CASE 1

A 45-Year-Old Woman Undergoing Hysterectomy Requests Oophorectomy

Sarah Alhaddad Tout

History of Present Illness

A multiparous, 45-year-old woman presents for preoperative evaluation. She has a long history of abnormal uterine bleeding that has been inadequately managed with her current levonorgestrel intrauterine device. She now desires definitive surgical management by hysterectomy. During her visit today, she requests that her ovaries be removed during the surgery. She shares that a good friend recently passed away after a long battle with ovarian cancer and she wants to lower her own risk of ovarian cancer as much as possible. Her past medical history includes depression managed on escitalopram 20 mg daily, and borderline hypertension currently managed with lifestyle modification. She has had no prior surgery.

Her gynecologic history is otherwise unremarkable. Her social history is remarkable for moderate alcohol use. There is no family history of ovarian cancer or premature atherosclerotic disease. She has a paternal aunt with postmenopausal breast cancer and her mother developed dementia at age 77.

Physical Examination

General appearance: 45-year-old adult, well-developed and well-nourished, in no apparent distress

Vital signs:

Temperature: 37.1°C

Pulse: 78 beats/min

Blood pressure: 138/89 mmHg

Respiratory rate: 16 breaths/min

Height: 65 inches

Weight: 172 lb

BMI: 28.6 kg/m^2

Cardiopulmonary: Unremarkable

Abdomen: Soft, non-tender, non-distended, normal active bowel sounds, no rebound or guarding, no masses or hernias, no hepatosplenomegaly

Pelvic: Normal external genitalia, vaginal and cervical mucosa normal, cul-de-sacs unobstructed, uterus slightly enlarged with several small fibroids palpable, mobile with grade 1 prolapse and good descensus, normal adnexa with no masses or tenderness appreciated

Neuro/psych: Alert, affect and mood appropriate to situation, good insight and judgment

Laboratory studies:

Hb: 11.4 g/dL (normal 12.1–14.4 g/dL)

Pathology: Endometrial biopsy demonstrates disordered proliferative endometrium with glandular and stromal breakdown

Imaging: Pelvic ultrasound demonstrates an anteverted, anteflexed uterus measuring 11.4 × 6.3 × 6.1 cm, endometrial thickness 8 mm with endometrial stripe slightly distorted by intramural and submucosal fibroids, the largest measuring 4.5 × 4.1 × 3.8 cm, and unremarkable adnexa

How Would You Manage This Patient?

This patient presents requesting oophorectomy at the time of hysterectomy. A careful review of her own medical and family histories is not suggestive of endometriosis, an inherited cancer syndrome, or otherwise increased risk of malignancy. Conversely, her personal and family history raises concern for the risk of several conditions that might be worsened by the loss of endogenous estrogen production. This premenopausal patient was counseled that, weighing the risks and benefits of the procedure, elective oophorectomy is not recommended. Specifically, she was informed of the potential risks of surgical menopause including effects on cardiovascular, neurologic, bone, and psychological/emotional health. She was also advised of option of salpingectomy at the time of hysterectomy as a risk-reducing strategy. The patient underwent total vaginal hysterectomy with bilateral salpingectomy. Intraoperative inspection of the ovaries was normal. She was discharged to home on the same day and was doing well at her visit six weeks postoperatively. Physical examination demonstrated a well-healed vaginal cuff. She was advised that, given her lack of any history of cervical dysplasia, she would no longer require routine screening for cervical cancer.

Elective Oophorectomy

This patient presents requesting additional surgical intervention, oophorectomy, which, on the surface, is not pertinent to her presenting complaint of abnormal uterine bleeding. As in all cases, however, in addition to providing the patient with evidence-based counseling and recommendations, careful attention must be paid to the patient's own history, as well as her background knowledge and values, which are driving her request. In this case, the patient has shared fears about ovarian cancer, a relatively rare condition, based on the experiences of a close friend, but non-relative. Historically, routine oophorectomy at the time of hysterectomy for benign indications was accepted practice to reduce ovarian cancer-related mortality. More recently, however, this practice has come to be generally discouraged, due to low rates of ovarian cancer, and findings from several large studies regarding potential long-term health impacts of oophorectomy. The lifetime risk of ovarian cancer in the general population is at 1.3%. The majority of ovarian cancers are diagnosed at a late stage, and, to date, no screening program has demonstrated effectiveness in decreasing mortality rates from this disease [1]. With no effective screening program available, primary prevention against ovarian malignancy, via

