not always be feasible, while optimal cytoreduction refers to residual tumor implants less than 1 centimeter (cm) in diameter, and suboptimal cytoreduction leaves tumor implants greater than 1 cm in diameter [17, 18]. These procedures can be associated with significant morbidity depend-

ing on the invasiveness and extent of surgery required, particularly in patients with more comorbidities or advanced age [19].

Pelvic Exenteration

Complete pelvic exenteration is a radical procedure involving the removal of the female reproductive organs, lower urinary tract, and/or anus and portion of the rectosigmoid colon. The urinary and gastrointestinal tracts may be diverted to a urostomy and colostomy, respectively. A complete pelvic exenteration also involves removal of the musculature of the pelvic floor and the soft tissue structures of the perineum. An anterior or posterior exenteration with preservation of the uninvolved pelvic organs may also be performed. Reconstruction can be vast and challenging, and the team performing a pelvic exenteration often includes multiple surgical subspecialties, including gynecologic oncology, colorectal surgery, urology and plastic surgery. Pelvic exenteration is offered only as an attempt to cure women with centrally located tumors (usually vulvar or cervical cancer), without evidence of metastatic disease [20]. Rarely, a pelvic exenteration may also be performed for palliation of unmanageable symptoms including pain, bleeding, or fistulae [21].

Given the extent and complexity of these surgeries, patients often require ICU-level care postoperatively. They often have high-volume blood loss intraoperatively, requiring significant resuscitation. Frequent labs (including complete blood counts, coagulation studies and electrolytes) are important monitoring tools. Drains are often left in place to avoid fluid collections and monitor bleeding or anastomotic leak; the volume and appearance of the drain output should be monitored postoperatively. Please refer to the "Diagnosis" section, under "Fever," for further discussion of assessment of drain output.

Up to 50 % of women will have a major complication after a pelvic exenteration [22]. Early complications include hemorrhage (both intraoperative and delayed), infection, wound

breakdown, ileus, anastomotic leak (urinary or bowel), and decline in body image [20]. Late complications include fistula (urinary or bowel), and chronic failure of wound healing. In the delayed postoperative period, it is important to consider the possibility of recurrent cancer. Please see the following section for management of reconstructive flaps.

Vulvectomy

Vulvar lesions can be treated with multiple different modalities, including laser (to vaporize the layer of abnormal cells, not used to treat invasive cancer), topical immunomodulators (also not used to treat invasive cancer), and excision. The type and extent of excision, with or without inguinal lymph node dissection, is highly dependent on the size and location of the lesion [23]. Following radical resections, reconstruction may be required using skin grafts or flaps [24].

Postoperative management after vulvectomy is highly dependent on the extent and location of resection. Patients may have drains in place, particularly following lymphadenectomy; the color and volume of drain output should be closely monitored. In patients with wound reconstruction, strict movement limitations (bed rest and no sitting) are often imposed to preserve the integrity and blood supply of the flap; adequate thromboembolism prophylaxis should be provided during this period of immobility [25]. Vulvar flaps should be assessed regularly, noting color (pale versus congested) and edema. Vulvar incisions must be monitored closely and cleaned frequently, usually with sterile saline or sitz baths.

The most common complication following vulvectomy is wound breakdown, occurring in approximately 15 % of cases [26]. Wound breakdown can predispose the patient to more serious complications, including infection ranging from cellulitis to necrotizing fasciitis. Please refer to Chap. 16, Complications of Minimally Invasive Gynecologic Surgery for the diagnosis and management of postoperative infections. There is also a risk of flap loss if arterial supply or venous drainage is compromised, which may require reoperation.

Lymphadenectomy

Removal of lymph nodes is performed when the risk of metastasis to lymphatic channels is high, determined according to specific criteria for each type of gynecologic cancer. Complications of lymphadenectomy include lymphedema (swelling) and nerve damage; the latter is discussed in Chap. 16, Complications of Minimally Invasive Gynecologic Surgery [27–29]. An extremity with lymphedema must be monitored closely for ulceration and cellulitis.

Chemotherapy

Chemotherapeutic agents for treatment of gynecologic cancers are associated with a range of toxicities, which is beyond the scope of this chapter. Chemotherapeutic drugs commonly encountered in the care of gynecologic oncology patients include platinum-based therapies (cisplatin and carboplatin) and taxanes (paclitaxel); toxicities of these include but are not limited to myelosuppression, nephrotoxicity, and peripheral neuropathy. Gastrointestinal toxicity (nausea and vomiting, in particular) is the most common chemotherapeutic toxicity; please refer to Chap. 14, Common Postoperative and Inpatient issues for more information for more information on the management of nausea.

Acute, severe complications of chemotherapy can occur. Patients may develop acute allergic reactions to any chemotherapy, which may be evidenced by diffuse rash, erythema, respiratory compromise, and/or hypotension. Hypersensitivity reactions to taxanes usually occur with the first or second infusions, while reactions to platinum-based chemotherapy may begin following repeated exposures due to priming of the immune response [30]. Please see Chap. 15, High-Acuity Postoperative and Inpatient Issues and Inpatient Issues, for more information on the diagnosis and management of anaphylaxis. Of note, bevacizumab, a vascular endothelial growth factor (VEGF) inhibitor that is FDA approved for the treatment of recurrent ovarian cancer and metastatic cervical cancer, carries a risk of spontaneous bowel perforation of

0.9 %, associated with a mortality rate of 21.7 % [31]. Bevacizumab may also cause malignant hypertension or wound breakdown.

Definitions

Neutropenic Fever Neutropenic fever is a single oral temperature of 38.3 °C (101 °F) or more, or a temperature of 38.0 °C (100.4 °F) or more sustained for at least 1 h, in a patient with neutropenia [32]. Neutropenia is defined as an absolute neutrophil count (ANC) less than 1,500 neutrophils/microliter (μL), and severe neutropenia is usually defined as an ANC less than 500 neutrophils/μL or an ANC that is expected to decrease to less than 500 neutrophils/μL over the next 48 h [32]. If not reported by the laboratory, ANC can be calculated by multiplying the total white blood cell (WBC) count by the fraction of polymorphonuclear cells (PMNs) and bands. Common pathogens in neutropenic fever include gram-positive species such as coagulase-negative staphylococci, *Staphylococcus aureus*, *Enterococcus* species, the *Viridans* group streptococci, *Streptococcus pneumonia* and *S. pyogenes*, and gram-negative species including *Escherichia coli, Klebsiella species, Enterobacter, Citrobacter, Acinetobacter,* and *Pseudomonas aeruginosa* [32].

Tumor Fever The mechanism is poorly understood and likely related to alterations in cytokines. While non-gynecologic malignancies are more commonly associated with fevers—including leukemia, lymphoma, and renal cell carcinoma—any malignancy can be considered as a cause of fever; fever may be more common in patients with sarcoma and liver metastases [33]. Attribution of fevers to tumor burden is a diagnosis of exclusion; in patients with hemodynamic changes, the diagnosis of tumor fever should be questioned and other alternatives pursued [34, 35].

Bowel Resection Bowel resection is removal of a part of the bowel (small bowel, large bowel, or both), repaired with

either primary reanastomosis (reattachment of healthy proximal and distal portions of bowel) or diversion of the gastrointestinal tract through the abdominal wall; the exposed portion of bowel at the skin is called the stoma. Ileostomy refers to a stoma created by bringing the ileum through the abdominal wall, while a colostomy involves the colon. Complications of stomas include stomal necrosis, stenosis, retraction, prolapse, and parastomal hernia formation, none of which generally require emergent intervention [36]. Complications of bowel reanastomosis include ileus, anastomotic strictures, leaks, and bowel obstruction, discussed under Management.

Bowel Obstruction Bowel obstruction is mechanical blockade of normal bowel peristalsis, occurring most commonly in the small bowel; small bowel obstruction is discussed in Chap. 16, Complications of Minimally Invasive Gynecologic Surgery. Large bowel obstruction accounts for up to 25 % of all intestinal obstructions, and approximately 70 % of large bowel obstructions occur at or distal to the transverse colon [37]. Risk factors for bowel obstruction postoperatively include intraoperative lysis of adhesions and/or concomitant bowel surgery, blood transfusion, and cystotomy [38]. Specific to gynecologic oncology, risk factors include extensive disease burden, particularly tumor causing extrinsic bowel compression, or radiation therapy.

Abdominal Wound Separation Fascial dehiscence refers to the separation of the fascia, usually occurring 3–7 days postoperatively, in up to 1.2 % of laparotomies [39, 40]. Fascial dehiscence is a surgical emergency, associated with a high mortality rate of up to 24 % [41]. Risk factors include wound infection, sepsis, age over 65 years, the presence of an ostomy within the incision, hypoproteinemia, poor nutrition, pulmonary disease, hypertension, obesity, and steroid use [42]. Superficial wound separation, involving just the suprafascial layers, may also occur and usually represents a far more mild complication. Please refer to Chap. 16, Complications of Minimal Invasive Gynecologic Surgery, for the diagnosis and management of vaginal cuff dehiscence.

Differential Diagnosis by Primary Complaint

Fever

- Superficial surgical site infection
- Vaginal cuff cellulitis
- Pelvic hematoma or abscess
- Cystitis
- Pyelonephritis
- *Clostridium difficile* colitis
- Retained foreign body
- Toxic shock syndrome
- Necrotizing fasciitis
- Septic pelvic thrombophlebitis
- Ovarian vein thrombosis
- Deep vein thrombosis (DVT)
- Pulmonary embolism (PE)
- Pneumonia
- Medication effect (drug fever)
- Tumor fever
- Neutropenic fever
- Pancreatic leak following pancreatic resection or splenectomy
- Urinary tract injury
- Bowel perforation, injury or anastomotic leak
- Alcohol withdrawal
- Transfusion reaction (hemolytic, febrile non-hemolytic, and Transfusion-Related Acute Lung Injury)

Pain

- Bowel injury
- Small or large bowel obstruction
- Bowel anastomotic stricture

(continued)

(continued)

Bowel anastomotic leak
Urinary tract injury
Pancreatic leak following pancreatic resection or splenectomy
Cystitis
Pyelonephritis
Superficial surgical site infection
Vaginal cuff cellulitis
Pelvic hematoma or abscess
Ovarian vein thrombosis
Necrotizing fasciitis
Vaginal cuff dehiscence
Abdominal wound dehiscence
Urine retention
Inadequate analgesic medications
Oncologic pain (tumor burden)

Nausea/Vomiting

Ileus
Small or large bowel obstruction
Bowel injury
Bowel incarceration due to an incisional or peristomal hernia, stoma retraction, or prolapse
Bowel anastomotic stricture
Bowel anastomotic leak
Pancreatic leak following pancreatic resection or splenectomy
Urinary tract injury (particularly urinary ascites causing ileus)
Chemotherapy-related nausea
Medication effects (including anesthetics and narcotics)
Nonsurgery related (i.e., viral gastroenteritis)

Vaginal Hemorrhage

Bleeding due to tumor will be addressed in this chapter. Please see Chap. 2, Vaginal Hemorrhage, for alternative diagnoses.

As with any gynecologic surgeries, risks of oncologic surgery include infectious, vascular, urologic, gastrointestinal, and nerve injuries or complications; please see Chap. 16, Complications of Minimally Invasive Gynecologic Surgery, for more information. Unique to surgical intervention for gynecologic cancer, procedures such as splenectomy, bowel resection, and pancreatectomy may be required, each with unique considerations and complications [43, 44].

When You Get the Call Ask for the most recent set of vital signs. Ensure that basic labs (such as a complete metabolic panel, complete blood count, and coagulation studies) have been ordered in clinically ill or unstable patients and at least one IV has been placed. Consider ordering an electrocardiogram (ECG) and chest radiograph while in route to see the patient as clinically indicated.

When You Arrive Review the full vital sign flow sheet, noting whether the patient is febrile, tachycardia, hypotensive, or tachypneic. In addition, in an oncologic patient, it is important to review the patient's cancer type, stage, and any prior treatments (radiation, chemotherapy, surgery). If the patient is postoperative, review the operative report for the extent of dissection, and whether any bowel injury or resection occurred.

History

Review with the patient when her primary symptoms began and any associated symptoms, including but not limited to fever, abdominal distention, nausea, vomiting, or diarrhea. In patients with nausea or vomiting, ask about recent flatus or bowel movements, the absence of which may be concerning for bowel

obstruction. If the patient is presenting with vaginal bleeding or discharge or abdominal pain, review her activities at the time of symptom onset, including heavy lifting or intercourse, which, within 6-8 weeks of total hysterectomy (and sometimes longer), may predispose to vaginal cuff dehiscence.

Review the patient's full medical history, including any chronic diseases such as diabetes or a history of venous thromboembolism. Make note of any current medications, including anticoagulant therapy and chronic steroid use. Review whether the patient has received hematopoietic growth factors—such as granulocyte-macrophage colony-stimulating factor (GM-CSF) or granulocyte colony-stimulating factor (G-CSF)—which are used for prophylaxis against febrile neutropenia resulting from chemotherapy and may result in leukocytosis. Dexamethasone is often given during chemotherapy and may also cause leukocytosis and hyperglycemia. Review her prior surgical history, as prior surgeries may increase the risk of adhesions and intraoperative injury to other organs.

A complete oncologic history includes the date of diagnosis, primary tumor site, stage, grade, and histology, and initial presenting symptoms at diagnosis, as well as the dates and nature of any subsequent treatments, including chemotherapy, radiation, and surgical treatments. Be sure to note any recurrences or complications during the patient's treatment course. Note the plan for any further treatments, such as upcoming chemotherapy or radiation treatments.