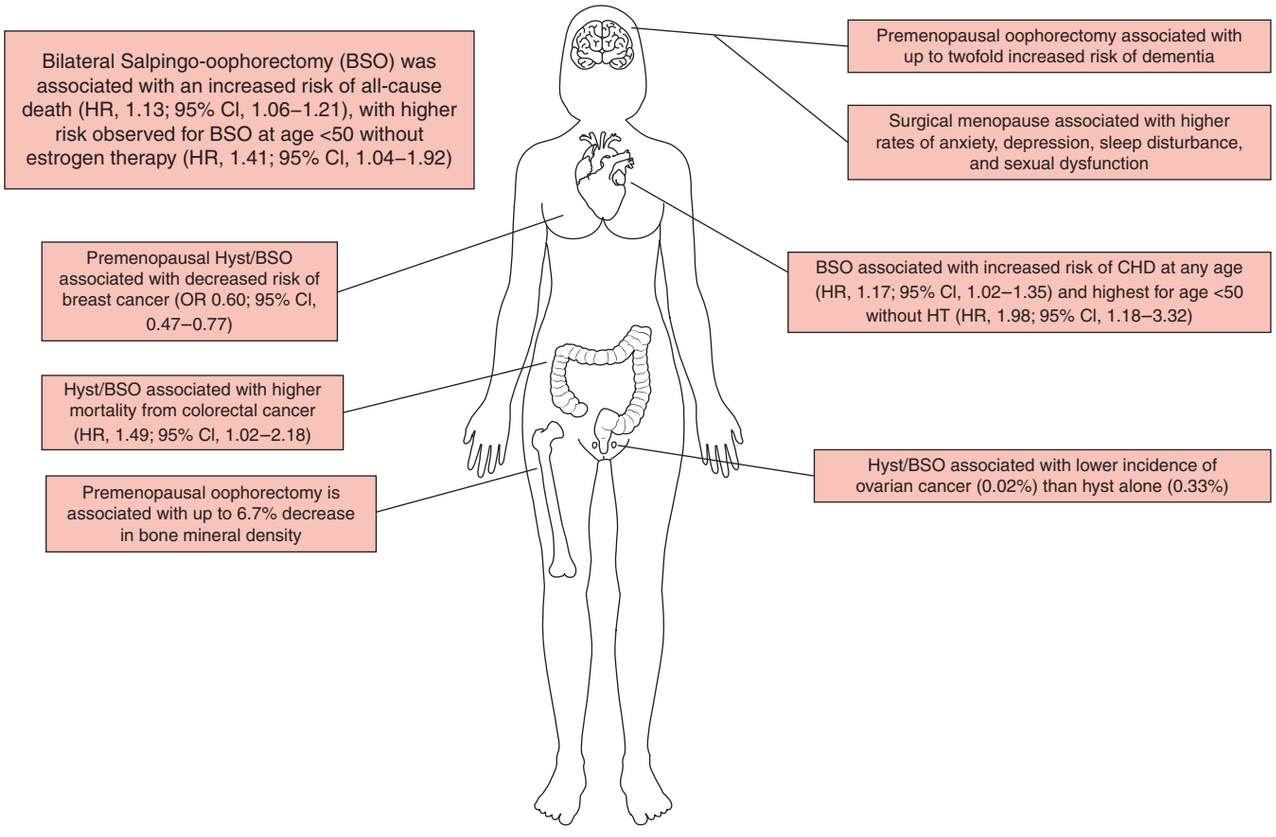

Figure 1.1 Effects of bilateral salpingo-oophorectomy.

oophorectomy, for those women approaching the age of menopause therefore once seemed a reasonable strategy. Additionally, ovarian retention was thought, potentially, to expose the patient to the risk of additional surgery for subsequent benign ovarian pathology. Ovarian retention was also posited to leave the patient at increased risk of breast cancer due to ongoing estrogen exposure. The sequelae from loss of endogenous estrogen production for those women, who underwent oophorectomy, it was reasoned, could be avoided via exogenous replacement. Unfortunately, more recent research has demonstrated that hormone therapy is not a viable strategy for the primary prevention of serious and potentially fatal conditions such as coronary heart disease (CHD), breast cancer, dementia, or osteoporosis, and increases the risk of stroke and thromboembolic disease [2, 3]. Data now show that, while those with elective oophorectomy at the time of hysterectomy were at lower risk of death from ovarian cancer, rates of all-cause mortality were higher after elective oophorectomy than with ovarian preservation [4, 5]. Additional concerns related to the early loss of endogenous estrogen production include elevated rates of cognitive decline, depression, anxiety, sexual dysfunction, and osteoporosis (Figure 1.1) [5, 6].

The routine practice of oophorectomy at the time of hysterectomy also confers additional surgical risk beyond that of the hysterectomy itself. For instance, that ligation of the infundibulopelvic ligament is a common point of ureteral injury during gynecologic surgery. Thus, oopherectomy for this patient would increase surgical risk without added benefit in the treatment of her presenting complaint. Evidence against the practice of elective oophorectomy has become so abundant that the majority of societies related to the field of obstetrics and gynecology recommend against it. The preponderance of evidence led the American Association of Gynecologic Laparoscopists to recommend, as the second item in its top-five list of practices to be avoided, "Do not perform routine oophorectomy in premenopausal women undergoing hysterectomy for non-malignant indications who are at low risk for ovarian cancer." [7]

However, while oophorectomy in premenopausal women should not be done routinely, there are, of course, situations in which oophorectomy should be considered, or even recommended, for women prior to the age of menopause. The performance of risk-reducing salpingo-oophorectomy (RRSO) in premenopausal women with hereditary breast and ovarian cancer syndrome is accepted practice [8]. In women for whom the risk of ovarian cancer is high, RRSO is preferred and hormone therapy is considered safe and effective for the treatment or prevention of a multitude of sequelae from the loss of endogenous estrogen production [6].