Physical Examination

Assess whether the patient is alert and oriented, and whether she is in distress (visibly uncomfortable, pale, diaphoretic or tachypneic). Check for capillary refill by pressing on the fingernails; delayed reperfusion of the nail beds is evidence of decreased perfusion, associated with sepsis or anemia. Perform a complete physical exam, including examination of the heart, lungs, abdomen (noting distention, a fluid wave due

to ascites, rebound, or involuntary guarding, and assessing any surgical incisions, drains, and ostomies), and the lower extremities (noting edema, and asymmetrical swelling or tenderness). Particularly in patients with fever or sepsis, assess for sacral decubitus ulcers in chronically ill or immobile patients, and any other skin disruption. Assess percutaneous nephrostomy tubes (for urinary diversion), subcutaneous ports (for central venous or peritoneal access), peripherally inserted central catheters (PICCs), and any other indwelling catheters for evidence of thrombophlebitis or abscess. In patients with bleeding, a physical examination is required to determine the source of bleeding—including uterine, cervical, vaginal, vulvar, or rectal sources—and to assess for the presence of any obvious tumor. Oncologic patients often have more complex histories and comorbidities, so it may be necessary to complete further portions of the physical exam as well (such as a neurologic exam in patients with altered mental status or musculoskeletal exam in patients presenting with pain).

In postoperative patients with abdominal pain or fever, and surgical wounds with erythema or drainage, the skin should be opened to release any collections (seroma, hematoma, or purulence), and the fascia should be probed with a sterile cotton swab to assess for dehiscence [48]. If a patient has drains or a vacuum-assisted wound closure device, assess the output for increased volume, blood, purulence or any other concerning changes. In patients with postoperative drains in place, Jackson-Pratt drains are among the most common closed systems; these consist of thin plastic tubing placed through the abdominal wall, usually sutured into place, and connected to a small reservoir outside, which is attached in a collapsed position to generate suction. Review the drain location (near certain organs or anastomoses intra-abdominally, or in the subcutaneous tissue). Drains may be placed near bowel anastomoses, cystotomy repairs or pancreatic resections because drain output can provide evidence of a leak; hemorrhage may also be revealed in drain output.

Diagnosis

Fever

Postoperatively, a temperature of 100.4 °F (38 °C) on two occasions more than 4 h apart, or a single temperature of 101 °F (38.3 °C), constitutes a fever [45]. In a patient with neutropenia, neutropenic fever is defined as a single oral temperature of 38.3 °C (101 °F) or more, or a temperature of 38.0 °C (100.4 °F) or more sustained for at least 1 h [32]. Always assess for physiologic or laboratory findings suggestive of sepsis (Table 18.1), which requires rapid intervention [46, 47].

The differential diagnosis for fever depends on the patient's recent treatment, and, if applicable, her interval from surgery. Fevers in the first 24 h after surgery are typically noninfectious, due to inflammation or medication reactions [48].

Table 18.1 Clinical criteria of sepsis and severe sepsis

Sepsis	**Severe sepsis**
Suspected source plus 2 or more: 1. Temperature >38.3 °C (101 °F) or <36 °C (96.8 °F) 2. Heart rate >90 beats per min 3. Tachypnea (>20 breaths/min) 4. WBC >12,000 μ/L or <4000 μ/L or normal with >10 % immature (band) forms	Sepsis plus one or more: 1. Systolic blood pressure <90 mmHg or decrease from baseline by 40 mmHg 2. Elevated lactate (>1 mmol/L; >4 particularly concerning, sign of organ hypoperfusion) 3. Acute lung injury: PaO_2/FIO_2 <250 (in the absence of pneumonia) or <200 (with pneumonia) 4. Acute oliguria: <0.5 mL/kg/h despite fluid resuscitation 5. Creatinine >2 mg/dL 6. INR > 1.5 7. Platelets <100,000/uL 8. Bilirubin >2 mg/dL

Adapted from Dellinger et al. [46] and Fischerova [47]

Infectious complications usually present beyond 48 h after surgery. Pneumonia (particularly aspiration) and urinary tract infections may present as early as the first 2-3 days postoperatively, while the presentation of surgical site infections, vaginal cuff complications and pelvic abscesses commonly may be delayed by 5 or more days. Bowel and urinary tract injuries typically present in the days following surgery, but may be delayed by 1-2 weeks. Neutropenia (and associated neutropenic fevers) depends on the chemotherapeutic agent and dosing schedule. Thrombosis-associated fever can occur at any time, but fever greater than 101°F is rarely related to thrombosis and should prompt exclusion of infectious etiologies first. Postoperative infections are more common in older patients with immunosuppression, diabetes, obesity, longer operative times (greater than 3 h), and smokers [49].

Laboratory testing should include a complete blood count with a differential, and urinalysis. In patients with a fever of 38.3 °C (101 °F) or more, obtain blood cultures (including one drawn from any central venous catheter), in addition to a urine culture, and cultures of any purulent wound exudate. Order a stool study for *Clostridium difficile* (polymerase chain reaction or enzyme immunoassay for microbe or toxin detection) in any patient with diarrhea and recent antibiotic exposure and/or prior *Clostridium difficile* infection. 1,3 [beta]-d-glucan, mannan, and anti-mannan antibody assays can be obtained in patients taking steroids or those with neutropenia, to assess for disseminated candidiasis. In patients with possible sepsis, check a lactate, liver function tests, electrolytes and creatinine. Also obtain coagulation studies (prothrombin time (PT), activated partial thromboplastin time (aPTT) and fibrinogen) to assess for disseminated intravascular coagulation.

Assess surgical drain output and consider sending laboratory testing, which can provide evidence of a postoperative complication resulting in fever or sepsis. Visual examination of output from a drain near a leaking bowel anastomosis may reveal obvious bowel contents, prompting imaging and/or intervention. Fluid from a drain near the bladder following cystotomy repair or a urinary conduit will have a much higher

creatinine level than the serum in the setting of a urine leak (usually several fold higher). Fluid from a drain near a pancreatic or splenic resection may be sent for amylase levels after a patient has resumed a regular diet (and the pancreas is stimulated) to rule out pancreatic leak; drain fluid levels that are triple the serum levels are consistent with pancreatic disruption [50]. If a patient has a chest tube in place, assess the color of the fluid for blood, pus, or chyle (which will separate into fatty layers inside the Pleur-evac® drainage system, Teleflex, Morrisville, NC). Any bubbles in the water seal chamber should also be noted, as these indicate continued passage of air into the pleural space.

Obtain imaging as indicated by the history and physical exam, including chest radiograph, pelvic ultrasound, or abdominal CT scan. Abdominal CT scans are particularly helpful in identifying pelvic hematomas or abscesses, but can also identify other sources of fever and pain, including bowel injury or obstruction, anastomotic leak, and urinary tract injury, while also characterizing tumor burden or progression. Oral and intravenous contrast should be given whenever possible.

Pain

The assessment of patients with gynecologic cancers with pain should be tailored to the acuity of their presentations. Patients with new-onset or postoperative pain should also have a complete blood count to assess for leukocytosis and anemia and a basic metabolic panel to assess for electrolyte derangements and creatinine elevation. A urinalysis may reveal urinary tract infection. Relevant tumor markers can also be sent if disease recurrence or progression is suspected. Abdominal imaging should be obtained, targeted to the suspected source of pain. If the differential diagnosis remains broad, an abdominal CT scan with oral and IV contrast can be helpful, revealing tumor burden, hemorrhage or progression, urinary or gastrointestinal tract injuries or obstructions,

pelvic fluid collections (hematoma, abscess, or urinary ascites), thromboses in pelvic vessels, or wound dehiscence [48].

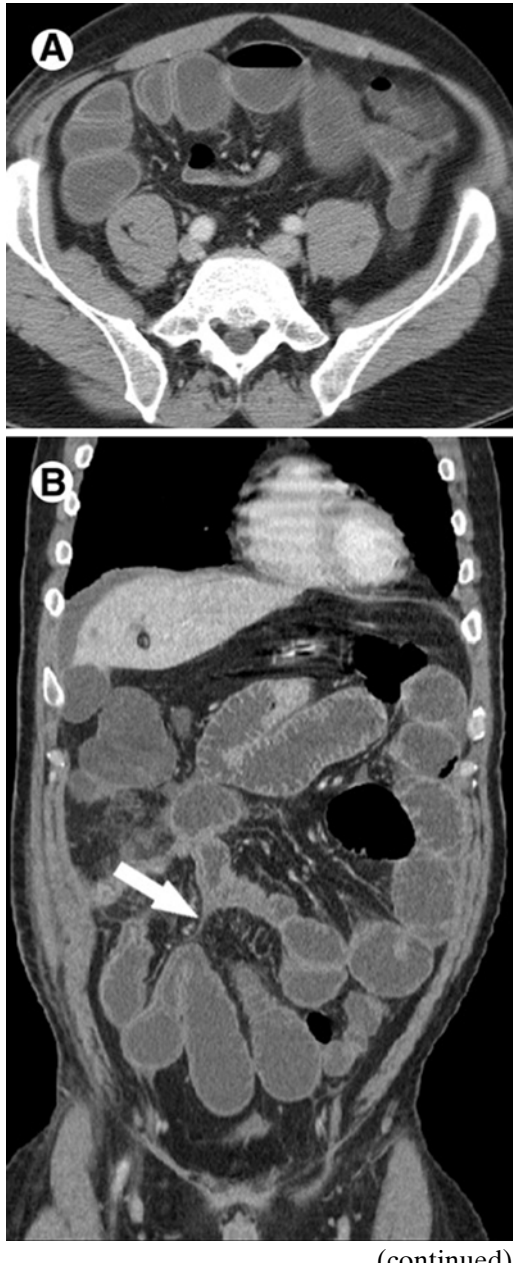
In an oncologic patient with advanced disease, her disease may be the source of her pain—through mechanisms such as tumor invasion or compression of other structures and pathologic bone fractures—though this is a diagnosis of exclusion. Tumor-related pain is not a reason to forgo a full assessment, as many of these sources of pain can be addressed or palliated.

Nausea/Vomiting

In patients with emesis, check a complete metabolic panel to assess for electrolyte and metabolic derangements. In a patient with hypotension, tachycardia, fever, or acute pain on exam, obtain a complete blood count and complete metabolic panel; serum lactate should also be sent, which may be elevated in conditions including (but not limited to) sepsis and bowel ischemia [51]. Relevant tumor markers can also be sent if disease recurrence or progression is suspected. A urinalysis, particularly in postoperative patients, can be sent to assess for infection.

The specificity of abdominal radiographs for the diagnosis of ileus or bowel obstruction is poor, and in patients with prolonged symptoms of ileus or obstruction, an abdominal CT is recommended [52, 53]. On abdominal CT, in patients with postoperative ileus, oral contrast will pass through the entire digestive tract, and the colon will contain air and fluid [54]. In patients with obstruction, a transition point may be identifiable by CT—potentially associated with tumor—with proximally dilated and distally collapsed bowel (Fig. 18.1) [54–58].

FIG. 18.1 (continued) Small bowel obstruction. (**a**) Axial image shows dilated loops proximal to decompressed loops, diagnostic of SBO. (**b**) Coronal reformatted image shows a linear band (*arrow*) extending toward the dilated loops, representing the adhesive band (Reprinted from Desser and Gross [55], with permission from Elsevier)



(continued)

Diagnosis of a bowel injury or anastomotic leak is optimally made using abdominal CT with oral contrast, which may extravasate [48, 59].

Please refer to Chap. 16, Complications of Minimally Invasive Gynecologic Surgery, for the diagnosis and management of ileus, small bowel obstruction, bowel and urinary tract injury.

Bleeding Due to Tumor

Please see Chap. 2, Vaginal Hemorrhage, for more information on diagnosis and initial resuscitation in patients with vaginal hemorrhage. Briefly, a complete blood count, coagulation studies, and blood type and antibody screen should be collected.

Patients with gynecologic malignancy—most commonly cervical, uterine, or gestational trophoblastic neoplasia—may develop bleeding either due to tumor invasion into vascular structures or due to friable tumor blood supply [60]. Of note, radiation can cause mucosal irritation and bleeding, but this would less commonly present as hemorrhage [61].

If a patient with vaginal hemorrhage is sufficiently stable, imaging to evaluate tumor size and location can be helpful, usually performed by CT scan with IV contrast, which may reveal contrast extravasation due to acute bleeding. If tumor is visualized in the cervix, vagina, or vulva by physical exam, specimen removal or biopsy may exacerbate acute hemorrhage. Malignancy-related bleeding is likely to be visible vaginally; hemorrhage of an intra-abdominal tumor is less common, but may be detected by serially declining hemoglobin and evidence of hemorrhage—either hemoperitoneum or enhancement within the tumor consistent with hemorrhage—by pelvic ultrasound or CT scan [62, 63].

Management

Please see Chap. 14, Common Inpatient and Postoperative Issues, for general management of nausea and vomiting.

Fever

In patients with clinical indicators of sepsis, initial management includes the placement of two large-bore IVs and supplemental oxygen by high-flow facemask as needed [46]. If not obtained earlier, a complete blood count and complete metabolic panel including liver function tests, coagulation studies and lactate should be obtained. These labs (as indicated) should be rechecked frequently during resuscitation to assess progress. An arterial blood gas should be obtained in acutely ill patients. Antibiotics should be started within 1 h, and the source of infection must be identified and controlled. Please see Chap. 1, Acute Pelvic Pain, for more information on the management of sepsis.

In patients with central venous catheters with positive blood cultures (for the same organism) from the catheter and peripheral blood, persistent bacteremia after 72 h of antibiotic treatment, sepsis or hemodynamic instability, this catheter should be removed if clinically feasible [64]. Establishing whether a catheter-associated infection is truly present can be challenging, and the removal of long-term catheters (such as ports) is more involved; consider consulting infectious disease specialists. Obtain a culture of the catheter tip for confirmation if the catheter is removed. Following a catheter-related infection, resolution of bacteremia as demonstrated by negative blood cultures for 48 h should precede reinsertion of a new line.