Finally, for low-risk patients, such as the one in this case, the discussion of whether to perform any therapy should include, in addition to risks and benefits, a review of the alternatives to that

therapy. In this case, the patient was offered salpingectomy, sometimes known as "opportunistic salpingectomy," in order to reduce her already low risk of ovarian cancer. This recommendation is based on a growing body of evidence that the precursor lesions to the majority of ovarian malignancies arise in the fimbriae of the fallopian tube [9]. Such lesions were originally identified in RRSO specimens from women with *BRCA1/2* mutations and have subsequently been identified in women who were negative for any known deleterious mutations. Long-term data regarding the safety and efficacy of this practice are not yet available. However, short-term outcome and cost-effectiveness data suggest that, for women already undergoing other pelvic surgery such as hysterectomy or sterilization, there may be benefit from the performance of bilateral salpingectomy as a primary preventive strategy for ovarian cancer.

Key Teaching Points

- In premenopausal women at low risk of ovarian cancer, the practice of elective oophorectomy should be avoided
- Counseling regarding prophylactic oophorectomy at the time of hysterectomy for benign disease should be patient-centered
- All-cause mortality is increased in elective oophorectomy
- Opportunistic salpingectomy may be an effective strategy to decrease ovarian cancer risk in low-risk women

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CASE 2

A 40-Year-Old G0 Developmentally Delayed Woman Requires Hysterectomy

Amy Boone

History of Present Illness

A 40-year-old nulligravid woman with developmental disabilities presents to the office with her mother. She is being followed for a long-standing history of heavy menstrual bleeding and pelvic pain. She had previously been treated with depot medroxyprogesterone acetate but had persistent light bleeding that presented hygiene issues. Her past medical history is significant for hypertension and constipation. She has never had abdominal or pelvic surgery. She has never been sexually active. She is not employed. She lives with her mother who is her caregiver.

Physical Examination

General appearance: Intellectual delay, non-verbal, no acute distress

Vital signs:

Temperature: 36.9°C

Pulse: 86 beats/min

Blood pressure: 144/96 mmHg

Respiratory rate: 18 breaths/min

Chest: Clear to auscultation bilaterally, non-labored respirations

Cardiovascular: Regular rate and rhythm, no murmurs

Abdomen: Uterus enlarged to 14-week size, mobile. Mild tenderness to palpation

Pelvic: Deferred due to patient discomfort

Extremities: Upper extremity contractures, shuffled gait

Neurologic: Alert, cooperative

Laboratory studies:

WBCs: 7500/μL (normal: 4000–11 000/μL)

Hb: 10 g/dL (normal: 11.3–15.2 g/dL)

Hct: 33% (normal: 33–45%)

Platelets: 251 000/μL (normal: 150 000–400 000/μL)

Urine pregnancy test: Negative

Imaging: Anteverted, enlarged uterus measuring 15.6 × 10.2 × 13.7 cm. Multiple fibroids seen without well-defined borders. The largest measurable fibroid is 7.5 × 6.2 × 6.3 cm. Endometrial echo complex measures 7 mm, which is normal. Right ovary measures 5.3 × 2.4 × 3.3 cm and has a fluid-filled, simple appearing 1.6 × 0.8 × 1.2 cm cyst. Left ovary measures 3.5 × 1.7 × 2.3 cm and appears normal. No free fluid is noted. Large stool burden noted

How Would You Manage This Patient?

This patient requires surgery but lacks capacity for informed decision-making based on her profound cognitive delay and non-verbal status. Her mother is her full legal guardian and thus is her surrogate decision maker. Her mother was counseled on the management options for fibroids and heavy menstrual bleeding refractory to medical therapy. The risks, benefits, and alternatives to the hysterectomy were presented. Additionally, the expected hospital and postoperative course were discussed in detail. Her mother was given time to ask questions and then signed a written consent for the procedure, as she felt it aligned with the patient's best interest and perceived values. The surrogate decision maker's identity and the details of the consent process were included in the preoperative note.

Informed Consent

The process of informed consent occurs when communication between a patient and physician results in the patient's agreement to undergo specific medical treatment. The concept of informed consent is based on the ethical principles of autonomy, beneficence, non-maleficence, and justice. The informed consent process has been described and refined by the law. In the landmark 1914 *Shloendorff* v. *Society of New York Hospital* case, Justice Benjamin Cardozo's stated, "Every human being of adult years and sound mind has a right to determine what shall be done with his own body; and a surgeon who performs an operation without his patient's consent commits an assault, for which he is liable in damages." This principle of self-determination became the primary basis of the legal mandate to obtain consent from patients prior to procedures [1, 2].

The exact term informed consent first appeared in 1957 in the case of *Salgo* v. *Leland Stanford Jr*. The decision in this case mandated that physicians are obliged to disclose any facts needed to form an informed agreement by the patient to proceed with the recommended treatment [1, 3]. Many cases since then have further defined informed consent as the process we know today: an ongoing interaction between a provider and a consenter in which information is thoroughly and mutually shared. The American College of Obstetrics and Gynecology (ACOG) has defined adequacy of disclosure as including the following: "1. The common practice of the profession, 2. The reasonable needs and expectations of the ordinary individual who might be making a particular decision, 3. The unique needs of an individual patient faced with a given choice." [4]. By default the informed consenter is the adult patient who has the capacity to comprehend and weigh the consequences of their decision. This requires the patient to understand the information presented and to be free from coercion. When these criteria are not met because the individual cannot comprehend, as in the case of this developmentally delayed adult patient, a surrogate decision maker is needed.

Capacity to Consent and Surrogate Decision Maker

It is imperative to distinguish competence from capacity. All adults are presumed competent, a legal term, unless a court had deemed said individual incompetent. Capacity, on the other hand, is a task-specific term. It implies the ability to understand, express a choice, appreciate the personal effects of, and reason through the implications of a decision. Lack of capacity may be short-lived as in a patient with altered mental status or long-term as in a patient with cognitive deficits [1]. The incidence of medical inpatients lacking decisional incapacity was estimated to be 26% in one 2011 comprehensive review [5]. There are many instruments available to assess healthcare decision-making capacity. However, consent capacity must take into account the context of the decision that the patient is being asked to make. This relative lack of standardization decreases the utility of these assessment tools. While assessing capacity, collateral information should also be collected to evaluate the consistency of a patient's currently expressed views with his/her long-standing values [5].

According to the AMA's 2019 Code of Medical Ethics, physicians must identify a suitable surrogate to make decisions on behalf of the patient when the patient does not have decision-making capacity. This surrogate is owed the same respect as the patient and deserves proper advice, guidance, and support. This decision maker should base choices on the patient's wishes as previously documented, previously expressed views about how life should be lived, as well as the patient's perceived attitudes regarding sickness and suffering. If this information is unknown, decisions should be based on her best interest considering the level of pain and suffering that will accompany the intervention or treatment, prospective benefit, resulting impairments from treatment, and patient's quality of life [6].

In the best-case scenario, the incapacitated patient has an advanced directive outlining his or her wishes. Unfortunately, only 20% to 29% of the United States population has a completed advanced directive. As a result, all 50 United States and the District of Columbia have enacted laws to address surrogate decision making for patients lacking capacity. Only 41 of those jurisdictions provide guidelines to appoint a surrogate decision maker for at least some medical decisions to safeguard those individuals who are, or who become incapacitated prior to completion of advanced directives. The process for both appointing and contesting surrogate decision makers varies widely among jurisdictions, which can lead to confusion when this process becomes necessary. This variation also limits efforts to research and improve compassionate decision-making [7]. In this case, full guardianship awarded to the mother in the family's state of residence is a formal recognition of incompetence on a permanent basis. Healthcare providers, patients, and healthcare systems must be aware of the laws surrounding the identification and appointment of a default surrogate in their jurisdiction. Hospitals are also required to have an ethics committee or other institutional resource to serve as a non-biased opinion to help settle decision-making disputes or when no default surrogate is identified [7]. In emergencies, decisions can be made solely based on what is determined to be in the best interest of the patient [4].

Key Teaching Points

- A surrogate decision maker is needed if a patient lacks decision-making capacity
- Assignment of a surrogate decision maker is made based on applicable state law
- Surrogate decision makers should respect the patient's preference and act in the patient's best interests
- In emergency situations when a surrogate is unavailable, physicians should proceed with care based on the best interests of the patient

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CASE 3 A 45-Year-Old Woman with Possible Penicillin Allergy Scheduled for Hysterectomy

Katherine Strafford

History of Present Illness

A 45-year-old presents for a preoperative visit. She reports regular menses that have become increasingly heavy in the past year and have not improved with hormonal management. Three weeks ago, she received a transfusion in the emergency department where imaging was notable for uterine fibroids. She received counseling on treatment options and desires hysterectomy. Her history is remarkable for two full-term vaginal deliveries. She has no history of abnormal cervical cytology or sexually transmitted diseases. Her past medical history is significant for exercise-induced asthma and surgical history for tonsillectomy. She is currently taking combined oral contraceptives, multivitamins, iron, and calcium with vitamin D. She is a non-smoker, does not drink alcohol, and is sexually active with one female partner. She reports a penicillin allergy characterized by the development of hives during prior treatment for a urinary tract infection 10 years ago.