Following Splenectomy

Patients with prior splenectomy are at increased risk for contracting infections with encapsulated bacteria, most commonly *Streptococcus pneumoniae, Neisseria meningitidis, Haemophilus influenza,* and *Streptococcus pyogenes* [65]. When a splenectomy is planned preoperatively, pneumococcal, meningococcal, and *H. influenzae* vaccinations should be given 2 weeks prior to surgery. In patients with an unanticipated splenectomy, these vaccines should be given 2 weeks

after surgery for the highest immunologic response, but from a practical perspective, these vaccines are often given immediately prior to hospital discharge [66].

Neutropenic Fever

Among hemodynamically stable patients presenting with fever, those with neutropenic fever are at greater risk of rapid progression of their infections as compared to immunocompetent patients; recognition and early treatment are crucial to prevention of progression to sepsis. Empiric antibacterial treatment should be initiated as soon as possible following collection of blood cultures [46, 67]. The infectious source must be identified and controlled as quickly as possible; the history, physical examination, and targeted imaging may identify the source.

Patients with neutropenic fever are stratified according to risk; high-risk patients are those with anticipated prolonged (greater than 7 days) or profound neutropenia (ANC less than 100 neutrophils/μL), or those with significant clinical illness, including identified infectious source, hypotension, hypoxemia, electrolyte abnormalities, nausea, emesis, diarrhea, significant pain, dehydration, chronic cardiopulmonary or renal disease, and those age > 60 years [32, 67]. Low-risk patients are those with anticipated brief neutropenic period (less than 7 days) and minimal clinical symptoms and comorbidities.

High-risk patients should be admitted immediately for empiric antibiotic therapy, whereas low-risk patients may be candidates for oral empiric therapy [32]. Intravenous empiric antibiotics include an antipseudomonal beta-lactam agent (such as cefepime 2 g IV every 8 h, meropenem 1 g IV every 8 h, or piperacillin-tazobactam 4.5 g IV every 6–8 h). Addition of further antimicrobials (vancomycin, an aminoglycoside, or fluoroquinolone) for broader coverage should be considered if microbial resistance is suspected or the patient is hemodynamically unstable. In particular, consider the addition of vancomycin in patients with skin or soft tissue infections, catheter- or drain-related infection, or ongoing hemodynamic instability.

Per the Infectious Diseases Society of America (IDSA) guidelines, a low-risk patient can be considered for an oral regimen. Initial regimens include ciprofloxacin (750 mg PO every 12 h) plus amoxicillin-clavulanate (500 mg/125 mg PO every 8 h), or ciprofloxacin plus clindamycin though the latter regimen is less well studied. Close outpatient follow-up is vital in these patients [32].

Large Bowel Obstruction

Patients with large bowel obstruction may report a longer duration of symptoms and less nausea and emesis than patients with small bowel obstruction, as the ileocecal valve provides an anatomic proximal point of dilation; severe large bowel obstructions will overwhelm the ileocecal valve and small bowel may become dilated as well [56, 58].

Unlike small bowel obstructions, for which conservative management is preferred, over 75 % of large bowel obstructions require surgical intervention [37]. Complete large bowel obstruction is a surgical emergency regardless of etiology, as perforation can lead to acute peritonitis and severe sepsis. Placement of a nasogastric tube may improve symptoms of nausea and emesis, but is insufficient treatment for a large bowel obstruction. A potential alternative to surgical management in carefully selected patients is the placement of a colonic stent, which can sometimes be used as a bridge to surgery if preoperative stabilization is required, or as palliation in nonoperative candidates or patients with advanced disease [68].

Anastomotic Leak

Anastomotic leaks should be considered as surgical emergencies, though treatment may vary somewhat depending on the clinical severity. All patients diagnosed with anastomotic leak should be started on broad-spectrum antibiotics (such as piperacillin-tazobactam 4.5 g IV every 8 h) and placed on

bowel rest [44, 69]. Patients presenting with evidence of peritonitis, severe sepsis, and/or hemodynamic stability require resuscitation and emergent exploratory laparotomy [70]. In a small subset of patients with localized peritonitis and/or evidence of mild infection only, a contained leak or abscess may potentially be managed with intravenous antibiotics and drainage by interventional radiology [70].

Abdominal Wound Separation

Fascial dehiscence is a surgical emergency, requiring immediate reoperation and repair. Conversely, superficially separated wounds with intact fascia can be managed with serial debridement of necrotic tissue and wet-to-dry dressings 2–3 times per day; wounds may heal by secondary intention or with placement of a negative pressure dressing (once any infection has been resolved) [71]. Alternatively, wounds can be surgically reclosed once healthy granulation tissue has formed, without evidence of ongoing infection [48, 72]. Vaginal cuff dehiscence is discussed in Chap. 16, Complications of Minimally Invasive Gynecologic Surgery.

Bleeding Due to Tumor

Significant vaginal hemorrhage due to cervical malignancy requires emergent radiation oncology consultation; hemorrhage from a uterine tumor can be treated with emergent radiation, emergent embolism by interventional radiology, or emergent surgical intervention, including hysterectomy or other tumor resection [73, 74]. The decision among these modalities depends on which resources and clinicians are available emergently, the patient's stability (as interventional radiology and radiation therapy require time for resource mobilization), and the patient's comorbid conditions and/or functional capacity, which may limit her eligibility for invasive surgery.

Hemorrhage within pelvic tumors and spontaneous hemoperitoneum are less uncommon in patients with gynecologic malignancies [75, 76]. Patients who are hemodynamically stable with stable hemoglobin levels may not require further intervention. Those with declining hemoglobin and/or hemodynamic instability may require embolization or operative management, depending on the source of the bleeding and the patient's clinical stability, treatment goals, and functional capacity [60].

Please see Chap. 13, Preparing for Urgent or Emergent Surgery, for more information on transfusion of patients with hemorrhage and anticoagulation reversal, as needed.

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Chapter 19
Urogynecology and Pelvic Reconstructive Surgery

Alexcis P. Thomson

Background

The goal of female pelvic reconstructive surgical procedures is to take advantage of the bony pelvis, relevant pelvic ligaments, and muscles to restore normal anatomy. These structures are reviewed briefly in the context of a survey of common urogynecological procedures (Fig. 19.1).

Definitions

Midurethral Sling Procedures

These procedures are performed to address stress urinary incontinence. The two most common variations are the tension-free vaginal tape and the transobturator tape. An incision is made in the anterior vaginal wall, and a portion of polypropylene mesh, approximately 1 centimeter (cm) in width, is placed below the midurethra. During times of increased

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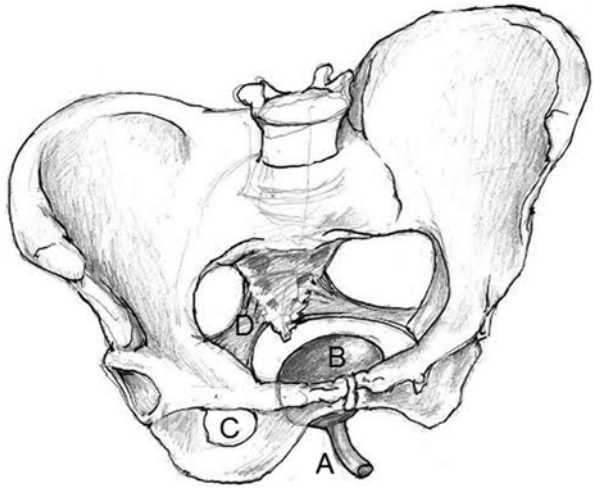

Fig. 19.1 Female pelvic anatomy. (*A*) Urethra, (*B*) bladder, (*C*) obturator foramen, (*D*) sacrospinous ligament

intra-abdominal pressure, the urethra is compressed superiorly against the pubic symphysis and inferiorly by the tape [1]. At rest, a correctly placed tape is tension-free. Each has several different techniques by which to perform the procedure, which is chosen according to surgeon preference and patient parameters.

Retropubic or tension-free vaginal tape (TVT): Placed lateral to the midurethra, through the retropubic space, emerging from the abdominal wall. This sling can also be placed in the reverse direction, entering at the abdominal wall. The TVT sling has a slightly higher incidence of cystotomy (4–7 %) and retropubic hematoma (1–2 %) as compared to the transobturator tape (TOT) sling [2, 3].

Transobturator tape (TOT): Passed through the obturator foramen laterally, typically emerging at the level of the clitoris. TOTs are associated with a higher incidence of major vascular injuries (1–2/1000) and neurologic injury but fewer complications overall, including bladder perforation, as

compared with the TVT sling [2, 4, 5]. Patients receiving TOT are more likely to report groin pain and even transient inner thigh weakness or numbness [6].

In addition to the TVT and TOT procedures, newer self-retaining slings have been developed, requiring only a vaginal incision. Depending on the device, these may be deployed through the retropubic space or the obturator canal.

Total Vaginal Hysterectomy (TVH)

Preferred route of hysterectomy, although increasingly marginalized into specialty urogynecologic practice since the advent of laparoscopic hysterectomy [7]. TVH involves removing the uterus with or without the adnexa through the vagina by successively ligating and transecting the lateral supportive attachments and blood supply from the cervix to fundus. Several critical steps occur during a vaginal hysterectomy, including (1) entering the anterior and posterior cul-de-sacs without causing a cystotomy or enterotomy, respectively, (2) transection of the cardinal-uterosacral ligament complex as close to the uterus as possible to avoid ureteral injury, and (3) transection of the utero-ovarian ligaments and/or infundibulopelvic ligaments if oophorectomy is planned. TVH is associated with faster recovery and lower cost than laparoscopic or abdominal hysterectomies [8]. Urinary tract injuries (bladder injuries, far more common than ureteral injuries) occur in an estimated 0.7–4 % of patients; bowel injuries occur in 0.1 % of patients [8].

Uterosacral Ligament Suspension (USLS)

Suspension of the vaginal vault apex from the uterosacral ligaments bilaterally using delayed absorbable sutures placed at the level of the ischial spine or higher (closer to the ligaments' sacral insertion) [9]. USLS is often performed after a concomitant TVH. A critical step is ensuring that the uterosacral sutures are placed sufficiently medially to avoid the ureters. The most common complications are ureteral obstruction (1.8 %) and bleeding (1.3 %) [10].

Sacrospinous Ligament Fixation (SSLF)

Fixation of the vaginal apex to the lateral third segment of the sacrospinous ligament, typically unilaterally and often on the right side as the rectum enters the pelvis from the left. The "Michigan Modification" affixes all four vaginal walls (anterior, posterior, left, and right) to the sacrospinous ligament. A critical step is the lateral placement of the sutures so as to avoid entrapment of the sciatic nerve. Care must also be taken to ensure placement at least 1–2 cm medial to the ischial spine to avoid injury to the pudendal vessels. Complications include hemorrhage and hematoma (2.3 %), injury to femoral, pudendal or sciatic nerves (1.8 %), injury to bladder or bowel (0.8 %), and ureteral kinking [11].

Sacrocolpopexy

Apical suspension of the vaginal vault after remote total hysterectomy or of the cervical stump after concomitant supracervical hysterectomy (more accurately called sacrocervicopexy) to the sacral promontory via nonabsorbable mesh. This can be performed abdominally, laparoscopically, or robotically. Critical steps are dissection of the vascular sacral promontory (with special care to avoid the middle sacral artery) and fine suturing of the mesh to the anterior and posterior portions of the vaginal vault as well as the sacrum, ensuring a robust repair. Complications include hemorrhage (4.4 %), cystotomy (3.1 %), bowel injury (1.6 %), and ureteral injury (1.0 %) [12].

Colpocleisis

An obliterative surgical repair of pelvic organ prolapse, typically performed in elderly women no longer desiring sexual function. The vaginal epithelium is removed, and the underlying anterior and posterior vaginal muscularis are sutured together; vaginal obliteration can be total (with hysterectomy) or partial. Complications include bleeding (5.7 %), followed by medical morbidity related to advanced patient age [11].

Anterior and/or Posterior Colporrhaphy

Employed to address anterior and posterior vaginal prolapse, respectively, separate from apical prolapse. Each involves plication of the vaginal fibromuscular layer and excision of redundant vaginal mucosa. For a more robust posterior repair, additional plication of the levator ani muscles is occasionally employed. Ureteral injuries occur during 1.7 % of anterior colporrhaphies; these and other urinary tract injuries are usually detected by cystoscopy, which is commonly performed after anterior colporrhaphy [13].

Cystoscopy

A commonly performed urogynecological procedure used to assess for transmural sutures and ureteral obstruction at the conclusion of a procedure. A cystoscope is used to visualize the urethra, trigone, ureteral orifices and jets, as well as bladder mucosa to ensure no cystotomy or sutures are present in the bladder. A thorough cystoscopy of the entire bladder and urethra can also visualize pathology that predated the surgery, such as masses or strictures.

Immediate Postoperative Issues: Calls from the Post-Anesthesia Care Unit (PACU)

Voiding Dysfunction

Background

For urogynecologic procedures in general, much of the focus of surgical manipulation is in close juxtaposition to the bladder and can involve frequent filling, emptying, and penetration of the urethra and bladder. This manipulation itself can cause voiding dysfunction secondary to irritation, inflammation, and edema of the surrounding soft tissue. More concerning is injury to the ureters, bladder, and urethra, though attempts are usually made to exclude these injuries at

the conclusion of the surgical case by performing cystoscopy [14, 15]. Other potential causes are an extremely tight midurethral sling or large retropubic hematoma causing urethral obstruction and intravascular depletion resulting in decreased urine output. Please see Chap. 14, Common Postoperative and Inpatient Issues, for more information on low urine output.

Definition

Voiding Dysfunction Variably categorized; familiarity with an institution's voiding trial practice and definition of voiding trial failure is important, as these are not universal and may vary widely. For anterograde trials of void, the catheter is removed without backfilling, allowing 6–8 h for the patient to void; a common benchmark for passing is the ability to void at least 50 % of the total amount of urine in the bladder and a post-void residual (PVR) of less than 150 milliliters (mL). If a retrograde trial of void is performed, the bladder is first emptied (or has been decompressed with a Foley catheter), and 300 mL of normal saline is backfilled into the bladder and the catheter is removed. If the patient voids at least 150 mL within 30 min, the trial is passed [16].

Differential Diagnosis

Postoperative edema
Urinary tract injury
Tight midurethral sling
Retropubic hematoma
Intravascular depletion
True voiding dysfunction (urinary retention)

When You Get the Call For a patient whose bladder was backfilled followed by an unsuccessful attempt to void, ask the nurse to replace the Foley immediately. For the urogynecologic patient population, particularly those who have had midurethral slings, acute bladder overdistension caused by

urinary retention can cause bladder wall ischemia within 30 min, as well as subsequent reperfusion injury, leading to prolonged bladder dysfunction [17, 18]. For patients undergoing anterograde trials of void, ask for a post-void residual (PVR), which is measured by a bedside ultrasound device.

When You Arrive Review the full vital signs flow sheet. Review the patient's full record of input and output intraoperatively and in the PACU. Ensure that the Foley catheter has been replaced and is not obstructed or kinked.

History

Assess whether the patient has a history of voiding dysfunction. Review the patient's medications, as urinary retention can be caused or exacerbated by many medications, including selective serotonin reuptake inhibitors, anticholinergics (which are often used intraoperatively), and antihistamines [19]. Review the patient's operative report to assess the degree of urinary tract manipulation and possibility of urinary tract injury. Review the duration of the surgery, whether laparoscopic or open, and note the amount of intravenous resuscitation and blood loss.

Physical Examination

Assess whether the patient is in pain or distress. Perform an abdominal exam, particularly to assess for suprapubic pain and distention, suggestive of urinary retention or less commonly retropubic hematoma.

Diagnosis

If there is concern for bleeding, either by symptoms of acute anemia (including tachycardia or hypotension) or evidence by physical examination (including large vaginal hematoma, suprapubic fullness, or bleeding from surgical sites), a complete blood count and coagulation studies (prothrombin time, activated partial thromboplastin time, and fibrinogen) should be checked. Please see the next section for diagnosis and management of retropubic hematoma.

In a patient who failed an anterograde voiding trial and has not yet had a Foley replaced, a PVR, either by bedside ultrasound device or by catheterization, is helpful in determining the cause of urinary retention. A PVR less than 150 mL in a patient with a low voided amount suggests that the patient is intravascularly depleted. If the patient appears to be under resuscitated, a fluid bolus may improve urine output. If a patient appears adequately resuscitated with a PVR of more than 150 mL, she likely has true voiding dysfunction.

Management

Management is dependent upon the cause of the voiding dysfunction. Patients with acute bleeding may require transfusion or further interventions depending on the acuity and source of the bleeding. If a patient with true voiding dysfunction is admitted postoperatively, a repeat trial of void can be attempted the following morning. Limit exposure to causal medications if possible, including anticholinergic medications (such as scopolamine patches, commonly used for postoperative nausea). If a patient fails her trial of void again, or will be sent home immediately postoperatively, she should be sent home with an indwelling catheter, to be removed in the outpatient setting in 2–3 days. A safe and viable alternative to an indwelling catheter is intermittent home self-catheterization 4–5 times per day; this requires patient education and ideally, a patient will have been taught to do this preoperatively [20]. If the patient is catheter-dependent upon discharge, antibiotics for prophylaxis of urinary tract infection are not routinely prescribed [21].

Suprapubic Pain/Swelling

Definition

Retropubic Hematoma Hematomas in the space of Retzius, also called the retropubic space, which is a potential space between the pubic symphysis and anterior bladder. Hematomas less than 100 mL in volume rarely cause

symptoms; hematomas 100–200 mL in volume may cause moderate pain, while hematomas 300 mL or more in volume may cause severe pain requiring surgical evacuation [22]. Venous injury is typically self-limited but may take 1–5 months to resolve [22]. In a minority of cases, the hematoma is large enough to compress the bladder and urethra and cause voiding dysfunction, become a nidus for infection, or represent a significant blood loss.

Differential Diagnosis

Physiologic tissue edema
Retropubic hematoma
Enlarged bladder due to acute urinary retention

When You Get the Call Ask for a recent set of vital signs and the volume of voided urine output. Review the operative report if available.

When You Arrive Review the full vital signs flow sheet, assessing for hemodynamic stability. Assess the patient's distress and pain. If the patient does not have a Foley catheter in place, exclude urinary retention by requesting a bedside ultrasound of the bladder volume (a bladder scan) or catheterization. Unstable patients with significant suprapubic swelling and pain (not attributed to urinary retention) likely have a retropubic hematoma and may require emergent intervention, either embolization by interventional radiology or operative evacuation of a hematoma and control of ongoing bleeding.

History

Review when the pain started and its severity. Review of the operative report is crucial to clarify whether the retropubic space was entered. Review whether the patient has baseline

voiding dysfunction or history of a bleeding diathesis or use of anticoagulant medications.

Physical Examination

Assess the suprapubic space to judge the degree of distention. Perform an abdominal exam to assess for peritoneal signs, including rebound (pain when abdominal pressure is withdrawn) or involuntary guarding.

Diagnosis

If a patient has pain and swelling consistent with retropubic hematoma, obtain a complete blood count and coagulation studies. In patients who are hemodynamically stable but with ongoing pain and distention, an ultrasound may be obtained to visualize a retropubic hematoma, either transabdominally or transvaginally (Fig. 19.2). Alternatively, a CT scan of the pelvic with IV contrast can be obtained (Fig. 19.3); extravasation of contrast may be identified in the retropubic space.

If a stable patient has not voided and does not have an indwelling Foley, a bladder scan can be performed to assess for urinary retention as the cause of suprapubic fullness; alternatively, consider presumptive catheterization for a potentially distended bladder, which would be both diagnostic and therapeutic. Of note, bladder distention and pain may elicit vasovagal symptoms (including transient hypotension and bradycardia).

Management

In a patient with hemodynamic changes (tachycardia, hypotension), severe pain, massive or enlarging suprapubic mass, and/or urinary retention, the retropubic space should be manually compressed while mobilizing resources. Severe hemorrhage can be managed with embolization by interventional radiology, or if this resource is unavailable, by laparotomy [23].

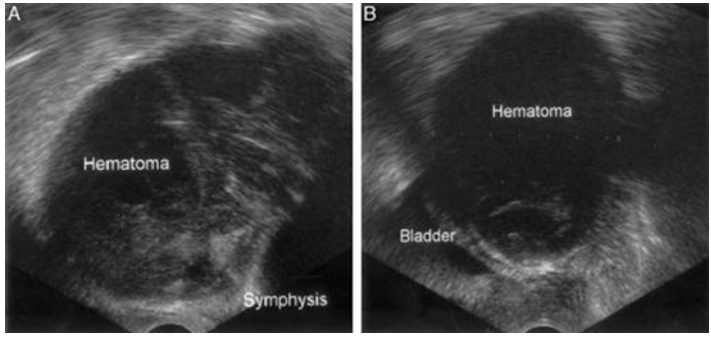

Fig. 19.2 Retropubic hematoma by transvaginal ultrasound, following a tension-free vaginal tape procedure. (**a**) Sagittal view. (**b**) Horizontal view. A nonhomogeneous mass behind the symphysis representing a clotted hematoma is displacing the bladder to the right (Flock et al. [22], with permission of the American College of Obstetricians and Gynecologists)

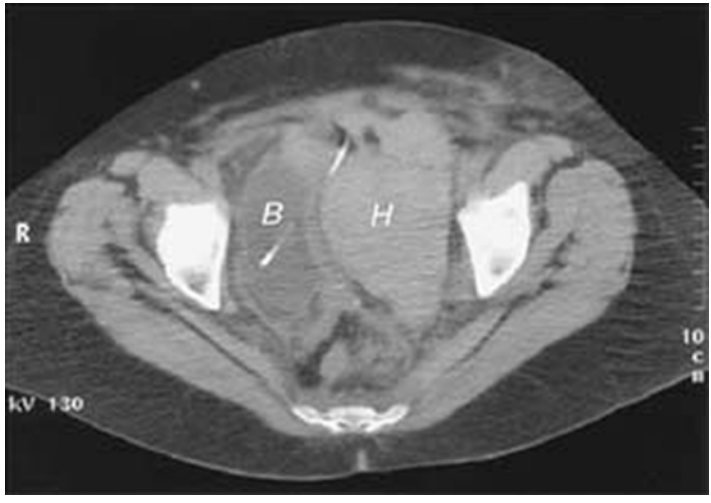

Fig. 19.3 Pelvic computed tomography scan of patient with a 10-cm hematoma (*H*) in the space of Retzius next to the bladder (*B*) (Walters et al. [24], with permission of the American College of Obstetricians and Gynecologists)

Management of transfusions are discussed in Chap. 13, Preparing for Urgent and Emergent Surgery.

Patients who are stable but with pain and a progressive decline in hemoglobin may require blood transfusion; a drain can also be placed in the suprapubic space by interventional radiology [24, 25]. If a patient is hemodynamically stable, with stable hemoglobin, able to void, and with well-controlled pain, her retropubic hematoma can be expectantly managed.

In cases of suprapubic swelling caused by urinary retention, the mass should resolve with an indwelling Foley catheter. These patients may have a repeat trial of void in the morning if they are admitted; if they are discharged, they should have a repeat trial of void in the office in 2–3 days.

Calls from the Emergency Room

Fever and/or Pelvic Pain

Please see Chap. 16, Complications of Minimally Invasive Gynecologic Surgery, for a full discussion of diagnosis and management of postoperative fever and pain, as well as management of urinary tract injury. Comment on conditions that should be considered in urogynecology patients in particular is provided here.

Urinary Tract Injuries

Injuries to the urinary tract may present as postoperative fever, pelvic pain, ileus (due to intraperitoneal urine), or leakage of urine through the vaginal cuff. In patients who have had urogynecologic surgery, urinary tract injury should be strongly considered. Urinary tract injuries are more common in procedures for correction of pelvic organ prolapse and urinary incontinence; cystoscopy is often performed at the time of surgery in an effort to identify urinary tract injury intraoperatively [26].

In a TVT sling placement, a bladder injury is most likely to occur as a puncture (through and through) at the anterior

aspect of the bladder dome, attributable to a medial placement of the sling trocars [27]. Rarely, the trocars can cause injury to the midurethra if placed too close to the midline. In a sacrospinous ligament fixation, the ureter may become kinked at the location of the sacrospinous ligament suture. During hysterectomy, the ureter is in greatest danger of injury at the following points: (1) the pelvic brim, running medial to the infundibulopelvic ligament; (2) when attached to the medial leaf of the broad ligament, descending into the pelvis; (3) at the level of the internal cervical os, traversing below the cardinal ligament containing the uterine vessels; and (4) entering the posterior aspect of the bladder at the anterolateral fornix of the vagina [28].

Mesh Exposure or Erosion

Mesh complications should be considered as a source of pain and, less commonly, fever. Mesh erosions occur following 0.8–4.2 % of midurethral sling procedures and complicate 10 % or more of other vaginal mesh procedures [29–31]. Risk factors for mesh exposure include advanced age, diabetes, smoking, steroid use, elevated body mass index (BMI), vaginal incisions greater than 2 cm, and prior surgery for incontinence or prolapse [29, 31]. Patients may complain of vaginal bleeding, vaginal discharge, dyspareunia, and/or pelvic pain [32]. Of note, patients may also have pain from mesh contraction (shrinkage).

On physical examination, mesh may be visible in the vagina, usually through a separated suture line [31]. Limited mesh exposure (less than 0.5 cm) may be managed with trimming of the visible mesh by the patient's urogynecologist and use of intravaginal estrogen (1 g, twice per week) [31]. Larger erosions often require operative excision of exposed mesh. Mesh may also erode into viscera, including the bladder and bowel (depending on the mesh implantation location), which may be diagnosed with cystoscopy and/or anoscopy, as indicated; these erosions require far more complex and multidisciplinary repair.

Mesh erosion may also rarely lead to infection; patients with infected mesh may have mesh-related abscess, fistulae, or necrotizing infection [33]. Rarely, patients may develop osteomyelitis following sacrocolpopexy [34]. Patients may present with fever, leukocytosis, worsening pain at the location of mesh, and/or imaging showing abscess associated with mesh; patients with infections associated with pelvic mesh usually require removal by a specialist and treatment with antibiotics [33, 35].

Vaginal Bleeding

Definition

Variably defined but soaking two pads per hour would be considered excessive. Early and late postoperative hemorrhage occurs in 2 % of cases [36]. Please see Chap. 2, Vaginal Hemorrhage, for diagnosis and management of this complaint.

Pessaries

Definitions

Pessaries Utilized to reduce pelvic organ prolapse and improve stress urinary incontinence. A wide range of shapes and sizes of pessaries are available, depending upon the degree and nature of support needed (Fig. 19.4). In general, these should be removed, cleaned, and replaced at least every 3 months, accompanied by a pelvic exam to assess for vaginal erosions or ulcerations. Pessary management is largely relegated to the outpatient setting; however, rare serious complications from prolonged pessary neglect can result in emergency room visits. These can present as severe mucosal erosion or infection, or pessary migration into adjacent structures, such as bladder and bowel.

The proper placement of several common pessaries is shown below. The ring pessary with knob (Fig. 19.5) is used

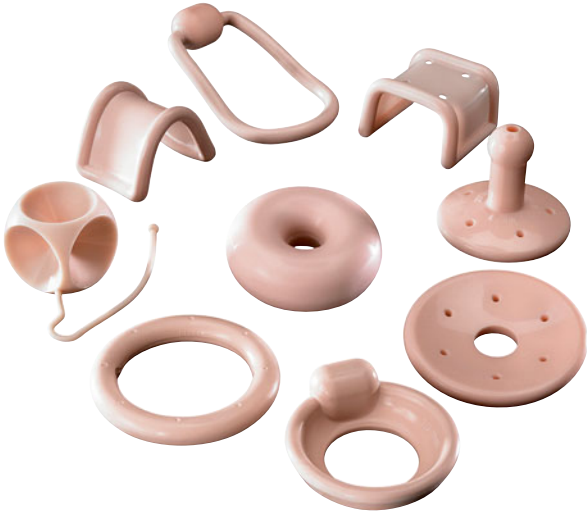

Fig. 19.4 Pessaries. Clockwise from 12 o'clock: Hodge with knob, Regula, Gellhorn, Shaatz, incontinence dish, ring, cube, Gehrung, with a donut pessary at the center (Photography supplied by CooperSurgical Inc.)