Physical Examination

General appearance: Well-groomed, alert and oriented, no apparent distress

Vital signs:

Temperature: 37.1°C

Pulse: 78 beats/min

Blood pressure: 114/74 mmHg

Respiratory rate: 18 breaths/min

Height: 64 inches

Weight: 140 lb

BMI: 24 kg/m^2

Abdomen: Normal bowel sounds, soft, non-distended, no guarding or rebound, no palpable masses

External genitalia: Normal

Vagina: Normal rugae, normal discharge

Cervix: parous, no bleeding noted, no cervical motion tenderness

Uterus: Mid-position, non-tender, mobile, bulky, 10-week size

Adnexa: No palpable masses

Laboratory studies:

Urine pregnancy test: negative

Hb: 9.0 g/dL (normal 11.4–15.2 g/dL)

Endometrial biopsy: secretory endometrium

Imaging: Transvaginal ultrasound shows uterus is homogeneous in echotexture and measures 11.2 × 6.6 × 5.3 cm. The endometrial stripe is distorted by a submucosal fibroid measuring 3.2 × 2.3 × 3.0 cm. An additional fibroid extending into the left adnexal region measures 4.1 × 3.2 × 3.0 cm. The right ovary measures 2.7 × 1.9 × 1.6 cm, and the left ovary measures 2.7 × 1.5 × 2.4 cm. They are normal in appearance

How Would You Manage This Patient?

This patient's history is significant for a report of penicillin allergy that could influence the choice of prophylactic antibiotic for her hysterectomy. Obtaining additional details is important, so the following information questions were posed: What was her allergic response to penicillin? How recent and how rapid was it? Was treatment required? Has she ever taken a cephalosporin? Are there other antibiotics that she has tolerated well? Has she ever had an anaphylactic or life-threatening allergic event? The patient reported that her reaction was 10 years ago when she developed hives on the fifth day of a seven-day course of amoxicillin. She discontinued the antibiotic and the reaction resolved without treatment. She has since been treated twice with antibiotics for sinus infection without difficulty. She has never had anaphylaxis. With this additional information in mind, after counseling on the relative risks of allergic cross-reaction to cefazolin and the limitations of second-line antibiotics, she received cefazolin at the time of surgery. She was referred for allergy evaluation postoperatively and with negative testing was able to have penicillin allergy removed from her medical record.

Penicillin Allergy

Ten percent of the US population reports an allergy to penicillin. The most common reactions found in medical records include rash (38%), "unknown," (26%) and hives (18%) in comparison to reports of anaphylaxis (5%). The rash reported most commonly in reaction to penicillin exposure is a delayed benign rash, likely a type IV hypersensitivity reaction, which may or may not recur. More than 95% of allergy reporting individuals are actually able to tolerate the drug. Furthermore, serious IgE-mediated allergies wane with age and 80% of individuals become tolerant over the course of a decade. Evaluation with amoxicillin challenge and/or penicillin skin testing may give the patient and future healthcare providers the confidence to utilize these drugs safely and remove the penicillin allergy label [1]. True type I IgE-mediated or severe T-lymphocyte-mediated penicillin hypersensitivity is uncommon. IgE-mediated reactions include anaphylaxis, rapid (minute to hours) development of raised pruritic lesions, flushing, difficulty breathing, chest tightness or arrhythmia and significant abdominal pain, nausea, and vomiting. Severe T-cell-mediated reactions may have a more delayed onset (days to weeks) with blistering, desquamation, organ and/or mucosal involvement,

and requirement for hospitalization including severe cutaneous adverse reaction, Stevens–Johnson syndrome, and toxic epidermal necrolysis. These patients often require ICU care [1].

Antibiotic Prophylaxis

The purpose of antibiotic prophylaxis is to reduce the risk of postoperative surgical site infections (SSI) by limiting the burden of microorganisms introduced. Antibiotics chosen should be safe and inexpensive, with coverage effective against likely flora, and the ability to reach appropriate levels in serum and tissue. Cephalosporins are commonly recommended for antibiotic prophylaxis due to wide utility and general tolerability [2]. Risks of antibiotic exposure include drug cost, allergic reactions, development of antibiotic resistance or altered flora, and pseudomembranous colitis [3]. Antibiotic prophylaxis should be initiated within 1 hour prior to incision. The American College of Obstetrics and Gynecology (ACOG) and the Centers for Disease Control and Prevention (CDC) recommend routine preoperative antibiotic coverage for patients undergoing hysterectomy based on its status as a Class II/Clean-Contaminated procedure. This designation is due to the entry into the vagina [4]. Skin and vaginal organisms that require antibiotic coverage for hysterectomies include aerobic gram-positive cocci such as staphylococci species, anaerobic bacteria, and gram-negative aerobes [5]. Rates of postoperative infection vary by route of hysterectomy and by depth of infection classification. The superficial incisional infection rate ranges from 2.3% to 2.6% for abdominal hysterectomy and from 0.6% to 0.8% for laparoscopic hysterectomies. Rates of deep or organ-space infection post-hysterectomy are in the 0.5–1.2% range for all routes [1]. Overall SSI rate for all forms of hysterectomy is 2.53% [6].