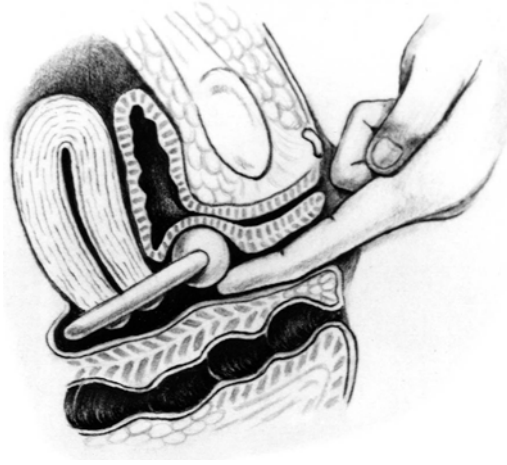

Fig. 19.5 Ring incontinence pessary with knob (image supplied by CooperSurgical Inc.)

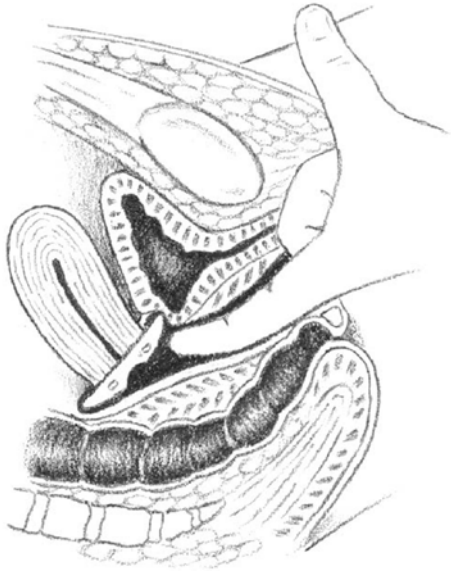

FIG. 19.6 Shaatz pessary (image supplied by CooperSurgical Inc.)

for incontinence, as the knob partially obstructs the urethra. The ring, donut, or Shaatz pessary (Fig. 19.6) is used for uterine prolapse and cystocele. The Gellhorn pessary (Fig. 19.7) is used for more advanced prolapse.

When You Get the Call Routine issues of pessary maintenance can generally be referred to the outpatient setting.

When You Arrive Review the full vital signs flow sheet to assess for hemodynamic stability. Observe whether the patient is in pain or distress.

History

Review with the patient how long she has been using the pessary and the indication for use. Review when she was last examined for vaginal erosion and whether she has been diagnosed with erosions in the past. Particularly if the patient is

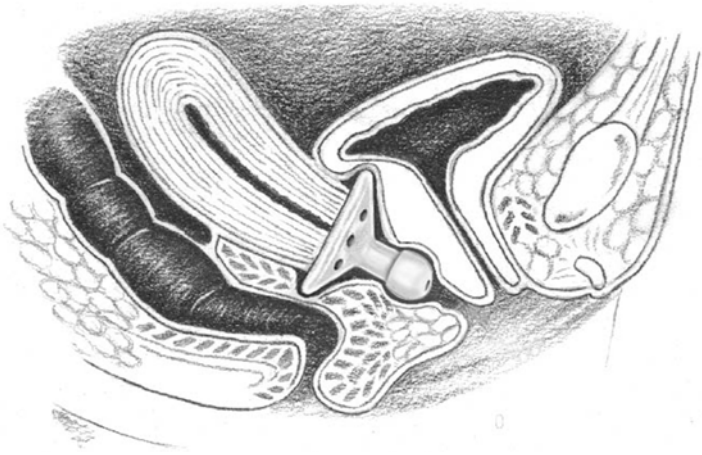

Fig. 19.7 Gellhorn pessary (image supplied by CooperSurgical Inc.)

postmenopausal, review whether she is using vaginal estrogen, which can be protective against vaginal erosions.

Physical Examination

If the pessary is visible and mobile, it should be removed to allow for a more thorough exam. Pessaries are usually somewhat pliable and can be bent in an examiner's fingers to allow for less traumatic removal. Lidocaine jelly (1 or 2 %) can be applied to the perineum to allow for more comfortable removal. After pessary removal, a speculum exam should be performed, during which the location and depth of erosions should be noted. If pelvic anatomy is obliterated or unrecognizable due to chronic infection, scarring, or fistulization, perform a rectovaginal exam to assess the anatomy.

Diagnosis

Vaginal erosions are diagnosed by physical examination. In the rare event of a significant erosion into surrounding

structures, a CT of the abdomen and pelvis can help locate the pessary and visualize the tissue injury. In these extreme cases, an exam under anesthesia may be required to locate and remove the pessary and to assess a rectovaginal fistula or other erosive damage [37].

Management

For uncomplicated vaginal erosions, the pessary should remain out of the vagina, pending reexamination and replacement by the patient's primary provider. In the interim, the vagina should be coated with an estrogen cream (such as Premarin®, Wyeth Pharmaceuticals, Philadelphia, PA, or Estrace®, Actavis, Parsippany, NJ) to help strengthen the vaginal epithelium [38]. One gram of estrogen cream can be applied nightly for severe erosions, with close interval follow-up in 1–2 weeks, at which point the dose can be lowered and/or spaced to twice per week. In the very unlikely event of pessary migration or fistulization, nonemergent surgical intervention is usually required, sometimes with colostomy in patients with rectovaginal fistula [39].

Rectovaginal and Vesicovaginal Fistulae

Definition

Rectovaginal or Vesicovaginal Fistula An abnormal communication between either the rectum or bladder and the vagina. Fistulae occurring below the dentate line are referred to as anovaginal. Globally, the most common cause of fistulae in women is obstetric trauma; however in the United States, fistulae may occur following surgeries involving dissection or injury of the posterior vaginal wall, perineum, anus, or rectum or as a complication of infection, pelvic or perineal cancers, inflammatory bowel disease, or radiation treatment [40]. Patients may complain of stool and/or urine per vagina or malodorous vaginal discharge.

Differential Diagnosis

Urinary or fecal incontinence
Vaginitis or vaginal discharge
Deep perianal or pelvic abscesses (often with imaging that suggests, potentially erroneously, communication with the vagina, uterus, bladder, or gastrointestinal tract)

When You Get the Call Ask for a full set of vital signs.

When You Arrive Review the full vital signs flow sheet to assess for hemodynamic stability. Observe whether the patient is in pain or distress. Assess for signs of sepsis, as fistulous tracts to the urinary tract may introduce severe infection.

History

Review the patient's symptoms associated with pelvic fistulae, including leakage of urine or stool from the vagina and foul smelling vaginal discharge. Review when her symptoms started. Ask whether she has any preexisting urinary or fecal incontinence, which may result in poor hygiene that can be mistaken for leakage from the vagina. Review her medical and surgical history, including pelvic surgery, inflammatory bowel disease, and malignancy (particularly those treated with pelvic radiation).

Physical Examination

Perform a sterile speculum exam. In addition, take the speculum apart and use one blade at a time, to allow for better visualization of the vaginal mucosa and any fistulous tract. A cotton swab, lacrimal duct, or silver wire probe may be used to identify a fistulous tract, though fistulous tracts are often

not visible. In patients with possible rectovaginal fistula, perform a rectovaginal exam to assess sphincter tone, as sphincter injury or deficiency may cause fecal incontinence, which may be mistaken from stool leaking from the vagina.

Diagnosis

There is no consensus regarding optimal diagnostic approach to fistulae of the female reproductive tract. Abdominal and pelvic CT scans are often a first step, which may reveal an abscess resulting in fistulous connections among viscera or malignancy [41]. Patients with vesicovaginal fistula may also have air bubbles visualized in the bladder by CT scan, though air bubbles may also be introduced by catheterization [42].

Regarding patients with vesicovaginal fistula, a voiding cystourethrogram is often helpful. In patients with fistulous connections to the distal gastrointestinal tract, MRIs are particularly helpful in delineating anovaginal collections or fistulae [41]. Fluoroscopy is available at many institutions but has relatively low sensitivity in the detection of rectovaginal or anovaginal fistulae [41]. Ultimately, exam under anesthesia may be needed for diagnosis; in patients with fistulous tracts between the urinary and gynecologic tracts, vaginoscopy and cystourethroscopy may be helpful, while protocoscopy can be revealing in patients with rectovaginal fistulae [42].

A simple tampon test may also be helpful. If a vesicovaginal or ureterovaginal fistula is suspected, a tampon is placed in the vagina, and the patient ingests oral phenazopyridine 200 mg; meanwhile, the bladder is emptied and filled with a dilute solution of normal saline and methylene blue [43]. If the tampon is stained orange, a ureterovaginal fistula is likely, whereas if the tampon is stained blue, a vesicovaginal fistula is more likely. If a rectovaginal fistula is of concern, a tampon is placed in the vagina, and an enema of warm saline dyed with a few drops of methylene blue can be instilled in the rectum using a syringe. If the tampon is stained blue, a rectovaginal fistula is likely [40].

Management

The management of vesicovaginal, ureterovaginal, rectovaginal, and anovaginal fistulae is beyond the scope of this chapter. If a fistula is diagnosed, the appropriate specialists should be consulted: urogynecology, colorectal surgery, and/or urology services. Fistulae, when requiring surgical intervention, are often repaired on an outpatient basis. In the emergent setting, however, immediate intervention is seldom indicated, except in the case of patients with abscesses or urinary tract infections, who require antibiotics and source control if possible. Please see Chap. 16, Complications of Minimally Invasive Gynecologic Surgery, for the management of urinary tract infection and pelvic abscess.

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Chapter 20
Reproductive Endocrinology and Infertility

Paula C. Brady and Elizabeth S. Ginsburg

Definitions

Infertility

Defined as the failure to achieve pregnancy after 12 months of unprotected intercourse in women under 35 years, and after 6 months in women aged 35 years and older. It is estimated to affect up to 15 % of couples [1, 2].

Clomiphene Citrate

A selective estrogen receptor modulator used to induce ovulation. Clomiphene acts as an estrogen antagonist in the hypothalamus which leads to increased endogenous gonadotropin secretion by the pituitary, stimulating ovarian follicular development [3]. It is administered in the early follicular

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phase of the menstrual cycle, starting on day 3–5 of the cycle and continued for 5 days. Common side effects include abdominal distention or discomfort, nausea, and breast tenderness; patients may rarely report visual disturbances, which are reversible but the clomiphene should be stopped [4, 5]. Ovarian enlargement may occur, though torsion and ovarian hyperstimulation syndrome (OHSS) are rare [6].

Gonadotropins

Injectable purified or recombinant luteinizing hormone and follicle-stimulating hormone, used in ovarian stimulation. Complications can include ovarian enlargement, torsion, and OHSS.

Intrauterine Insemination (IUI)

Introduction of a processed and concentrated sperm sample (either fresh from a partner or a previously frozen sample) into the uterus, using a catheter placed through the cervix. IUIs are performed for both female and male infertility indications. Women may take medications for ovulation induction (such a clomiphene citrate, letrozole, or gonadotropins), with or without an injection of human chorionic gonadotropin (hCG) to promote final oocyte maturation. IUIs are timed with a patient's ovulation using the hCG injection or home ovulation predictor kits. IUI is a very low-risk procedure, with a very low risk of upper genital tract infection [7].

In Vitro Fertilization (IVF)

IVF begins with ovarian stimulation, most commonly achieved with exogenous injectable gonadotropins. Ovarian follicular development and serum estradiol are closely monitored during this process. Once adequate follicular development is achieved according to an IVF program's protocols, final oocyte maturation is triggered with hCG or gonadotropin-releasing hormone (GnRH) agonists.

Thirty-six hours after the trigger injection, oocytes are retrieved transvaginally, or less commonly transabdominally, by ultrasound-guided needle aspiration of ovarian follicles. The oocytes are then fertilized, and the embryos are returned to the patient's uterus 2–6 days later, as dictated by an IVF program's protocols and the patient's clinical details.

For a variety of reasons, including but not limited to high risk of ovarian hyperstimulation syndrome or medical illness, patients' embryos or unfertilized oocytes may be cryopreserved (frozen) and not transferred. Conversely, patients may receive cryopreserved embryos or embryos derived from donated oocytes, meaning that these patients have not undergone ovarian hyperstimulation prior to embryo transfer. Instead, they receive various formulations of estrogen and progesterone for endometrial preparation.

To assess for successful implantation, patients' hCG levels are checked approximately 12 days after embryo transfer. If hCG levels are checked too soon, the result may be a false positive, as patients who received hCG for oocyte maturation may have residual serum hCG levels for up to 10 days [8]. Serum hCG levels after either subcutaneous or intramuscular hCG trigger injections peak at 24–36 h afterward, at levels of approximately 300 milli-international units per milliliter (mIU/mL) [8, 9].

IVF is an independent risk factor for ectopic pregnancy. The rate of ectopic pregnancy is estimated at 2–5 % among patients who have utilized assisted reproductive technologies [10, 11]. Risks of oocyte retrieval and OHSS are discussed in the following sections.

Oocyte Retrieval

Removal of oocytes from a patient's ovaries following controlled ovarian hyperstimulation using an ultrasound-guided needle introduced transvaginally (Fig. 20.1), though rarely obesity or anatomic variants may require transabdominal aspiration. This is an ambulatory, low-risk procedure, and complications occur in less than 0.5 % of cases [12].