Recommended Antibiotic Prophylaxis for Hysterectomy

Cefazolin is the recommended prophylactic antibiotic for all routes of hysterectomy. The starting dose is 2 g IV and should be increased to 3 g for patients >120 kg. The same dose should be repeated for blood loss >1500 mL and for cases exceeding 2.5 times the drug's half-life (4 hours) from time of initial antibiotic dose [1, 5]. Cefoxitin, cefotetan, and ampicillin-sulbactam are also considered appropriate first-line hospital formulary options for hysterectomy prophylaxis by the American Society of Health-System Pharmacists [6]. Second-line options include the combination of metronidazole or clindamycin with gentamicin or aztreonam. Ciprofloxacin may be used if gentamicin or aztreonam are not possible [1]. Patients with methicillin-resistant *Staphylococcus aureus* (MRSA) colonization or infection should receive vancomycin 15 mg/kg or local hospital-recommended MRSA protocol with their antibiotic prophylaxis for hysterectomy. Quinolones or vancomycin may be given up to 2 hours prior to incision [1]. When concern for increased risk of vaginal cuff infections associated with bacterial vaginosis (BV) exists, providers may screen for BV. Patients can be provided with metronidazole, or alternative BV coverage, for five to seven days preoperatively or four days perioperatively if treatment is not completed prior to surgery [1]. Use of second-line antibiotics carries a greater risk of postoperative infection (SSI) with an odds ratio of 1.5–1.7 [1, 7, 8]. Over-avoidance of recommended first-line antibiotic prophylaxis risks use of more broad-spectrum agents and resulting development of antimicrobial resistance. These alternatives also contribute to increased healthcare costs from both the drugs themselves and the additional resources needed to manage resulting higher rates of infection, resistance, and adverse drug effects. Adverse drug effects from second-line antibiotics include *Clostridium difficile,* associated with clindamycin, and nephrotoxicity from gentamicin or vancomycin [7]. Studies have reported inpatient penicillin allergy labeling to be associated with longer hospital stays; higher readmission rates, treatment failures, and ICU admissions; and greater exposure to antibiotics associated with *C. difficile*, vancomycin-resistant *Enterococcus* (VRE), and MRSA (Table 3.1) [9, 10].

Table 3.1 Antibiotic prophylaxis regimens for hysterectomy (all routes)

Antibiotic	Adult dose	Half-life (h)	Repeat dose (h)
Cefazolin	2 g (3 g > 120 kg)	1.2–2.2	4
Cefoxitin†	2 g	0.7–1.1	2
Cefotetan†	2 g	2.8–4.6	6
Ampicillin-sulbactam†	3 g (2 g-1 g)	0.8–1.3	2
Vancomycin, MRSA coverage	15 mg/kg	4–8	Not needed
Clindamycin*	900 mg	2–4	6
Metronidazole*	500 mg	6–8	Not needed
Gentamicin*	5 mg/kg	2–3	Not needed
Aztreonam*	2 g	1.3–2.4	4
Ciprofloxacin*	400 mg	3–7	Not needed

Dosage based on ideal body weight (IBW), normal renal function and typical case length.
† First-line cefazolin substitution.
* Second-line: Clindamycin or metronidazole given with either gentamicin or aztreonam (ciprofloxacin if gentamicin or aztreonam not possible).

Use of Cephalosporins in Penicillin Allergic Patients

Cefazolin is a first-generation cephalosporin. Its use in patients reporting penicillin allergy is sometimes avoided due to a concern for a cross-reactive allergic reaction. Approximately 2% of the general population has a reported cephalosporin allergy [1]. Overall anaphylaxis incidence from cephalosporins is rare with rates reported at 0.0001–0.1%. Reassuring penicillin histories include maculopapular or morbilliform rash (immediate or delayed), gastrointestinal side effects, isolated pruritus/dizziness, headache, and >10 years since last non-life-threatening reaction. These patients can safely receive typical surgical prophylactic cephalosporins [9]. In this case, the patient experienced

a delayed, benign, cutaneous reaction that occurred 10 years ago, thus routine prophylaxis with cefazolin was considered safe.

General cross-reactivity between penicillin and cephalosporins occurs in about 2% of cases [4]. The concern for cephalosporin reactions in patients with penicillin allergy stems from the existence of a beta-lactam ring in both drugs. More specifically, cross-reactivity risk is linked to similarities in the R1 side chain of the beta-lactam ring. These R1 chains vary independently from the cephalosporin generations [2]. Cefazolin possesses a unique R1 side chain that significantly reduces the risk for cross-reactivity in those with penicillin allergy. Cefotetan and cefoxitin also have R1 side chains with little similarity to penicillin [9]. Only the aminocephalosporins (cephalexin, cefadroxil, cefprozil, cefaclor) share an identical side chain with aminopenicillins and thus a significant risk for cross-reactivity in those confirmed to have life-threatening penicillin allergy [10]. Due to R1 side chain differences, some authors report that even those with immediate IgE-mediated penicillin reactions can receive cefazolin, cefotetan, and cefoxitin [2, 9, 10]. Those with life-threatening T-lymphocyte-mediated delayed reactions to penicillin are generally recommended to avoid all cephalosporins [2].

Key Teaching Points

- Charted penicillin allergies should be carefully evaluated to determine their severity
- Many patients with penicillin allergies can safely receive cephalosporins due to differences in chemical structure
- Cefazolin is the most commonly recommended prophylactic antibiotic for hysterectomy and has a unique structure that makes cross-reactivity with penicillin unlikely
- Clindamycin or metronidazole plus gentamicin or aztreonam are the recommended antibiotic prophylaxis for hysterectomy in patients with cephalosporin allergy or severe penicillin allergy
- Coverage with antibiotics other than cephalosporins results in increased infection risk, healthcare costs, and adverse events

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CASE 4 A 50-Year-Old Woman with Prior DVT Undergoing Hysterectomy

Jacqueline Rohl

History of Present Illness

A 50-year-old, gravida 1, para 1, with prior deep vein thrombosis (DVT) presents for a preoperative visit due to upcoming hysterectomy. She is scheduled for a total abdominal hysterectomy due to abnormal uterine bleeding and uterine fibroids. The patient's medical history is significant for obesity and prior history of DVT. Her DVT occurred 10 years ago and was unprovoked. She completed a course of anticoagulation with warfarin for three months. She takes aspirin 81 mg a day. She has no family history of thromboembolic disease. She does not smoke. She is sexually active with one female partner. She has had one prior cesarean section and one vaginal delivery.

Physical Examination

General appearance: Awake and alert, in no acute distress
Vital signs:

Temperature: 36.9°C
Pulse: 85 beats/min
Blood pressure: 120/76 mmHg
Respiratory rate: 16 breaths/min
Height: 60 inches
Weight: 210 lb
BMI: 41 kg/m^2

Heart: Regular rate, rhythm, no murmurs
Lungs: Clear to auscultation bilateral
Abdomen: Obese, soft, not tender, no masses
Pelvic: Normal external genitalia, normal vagina without discharge or lesions, normal cervix without lesions, uterus 20 weeks' size, irregular due to uterine fibroids, adnexa without enlargement or tenderness
Extremities: No edema, tenderness, pulses present
Laboratory studies:

Hb: 10.5 g/dL (normal 12.1–15.1 g/dL)
Platelets: 350 000/μL (normal 150 000–400 000/μL)

How Would You Manage This Patient?

The patient has a history of DVT and is not currently anticoagulated. DVT prophylaxis is indicated. Her risk for perioperative thrombosis is increased due to history of DVT, age, weight, and major open surgery planned. Utilizing a standardized assessment for perioperative DVT risk, the Caprini Risk Assessment Method (RAM) for venous thromboembolism (VTE), she has a score of 7, which places her in the highest risk category (age, BMI – 1 point each, major open surgery – 2 points, history of VTE – 3 points). Her assessment for major risk of bleeding revealed no history of easy bruising, need for prior transfusion, coagulopathy, bleeding disorders, or thrombocytopenia. Based on her Caprini RAM score, both pharmacologic and mechanical VTE prophylaxis are indicated. Intermittent pneumatic compression (IPC) devices were placed on her lower extremities prior to the start of surgery and continued during her hospital stay until discharge on postoperative day 2. In addition, unfractionated heparin (UFH), 7500 units subcutaneously, was administered prior to surgery and continued every 8 hours after surgery until discharge. After discharge, VTE prophylaxis was continued for an additional 14 days with a low molecular weight heparin (LMWH), enoxaparin 40 mg, subcutaneously twice daily.

Indications for Perioperative Venous Thromboembolism Prophylaxis

Venous thromboembolism (VTE) is a high concern in the perioperative period and the leading cause of perioperative morbidity and mortality in hospitalized patients. More than half of blood clots occurring in the outpatient setting (after discharge) are directly linked to a recent hospitalization or surgery [1]. Risk factors for VTE described in Virchow's triad are increased around the time of surgery and include stasis, vessel injury and hypercoagulability [2]. Thoughtful evaluation of patient's risk and implementation of perioperative VTE prophylaxis is of utmost importance. The type and timing of thromboprophylaxis must be judiciously weighed against the risk of bleeding due to surgery.

If pharmacologic VTE prophylaxis is recommended, risk for major bleeding should be obtained from the patient's history. Conditions that would likely preclude pharmacologic VTE prophylaxis would include those with history of active bleeding as the indication for surgery such as a gastrointestinal bleed or trauma; a history of moderate or severe coagulopathy such as patients with liver disease; and inherited bleeding disorders or thrombocytopenia. Relevant questioning should inquire about easy bruising, severe bleeding with resultant anemia, and prior need for transfusion.

Although there is variation, most societies and hospital VTE prophylaxis guidelines adhere to recommendations of the American College of Chest Physicians (ACCP), initially outlined in 2012 [3]. There are numerous risk factors for development of postoperative VTE and the ACCP recognizes that each clinical scenario will demand individualization despite these guidelines. The ACCP suggests use of a risk assessment model (RAM). The Caprini RAM is the most widely used and well-validated model to predict VTE in non-orthopedic post-surgical patients [4, 5]. Thirty-nine factors were included in the original score plus a box for additional risk factors. The scoring tool involves assigning a point value to each risk factor according to the significance of the risk factor

Deep Vein Thrombosis (DVT)

Prophylaxis Orders
(For use in Elective General Surgery Patients)

Thrombosis Risk Factor Assessment
(Choose all that apply)

BIRTHDATE

NAME

CPI No.