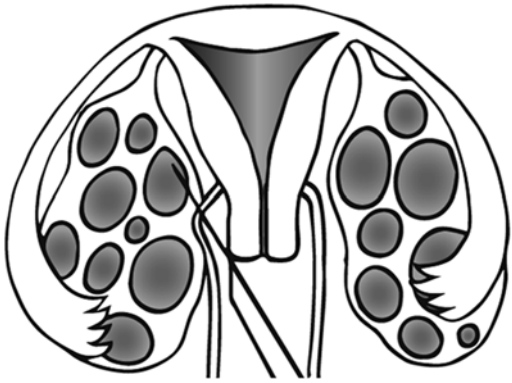

Fig. 20.1 Transvaginal oocyte retrieval following controlled ovarian hyperstimulation

Complications include (1) intra-abdominal bleeding usually ovarian in origin; (2) infection, including tubo-ovarian abscess, superinfected endometrioma, or other pelvic abscess; and (3) visceral injury.

Vaginal bleeding can occur but is usually identified and resolved with tamponade at the time of the retrieval. Intra-abdominally, some degree of bleeding after oocyte retrieval is to be expected. Studies have estimated the blood loss following an uncomplicated oocyte retrieval at 72–230 mL, with a mean hemoglobin decline of 1.6 g per dL (g/dL) [13, 14]. Even patients with stable post-procedural hemoglobin levels develop intraperitoneal free fluid on imaging [13].

Clinically significant intra-abdominal hemorrhage originates most commonly from the ovaries, though vascular injuries do rarely occur [12, 15]. Intra-abdominal hemorrhage is more likely in patients with bleeding disorders, including von Willebrand disease or coagulation factor deficiencies [12]. Most, though not all, patients with significant intra-abdominal hemorrhage following oocyte retrieval present within the first 24 h following the procedure [16]. Intraperitoneal hemorrhage is discussed in Diagnosis and Management.

Injury to intra-abdominal organs, usually the bowel, due to direct puncture with the oocyte retrieval needle, occurs rarely; injuries to the appendix, bladder, and ureter have also been detailed in case reports [17]. Intra-abdominal infections can also occur, including tubo-ovarian abscesses [18]. Infection of an endometrioma, likely due to bacteria introduced through a puncture, is less common but has been reported [19].

Finally, patients usually receive sedation for oocyte retrieval and are therefore subject to complications of anesthesia as well, including medication reactions and aspiration. Embryo transfers, conversely, do not generally require sedation and are performed with flexible catheters, with minimal risk of uterine perforation or other complications.

Ovarian Hyperstimulation Syndrome

An iatrogenic condition resulting from ovarian stimulation. It is usually a response to gonadotropin administration, though it can also occur after administration of clomiphene citrate [20]. Severe OHSS has been reported in 0.1–2 % of IVF cycles [21]. The clinical syndrome of OHSS results largely from capillary permeability, leading to ascites, electrolyte imbalances, and hemoconcentration. Elevated levels of vascular endothelial growth factor (VEGF), originating from ovarian follicles, are implicated in the pathophysiology of OHSS [22].

Symptoms of OHSS may begin as early as 48 h after administration of the hCG trigger injection and peak in 7–10 days [23]. Symptoms of OHSS are exacerbated and potentiated by pregnancy, likely due to rising hCG levels which increase VEGF levels [24]. Patients experience abdominal pain, nausea, and/or vomiting. Due to intravascular depletion, patients may develop hypotension, tachycardia, and oliguria. Patients with severe disease may develop ascites or pleural effusions and/or renal failure. All patients undergoing IVF are at increased risk of venous thromboembolism (VTE) due to elevated estradiol levels, with an incidence rate of 0.2 % or twice the rate of the normal population; in patients with

OHSS—due to elevated estradiol and hemoconcentration—the incidence is 1.7 % [25]. Patients are also at increased risk of ovarian torsion or rupture.

Risk factors for OHSS are shown in (Table 20.1) [26–29]. Patients with elevated antimüllerian hormone (AMH), which is a serum marker of ovarian reserve, may be at higher risk of OHSS as well; AMH levels greater than 3.3–3.75 nanograms (ng) per mL have been associated with an elevated OHSS risk [30, 31]. Serum estradiol (E2) during ovarian stimulation is also a predictor of OHSS; serum E2 greater than 5000–6000 picograms (pg) per mL is considered a risk factor, though even levels above 2500 pg/mL may carry some increased risk of OHSS [1, 26]. Rapidly rising estradiol (E2) levels, increasing by 50–75 % from the prior 1–2 days, are also considered a risk factor [26–29]. Risk of OHSS is also higher after triggering final oocyte maturation with hCG, whereas rates are much lower following triggering with a GnRH agonist [32].

Table 20.1 Risk factors for ovarian hyperstimulation syndrome

Risk factors	**Definition**
Age	Less than 33 years
Low body weight	
Polycystic ovarian syndrome	See Chap. 4 for diagnostic criteria of PCOS
High number of oocytes retrieved	Greater than 15 oocytes
Prior OHSS	
Elevated antimüllerian hormone (AMH)	Greater than 3.3–3.75 nanograms (ng) per mL
Elevated E2	Greater than 5000–6000 picograms (pg) per mL
Triggering with hCG	
Pregnancy	Results in "late OHSS," more likely to be severe

References are contained within the text

Pregnancy after IVF is a risk for "late" OHSS, which is more likely to be severe than "early" OHSS, occurring immediately after ovarian stimulation [33].

Differential Diagnosis

Patients may present in the emergent setting after fertility treatment with a variety of complaints, chief among these being abdominal pain and vaginal bleeding. Vaginal bleeding is usually light immediately following oocyte retrieval; heavier bleeding is likely to occur in patients who have become pregnant and are having a threatened or spontaneous abortion. Withdrawal bleeding (menses) may be heavier than usual in nonpregnant patients following a failed IVF cycle, usually occurring approximately 10–12 days after trigger. For more information on diagnosis and management of vaginal hemorrhage, please see Chap. 2. For assessment and management of spontaneous abortion, refer to Chap. 8. For a complete discussion of adnexal masses, refer to Chap. 4.

Vaginal Bleeding

- Post-oocyte retrieval bleeding from vaginal puncture
- Non-gravid vaginal bleeding (including withdrawal bleeding after failed IVF cycle)
- Threatened or spontaneous abortion
- Ectopic pregnancy

Abdominal Pain

- Ovarian torsion
- OHSS
- Post-oocyte retrieval: bleeding, visceral injury, pelvic infection/abscess
- Positive hCG: ectopic pregnancy, spontaneous abortion
- Ovarian enlargement due to stimulation

Adnexal Masses

- Tubo-ovarian abscess
- Endometrioma, rarely infected after oocyte retrieval
- Appendicitis or other gastrointestinal (GI)-related abscess
- Ectopic pregnancy
- Less acute issues: post-stimulation enlarged ovaries, ovarian cyst, hydrosalpinx

When You Get the Call Ask for a full set of vital signs, and request a pelvic ultrasound if one has not already been performed. In patients with pain, request that the patient not receive further pain medications prior to a physical examination by gynecology, if possible, to allow for an accurate assessment.

When You Arrive Review the patient's vital signs to assess for hypotension, tachycardia, or hypoxia. If possible, review the patient's records for details of the fertility treatments. If the patient underwent in vitro fertilization, review the patient's peak serum estradiol, number of oocytes retrieved and embryos transferred, in addition to the dates of retrieval or transfer. If the patient presents with pain or fever, review whether perioperative antibiotics were administered at her oocyte retrieval.

History

If not available through records, ask the patient for details of her infertility treatment, including dates of clomiphene administration or hCG or GnRH agonist trigger. If the patient underwent IVF, ask her for the peak serum estradiol level, number of eggs retrieved, and number of embryos transferred, as well as the dates of these procedures. If the patient is known to be pregnant following fertility treatment, calculate her gestational age, and review any available hCG values and obstetrical ultrasound.

Obtain a history regarding the onset of any abdominal pain, including whether the pain began acutely or gradually, and whether it followed any treatment steps (such as oocyte retrieval). Acute-onset pain may be more consistent with torsion or hemorrhage. Ask patients about nausea, vomiting, fevers, chest pain, dyspnea, calf pain, or vaginal bleeding.

Review the patient's past medical history, including a history of ectopic pregnancy, OHSS, bleeding disorders, or postoperative bleeding issues.

Of note, due to ovarian enlargement following ovarian hyperstimulation, and direct vaginal and ovarian punctures during oocyte retrieval, IVF patients commonly report abdominal or pelvic pain. Patients can be expected to have cervical motion tenderness after oocyte retrieval, due to peritoneal irritation caused by intra-abdominal blood. Differentiating expected pain from a true complication can be challenging.

Physical Exam

In patients with symptoms suggestive of OHSS, a lung exam should be performed to assess for pulmonary edema or pleural effusion. An abdominal exam should be performed to assess for pain, peritoneal signs, distention, or a fluid wave suggesting ascites. An examination of the extremities may reveal edema or evidence of a deep vein thrombosis. In general, a bimanual exam in a patient who has recently undergone IVF should be avoided, as the ovaries are enlarged and tender; significant complications, such as intra-abdominal bleeding or ovarian torsion, can be detected by peritoneal signs on the abdominal examination. A speculum exam can be performed in patients presenting with vaginal bleeding to quantify the amount of bleeding and to identify the source.

Diagnosis

In patients who are acutely unstable following fertility treatments (particularly more than 3 weeks after oocyte transfer), consider a urine hCG to triage for risk of ectopic pregnancy

and a focused assessment with sonography for trauma (FAST) scan—a bedside ultrasound assessing for free fluid in the perihepatic, perisplenic, and pelvic space—to assess for intra-abdominal free fluid [34]. Please refer to Chap. 3, Pregnancy of Unknown Location and Ectopic Pregnancy, for more information on the diagnosis of ruptured ectopic pregnancy.

In patients with either pain or bleeding, an hCG should be obtained—with the caveat that hCG may be detectable in the serum for up to 10 days after an hCG trigger injection. A complete blood count should also be obtained. In patients with pain and at risk of OHSS, additional laboratory tests should include electrolytes, creatinine, and liver function testing.

In patients with abdominal pain and who have received ovarian-stimulating medications, particularly gonadotropins, ultrasound should be obtained to assess for ovarian enlargement and ascites (Figs. 20.2 and 20.3). In patients who have undergone oocyte retrieval, a pelvic ultrasound may show adnexal masses, including multiple hemorrhagic follicles that were recently aspirated, ectopic pregnancy, endometrioma, or tubo-ovarian abscess, and may also reveal hemoperitoneum. Imaging may also be helpful in those with vaginal bleeding, to assess for intrauterine or ectopic pregnancies or other endometrial lesions such as polyps or fibroids.

Patients undergoing (or who recently underwent) controlled ovarian hyperstimulation commonly report dyspnea due to abdominal discomfort and distention; pleural effusions in patients with OHSS can be seen by ultrasound. Pulmonary embolism—and workup with a chest CT—should be considered in patients with respiratory symptoms, particularly those with hypoxia and without pleural effusion to explain their symptoms [23]. For diagnosis and management of pulmonary embolism, see Chap. 16, Complications of Minimally Invasive Gynecologic Surgery.

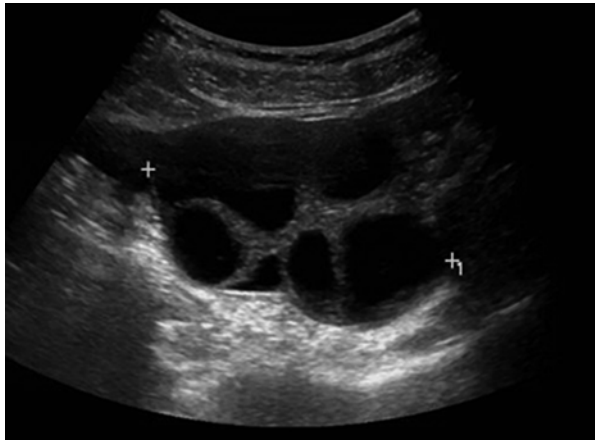

FIG. 20.2 Hyperstimulated ovaries. Transvaginal ultrasound reveals bilaterally enlarged multicystic ovaries (8 cm) in a patient undergoing controlled ovarian hyperstimulation

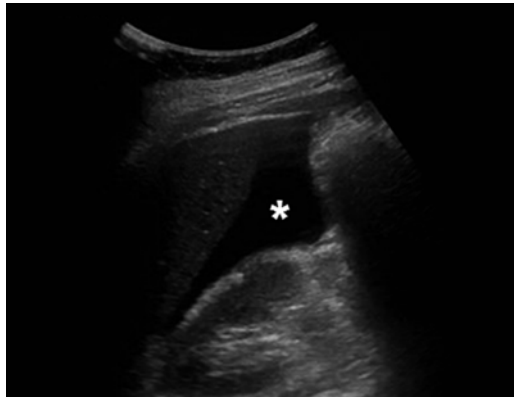

FIG. 20.3 Ascites from ovarian hyperstimulation syndrome. Transabdominal ultrasound reveals perihepatic free fluid following recent oocyte retrieval, indicated with an *asterisk* (*)

Intraperitoneal Bleeding

A patient with significant intraperitoneal hemorrhage may show signs of hemorrhagic shock, the first sign of which is tachycardia; hypotension may only occur after 30–40 % of a patient's blood volume is lost, particularly in young, healthy women. Please refer to Chap. 1, Acute Pelvic Pain, for the diagnosis of intra-abdominal hemorrhage and hemorrhagic shock. The patient may also show signs of peritonitis, including a rigid, exquisitely tender abdomen. A pelvic ultrasound may show free fluid, particularly echogenic, complex, free fluid concerning for hemoperitoneum (Fig. 20.4). Obtain repeat hemoglobin levels in 2–4 h in patients with suspected intra-abdominal bleeding; patients with ongoing bleeding will have progressively declining hemoglobin. In patients who are clinically worsening, or with declining hemoglobin, obtain coagulation studies to assess for underlying bleeding disorders or evolving coagulopathy, while beginning aggressive intravascular

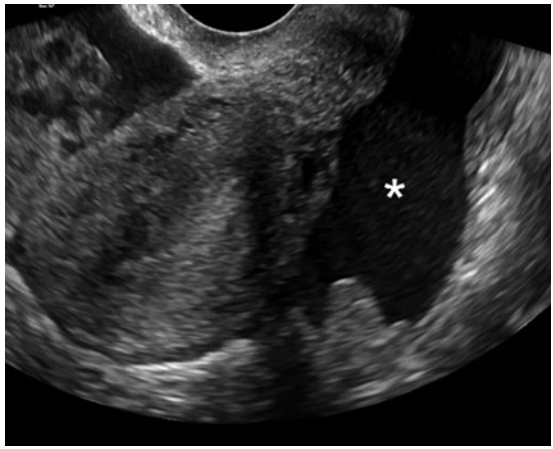

Fig. 20.4 Hemoperitoneum. Transvaginal ultrasound showing complex free fluid in the posterior cul-de-sac, indicated with an *asterisk* (*)

resuscitation with fluids and blood products as needed. For more information on intravascular resuscitation and transfusion, please see Chap. 13, Preparing for Urgent and Emergent Surgery.

OHSS

OHSS ranges from mild to critical in its clinical manifestations, and several classification methods have been proposed, summarized in Table 20.2. In general, laboratory parameters remain normal in mild and moderate OHSS, while severe and critical OHSS are accompanied by significant derangements

Table 20.2 Classification of OHSS

Severity	Clinical findings	Laboratory and Imaging
Mild	Mild abdominal pain Mild abdominal distention	Ovaries usually <8 cm in diameter No other laboratory abnormalities
Moderate	Nausea/vomiting or diarrhea Abdominal distention Ascites	Ovaries 8–12 cm in diameter No other laboratory abnormalities
Severe	Large ascites Pleural effusion Respiratory distress	Ovaries > 12 cm in diameter Hematocrit > 45% WBC > 15,000/uL Creatinine 1.0–1.5 mg/mL Elevated liver enzymes
Critical	Tense ascites Large pleural effusion Thromboembolism Oliguria Acute respiratory distress syndrome (ARDS)	Hematocrit > 55% WBC > 25,000/uL Creatinine > 1.6 mg/mL

From Navot et al. [35], Golan et al. [36], Mathur et al. [37]

in multiple organ systems, evidenced by laboratory results and physical examination [35–37]. In addition to findings noted in Table 20.2, severe disease may be accompanied by hyponatremia or hyperkalemia, and the risk of thromboembolism increases with worsening hemoconcentration. In patients who require paracentesis or thoracentesis, the fluid is exudative, with high protein (4.8 g/10 mL), many red blood cells, and few leukocytes [23].

Pelvic Infections

Following oocyte retrieval, patients with fever, abdominal pain, nausea, and leukocytosis may have a pelvic infection. Patients with pelvic infections may have peritoneal signs on abdominal exam, mucopurulent cervicitis on speculum exam (if performed), and leukocytes may be noted on a wet mount [38]. In patients also found to have complex adnexal masses on imaging, the most common etiologies are tubo-ovarian abscesses or, less commonly, infected endometriomas. Clinicians should also consider the possibility of appendicitis or other non-adnexal abscesses, potentially—though not necessarily—related to oocyte retrieval. For more information on other adnexal masses, please refer to Chap. 4, Adnexal Masses and Ovarian Cyst Rupture. In patients with signs of pelvic infection after oocyte retrieval and/or embryo transfer in the absence of an adnexal mass or other identifiable source, consider upper genital tract infection, treated with regimens for pelvic inflammatory disease or endometritis. For more information, please refer to Chaps. 6 and 16, respectively. Avoid teratogenic medications in patients who have undergone embryo transfer.

In general, for infectious adnexal masses, a CT scan may reveal surrounding inflammatory changes, including stranding or free fluid [38]. A CT scan may also help clarify any gastrointestinal involvement, including appendicitis or diverticulitis, which can lead to inflammation in the region of an

adnexa. By MRI, internal gas bubbles are highly specific for abscess [39].

Ultrasound sensitivity and specificity for tubo-ovarian abscesses are greater than 90 %; by ultrasound, TOAs may appear as a complex, septated cystic adnexal structure with irregular, thick walls, and sometimes with internal debris (Fig. 20.5) [38]. By CT scan, TOAs also appear as complex, thick-walled, septated masses (Fig. 20.6).

Conversely, by ultrasound, endometriomas appear as homogenous masses with low-level interval echogenicity and smooth, thick walls (Fig. 20.7) [40, 41]. By CT, endometriomas are nonenhancing (Fig. 20.8). By MRI, endometriomas demonstrate high signal intensity (brightness) on T1-weighted images (Fig. 20.9a), while on T2-weighted images, endometriomas have less intense signal intensity than simple cysts and may demonstrate fluid-fluid levels (Fig. 20.9b) [42].

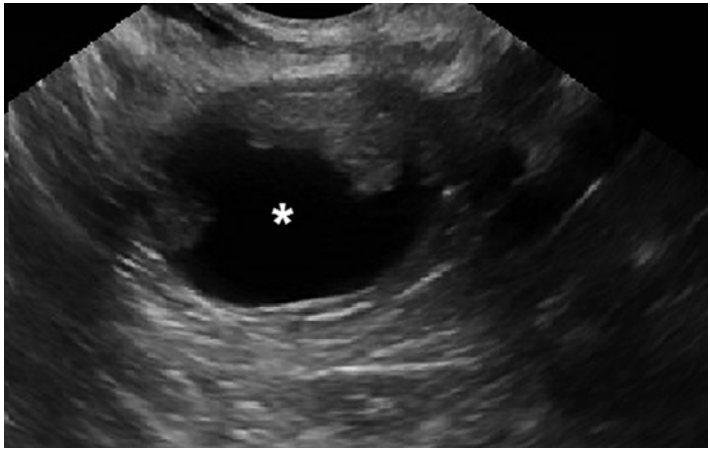

FIG. 20.5 Tubo-ovarian abscess by ultrasound. Transvaginal ultrasound showing an enlarged fallopian tube with debris, indicated with an *asterisk* (*)

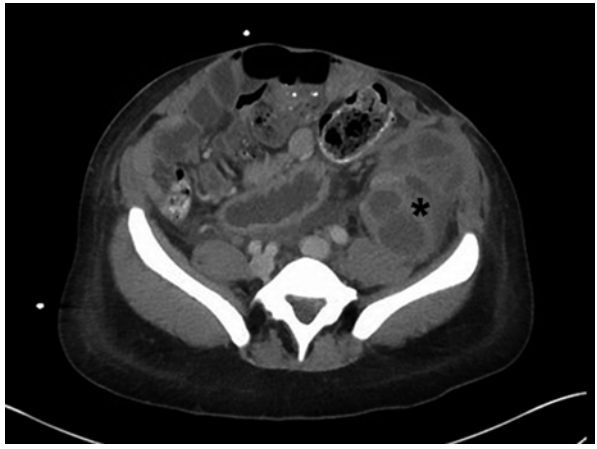

FIG. 20.6 Tubo-ovarian abscess by CT scan. Left-sided tubo-ovarian abscess is indicated with an *asterisk* (*)

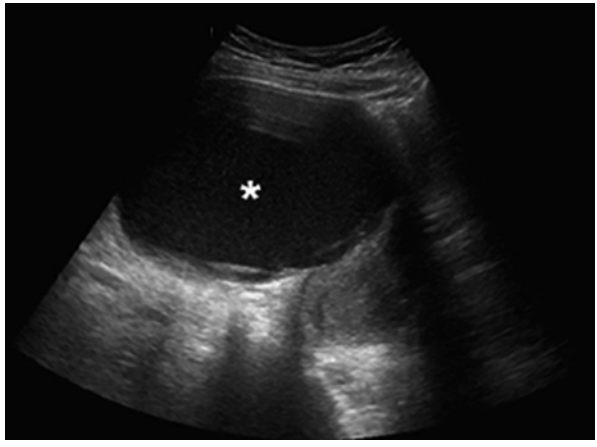

FIG. 20.7 Endometrioma by ultrasound. Transvaginal ultrasound showing an ovarian endometrioma, indicated with an *asterisk* (*)

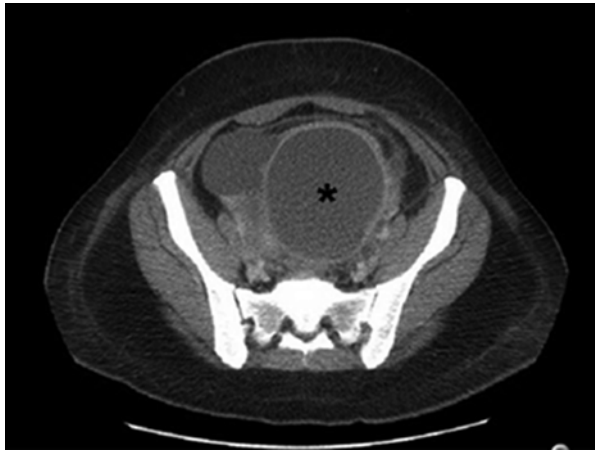

FIG. 20.8 Endometrioma by CT scan. Pelvic CT scan showing a large left adnexal endometrioma, indicated with an *asterisk* (*)

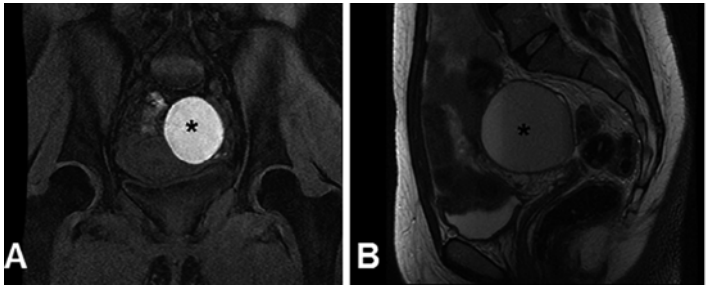

FIG. 20.9 Endometrioma by MRI. (**a**) Left adnexal endometrioma, indicated with an *asterisk* (*), by T1-weighted fat-suppressed MRI image. (**b**) Left adnexal endometrioma, indicated with an *asterisk* (*), by T2-weighted MRI image

Other Acute Diagnoses

Ovarian torsion should be part of the differential diagnosis for any patient with an enlarged ovary—simply from hyperstimulation or associated with a mass—and abdominal pain.

The rate of torsion following IVF is approximately 1 in 1000 women, though up to one-third of these have concomitant OHSS [43]. Please see Chap. 5 for the diagnosis and management of adnexal torsion.

Ectopic pregnancy should always be considered in a patient with abdominal pain and a positive serum or urine hCG. Please see Chap. 3, Pregnancy of Unknown Location and Ectopic Pregnancy, for more information on ectopic pregnancy.

Management

Intraperitoneal Bleeding

In patients with hemoperitoneum following oocyte retrieval, particularly those presenting within a few days following the procedure, bleeding most commonly originates from ovarian puncture sites [18]. In hemodynamically stable patients, first-line management of suspected intra-abdominal bleeding after oocyte retrieval is close observation and supportive care. Hemoglobin measurements should be obtained every 4 h until stable values are confirmed; if the hemoglobin continues to decline, provide transfusions as needed. Patients requiring transfusion should be admitted for close monitoring. Please see Chap. 1, Acute Pelvic Pain, for the management of intra-abdominal hemorrhage.

Patients who are hemodynamically unstable or have persistently declining hemoglobin—refractory to aggressive management with blood products—may require surgical management, either by interventional radiology or by laparoscopy or laparotomy, as determined by resource availability and the patient's clinical stability [16, 44]. Interventional radiology offers the advantage of identifying and embolizing vascular injuries using angiography. If a patient is taken to the operating room, suturing and electrocauterization of bleeding ovarian puncture sites have been described, in addition to application of hemostatic agents [16]. For persistent or

uncontrollable bleeding, patients may require oophorectomy. A full survey of the abdominal and pelvic organs should be performed at the time of surgery to assess for injuries to other pelvic organs or vessels.

OHSS

Mild OHSS in the properly counseled patient can be managed in the outpatient setting with hydration, pain medications, and antiemetics [1]. Patients should drink at least a liter of electrolyte-rich fluid per day and can be asked to keep a log of intake and outputs. Patients are at risk of ovarian torsion or rupture and should avoid intercourse or strenuous activity. Patients should be counseled to weigh themselves daily, and a weight gain of 2 lb or more per day is an indication for repeat laboratory assessment and discussion of symptoms. Patients should be followed with frequent office visits, to assess for worsening ascites or laboratory abnormalities. Patients who then become pregnant are at risk of "late" OHSS and should be followed particularly closely [33].

In both the inpatient and outpatient settings, patients with large ascites and significant discomfort may require paracentesis—transvaginally or transabdominally—under ultrasound guidance [23]. Large pleural effusions, particularly those resulting in respiratory compromise, may require thoracentesis.

Patients with severe OHSS require hospitalization. Findings that may prompt admission include intractable abdominal pain or vomiting, tachypnea, tachycardia, hypotension, syncope, significant hyponatremia, hyperkalemia, hemoconcentration (>45 %), or elevations in creatinine or liver function tests [1]. Patients who are admitted should have regular vital signs recorded, daily weights, physical examination (assessing for new or worsening pleural effusion or ascites), and laboratory testing (CBC, electrolytes, and creatinine). Electrolyte abnormalities should be addressed. Strict inputs and outputs should be recorded. Due to risk of thromboembolism, patients should receive subcutaneous heparin (5000 units every 12 h) [1].

Intravenous hydration, preferably with an isotonic fluid such as normal saline, should be administered to maintain a urine output of at least 20–30 mL/h [1]. Excessive hydration will only lead to more extravasation due to vascular permeability. Diuretics are not appropriate therapy, as patients with OHSS are already hemoconcentrated and intravascularly depleted.

TOA

Please see Chap. 6, Pelvic Inflammatory Disease and Tubo-Ovarian Abscess, for management for TOA.

Infected Endometrioma

Endometriomas may be difficult to penetrate with intravenous antibiotics, due to sparse blood flow and the presence of fibrosis [19]. Regardless, antibiotics should be started; options include regimens usually used for TOAs: (1) doxycycline (100 mg PO or IV every 12 h) for 14 days plus *either* (1) cefoxitin (2 g IV every 6 h) or (2) cefotetan (2 g IV every 12 h). An alternative regimen is clindamycin (900 mg IV every 8 h) plus gentamicin (2 mg/kg load, followed by 1.5 mg/kg every 8 h) or (3) ampicillin-sulbactam (3 g IV every 6 h) plus doxycycline (100 mg PO or IV every 12 h). Once a patient has been afebrile for at least 24 h, she can be transitioned to oral antibiotics; the CDC recommends doxycycline (100 mg PO every 12 h) plus *either* clindamycin (450 mg PO every 6 h) or metronidazole (500 mg PO every 12 h). Doxycycline should not be continued alone. Twenty-four hours of inpatient observation of the patient's clinical status following transition to oral antibiotics is recommended.

Ideally, teratogenic medications should be avoided in patients who have already undergone embryo transfer. All of the above regimens include a pregnancy class D medication (meaning fetal risk has been demonstrated); consider infectious disease consultation for further guidance. These medications

may ultimately be required in acutely ill patients with TOA or infected endometrioma.

In patients initially treated with intravenous antibiotics alone, persistent pain, fever, or leukocytosis indicates need for further intervention; in the past, intervention has usually been surgical. Patients with endometriomas are likely to have adhesive disease, and due to the inflammation caused by an acute infection, these cases are highly challenging and may result in oophorectomy.

As an alternative to surgical intervention, percutaneous or transvaginal drainage with ultrasound guidance has been described for the management of endometriomas, though the recurrence rate is high (at least two-thirds or more in studies) [45–47]. While endometriomas are likely to recur after drainage, decompression of the infection may have utility in the acute setting. Of note, malignant transformation of endometriosis occurs in less than 1 % of cases, and aspiration may theoretically lead to peritoneal spread [48].

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Chapter 21
Patient Communications

Paula C. Brady and Michelle R. Davis

Patient calls to a gynecologist—including subspecialists in minimally invasive surgery, gynecologic oncology, urogynecology, family planning, and reproductive endocrinology—include but are not limited to the following issues. Whenever a patient's complaints are difficult to parse over the phone but are concerning for any reason, urgent assessment is recommended in the emergency department, urgent care clinic, or outpatient setting as available and appropriate.

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When to Ask the Patient to Call an Ambulance

1. **Vaginal hemorrhage**. A report of completely soaking two pads or more per hour for 2 h is a rough estimate of excessive bleeding. Excessive bleeding resulting in symptoms of anemia, including palpitations, pre-syncope or syncope, or bleeding through a patient's pad or tampon and clothes—particularly in the setting of pregnancy or known bleeding diathesis—require emergent assessment, and may warrant activation of emergency medical services. Please see Chap. 2, Vaginal Hemorrhage, for more information.
2. **Chest pain**. Reported symptoms most suggestive of an acute coronary syndrome are exertional chest pain with radiation to one or both arms [1]. Chest pressure, nausea, and diaphoresis are moderately predictive, while pleuritic, positional, sharp, and reproducible pain is least consistent with an acute coronary syndrome. Risk factors include age greater than 65 years in women, prior coronary artery disease, current smoking, diabetes, hypertension, hyperlipidemia, obesity, and family history of coronary artery disease [2]. Please see Chap. 15, High Acuity Postoperative and Inpatient Issues, for more information on the diagnosis and management of acute chest pain.
3. **Altered mental status or somnolence**. Patients' family members or caregivers may call reporting these symptoms; acute changes to mental status require emergent assessment. Please see Chap. 15, High Acuity Postoperative and Inpatient Issues, for more information regarding the diagnosis and management of altered mental status.

When to Ask the Patient to Present to the Emergency Room the Same Night for Assessment

1. **Fever greater than 100.4 °F**. Fevers require urgent assessment, particularly in postoperative, pregnant, and neutropenic patients. More information on these subjects can be

found in Chap. 16, Complications of Minimally Invasive Gynecologic Surgery; Chap. 17, Induced Abortion; and Chap. 18, Gynecologic Oncology.

2. **Intractable nausea and vomiting**. Patients with severe nausea and vomiting, associated with inability to tolerate any oral intake and/or the absence of stools and flatus, are suggestive of a bowel obstruction or other complications requiring assessment, particularly in a postoperative or gynecologic oncology patient. Please see Chap. 16, Complications of Minimally Invasive Gynecologic Surgery, for more information.
3. **Dyspnea and/or pleuritic chest pain**. Patients calling to report these symptoms—particularly patients who are postoperative, pregnant (or recently pregnant), or being treated for gynecologic malignancy—should be assessed urgently for possible pulmonary embolism. Postoperative, pregnant, or oncology patients calling with unilateral, painful lower extremity edema should also be assessed urgently, given their increased risk for deep vein thrombosis; consider the patient's symptoms and risk factors for thromboembolism when determining the appropriate timeframe for evaluation, either overnight or the following day. Please refer to Chap. 15, High Acuity Postoperative and Inpatient Issues, and Chap. 16, Complications of Minimally Invasive Gynecologic Surgery, for more information on the diagnosis and management of pulmonary embolism.

   Patients undergoing in vitro fertilization (IVF), particularly after oocyte retrieval or in very early pregnancy, may also call with dyspnea potentially attributable to ovarian hyperstimulation syndrome (OHSS). Attempt to clarify the severity of the patient's symptoms over the phone and consider her risk factors for OHSS to determine whether the patient must be seen immediately. Please see Chap. 20, Reproductive Endocrinology and Infertility, for more information regarding the diagnosis and management of OHSS.

4. **Worsening pain after surgery**: Patients reporting significant pain not improved with pain medication as prescribed, including narcotic pain medications, acetaminophen, and ibuprofen—particularly when associated with fever, nausea and vomiting, or other concerning symptoms—require urgent assessment. Patients undergoing laparoscopic surgery should have continual improvement in pain post-operatively, and any patient with increased pain after laparoscopy while taking adequate pain medication should be evaluated urgently to rule out a serious post-operative complication such as port-site herniation or an occult bowel injury. Please see Chap. 16, Complications of Minimally Invasive Gynecologic Surgery, for more information.
5. **New or worsening abdominal or pelvic pain**. Patients reporting severe pain that does not improve with acetaminophen and ibuprofen or the patients' standard pain medications (such as narcotics in patients with chronic pain syndromes) require urgent assessment, particularly when associated with emesis or fever. A patient with a known or suspected ectopic pregnancy requires immediate assessment; please refer to Chap. 3, Pregnancy of Unknown Location and Ectopic Pregnancy, for more information.

   Patients undergoing IVF frequently develop abdominal discomfort due to ovarian enlargement; these patients are also, however, at risk for ovarian torsion and OHSS. Assessment of the severity of a patient's pain over the phone can be helpful in determining whether she needs to be seen immediately or within 24 h. Of note, ibuprofen and heating pads on the abdomen should be avoided in pregnancy (including after an embryo transfer). More information on ovarian torsion and OHSS can be found in Chap. 5, Adnexal Torsion, and Chap. 20, Reproductive Endocrinology and Infertility, respectively.

   Finally, patients with endometriosis or chronic pain managed with hormonal medications may have pain in

the setting of recently missing doses of their medications; most often, resumption of these medications and reassurance is sufficient. Assessment of patients with chronic pain by phone can be challenging; however, any new or different symptoms, particularly emesis or fever, warrant evaluation.

When to Refer Patients to the Outpatient Setting the Next Day

1. **Spotting and/or mild cramping in early pregnancy**. Patients can be given the reassurance that spotting in early pregnancy occurs in 27 % percent of first trimester pregnancies; spotting may not increase the risk of miscarriage, though heavy vaginal bleeding (like a menstrual period), which is less common, increases the risk of miscarriage [3]. Administration of anti-D immune globulin before 12 weeks of gestation age is debated, as alloimmunization at this gestational age is very rare, though most providers do provide this prophylaxis regardless of gestational age [4, 5]. In general, patients who are rhesus-D antigen (Rh) negative should be seen within 72 h for the administration of Rho(D) immune globulin after reporting any vaginal bleeding in early pregnancy.
2. **Incisional erythema**. Patients calling to report incisional erythema, particularly in the first 2 days after surgery, may be mistaking ecchymosis for infection. Patients reporting fever or associated symptoms—including copious and/or purulent wound drainage, acutely worsened abdominal pain, nausea, or vomiting—should be seen urgently to rule out wound complications. In the absence of these symptoms, patients can be assessed in the outpatient setting. To avoid antibiotic resistance, any wound should be evaluated prior to prescribing antibiotics; thus, referral to the outpatient clinic for evaluation within 48 h is the preferred man-

agement. Please see Chap. 16, Complications of Minimally Invasive Gynecology, for more information on the diagnosis and management of wound complications.

3. **Bloating and abdominal discomfort**. Patients undergoing IVF often develop these symptoms, but those who are tolerating oral intake, voiding, without shortness of breath or acutely worsened abdominal distention, and with pain adequately controlled can be followed closely as outpatients [6]. Postoperative patients who call with these symptoms should be assessed for return of bowel function and constipation. Patients who are able to tolerate oral intake and are passing flatus may be monitored as outpatients, and adherence to a bowel regimen (including stool softeners such as docusate and laxatives as needed) should be encouraged [7]. Patients receiving chemotherapy may experience nausea, vomiting, constipation, or diarrhea as a result of their chemotherapy. Patients who are passing flatus and able to hydrate with liquids may be managed with antiemetics and seen as outpatients within 48 h for evaluation of chemotherapy toxicity and hydration as needed. Please refer to Chap. 16, Complications of Minimally Invasive Gynecologic Surgery, for more information on postoperative bowel complications, Chap. 18, Gynecologic Oncology, for a discussion of chemotherapy and nausea, and Chap. 20, Reproductive Endocrinology and Infertility, for more information on the diagnosis and management of OHSS.
4. **Dysuria or suprapubic pain**. In the absence of fever or pregnancy, patients without a history of frequent urinary tract infections or those who are recently postoperative should be seen in the office for a urine dipstick for confirmation of infection [8]. Those with frequent urinary tract infections who are aware of their urinary tract infection symptoms can be offered presumptive treatment with antibiotics. Those who are pregnant and/or febrile should be seen urgently for assessment of pyelo-

nephritis. Please see Chap. 16, Complications of Minimally Invasive Gynecology, for more information on urinary tract infections.

Issues Managed Over the Phone

1. **Vaginitis**: Patients calling with symptoms of vaginal discharge or irritation can be seen in the outpatient setting, as these issues are generally nonurgent. Patients may call requesting treatment for vaginal candidiasis, with symptoms that can include itching, burning, dysuria, and thick white vaginal discharge. Studies have shown that patients' ability to self-diagnose yeast infections is poor [9]. However, patients can be offered a short course of presumptive treatment, with counseling to follow up as outpatients if their symptoms do not improve [10]. Please refer to Chap. 7, Vulvovaginal Dermatoses, Lesions, and Masses, for more information on the diagnosis and treatment of vulvovaginal candidiasis.
2. **Risk of pregnancy**: Patients may call following unprotected intercourse or contraceptive failure. Review whether the sexual encounter was consensual; if it was not, the patient can present to the emergency room for full assessment. Please see Chap. 9, Sexual Assault, for more information. Patients should be counseled regarding their options, which are listed in Table 21.1. Patients do not require physical examination or laboratory assessment before receiving emergency contraception, unless preexisting pregnancy is suspected by the patient's history or missed menses. Patients should be counseled regarding risk of sexually transmitted infection and can be seen in the outpatient setting for testing for these as needed.

Table 21.1 Summary of options for emergency contraception (EC) in the United States

Method	Mechanism of action	Considerations	Dose	Efficacy	Contraindications
Ulipristal acetate	Delays or prevents ovulation		30 mg PO once, within 120 h of exposure	Failure rate <2 %	Confirmed pregnancy
Levonorgestrel (progesterone-only pill)	Delays or prevents ovulation	Provide antiemetics for side effects of nausea and vomiting Retake dose if vomiting within 2–3 h of administration	1.5 mg PO once, within 120 h of exposure Alternatively, 0.75 mg PO every 12 h for 2 doses, associated with more nausea	Failure rate <2.5 %	Confirmed pregnancy Contraindications to progesterone contraception likely do not apply given short treatment duration. See CDC Medical Eligibility Criteria for Contraceptive Use, Appendix D

Combined estrogen–progesterone	Delays or prevents ovulation	Provide antiemetics for side effects of nausea and vomiting Retake dose if vomiting within 2–3 h of administration	Each dose should contain 100 micrograms of ethinyl estradiol and 0.5 mg levonorgestrel, given 12 h apart for 2 doses. The first dose is given within 72 h of exposure	Failure rate of 3.2 % Less effective than levonorgestrel and should be considered only if other options are unavailable	Confirmed pregnancy Contraindications to estrogen-containing contraception likely do not apply given short treatment duration. See CDC Medical Eligibility Criteria for Contraceptive Use, Appendix D

(continued)

Table 21.1 (continued)

Method	Mechanism of action	Considerations	Dose	Efficacy	Contraindications
Copper intrauterine device (IUD)	Oocyte toxicity, inhibition of sperm function, endometrial inflammation	Ideal for women also seeking long-term contraception Recommend testing for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* at time of insertion Significantly higher cost compared to other forms of EC	Intrauterine device, within 120 h of exposure Effective for up to 10 years	Most effective form of emergency contraception, with failure rate of 0.09 %	Confirmed pregnancy Cancer of genital tract Uterine malformation Copper allergy Mucopurulent cervicitis

From Li et al. [11], Glasier et al. [12], Centers for Disease Control and Prevention (CDC) [13]

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