SEX M F VISIT No. _____

Each Risk Factor Represents 1 Point

- ❑ Age 41–60 years
- ❑ Swollen legs (current)
- ❑ Varicose veins
- ❑ Obesity (BMI >25)
- ❑ Minor surgery planned
- ❑ Sepsis (<1 month)
- ❑ Acute myocardial infarction
- ❑ Congestive heart failure (<1 month)
- ❑ Medical patient currently at bed rest
- ❑ History of inflammatory bowel disease
- ❑ History of prior major surgery (<1 month)
- ❑ Abnormal pulmonary function (COPD)
- ❑ Serious Lung disease including pneumonia (<1 month)
- ❑ Oral contraceptives or hormone replacement therapy
- ❑ Pregnancy or postpartum (<1 month)
- ❑ History of unexplained stillborn infant, recurrent spontaneous abortion (≥ 3), premature birth with toxemia or growth-restricted infant
- ❑ Other risk factors _____

Subtotal:

Each Risk Factor Represents 2 Points

- ❑ Age 61–74 years
- ❑ Arthroscopic surgery
- ❑ Malignancy (present or previous)
- ❑ Laparoscopic surgery (>45 minutes)
- ❑ Patient confined to bed (>72 hours)
- ❑ Immobilizing plaster cast (<1 month)
- ❑ Central venous access
- ❑ Major surgery (>45 minutes)

Subtotal:

Each Risk Factor Represents 3 Points

- ❑ Age 75 years or older
- ❑ History of DVT/PE
- ❑ Positive Factor V Leiden
- ❑ Elevated serum homocysteine
- ❑ Heparin-induced thrombocytopenia (HIT)
  (Do not use heparin or any low molecular weight heparin)
- ❑ Elevated anticardiolipin antibodies
- ❑ Other congenital or acquired thrombophilia
  If yes: Type _____
- ❑ Family History of thrombosis*
- ❑ Positive Prothrombin 20210A
- ❑ Positive Lupus anticoaqulant

*most frequently missed risk factor

Subtotal:

Each Risk Factor Represents 5 Points

- ❑ Stroke (<1 month)
- ❑ Elective major lower extremity arthroplasty
- ❑ Hlp, pelvis or leg fracture (<1 month)
- ❑ Acute spinal cord injury (paralysis) (<1 month)
- ❑ Multiple trauma (<1 month)

Subtotal:

TOTAL RISK FACTOR SCORE:

Figure 4.1 Caprini risk scoring model. Earlier versions of this tool have been published in 2005 and 2009 [4, 5]. BMI, body mass index; COPD, chronic obstructive pulmonary disease; DVT, deep venous thrombosis; PE, pulmonary embolus. (Reproduced with permission from *Annals of Surgery* [6].

based on the available literature. The points are added to obtain an overall score (Figure 4.1) [6]. Many institutions use their own modified or empiric models as well.

In applying the Caprini RAM, different cutoff values have been used to categorize risk depending on the surgical population. The ACCP guidelines on VTE prophylaxis in non-orthopedic surgical patients are as below [7]:

1. Very low risk: Caprini score 0: corresponding to Estimated Baseline Risk of VTE (EBR) <0.5%. In very low-risk patients, no specific mechanical or pharmacologic therapy is recommended. Early and frequent ambulation is recommended to reduce VTE.
2. Low risk: Caprini score 1–2: corresponding to EBR approximately 1.5%. In low-risk patients, mechanical methods, preferably with intermittent pneumatic compression (IPC) is recommended over no prophylaxis.
3. Moderate risk: Caprini score 3–4: corresponding to EBR approximately 3%. In moderate risk patients wherein bleeding risk is low, mechanical methods (IPC) and/or pharmacologic prophylaxis (LMWH or UFH) over no prophylaxis is recommended. If bleeding risk is high, mechanical methods alone would be recommended.
4. High risk: Caprini score ≥5: corresponding to an EBR of at least 6%. In high-risk patients, wherein bleeding risk is low, mechanical (IPC) and pharmacologic prophylaxis with LMWH or low-dose UFH is recommended. If bleeding risk is high, mechanical methods alone would be recommended.

Types of Thromboprophylaxis

Early ambulation is recommended and reduces VTE by reducing stasis. Intermittent pneumatic compression stockings are also felt to reduce stasis by promoting blood flow in the deep veins of the legs. Pharmacologic agents commonly used are LMWH and UFH. Both have been shown to be superior to no prophylaxis or mechanical methods alone to prevent VTE as described in multiple studies [8]. The frequency with once daily dosing of LMWH makes it more convenient than that of BID or TID dosing of UFH. However, UFH can be used when availability or cost of LMWH is limited or if there is concern for renal insufficiency. Enoxaparin is a commonly used LMWH with dosing of 40 mg subcutaneously daily for VTE prophylaxis. This may be increased to twice daily in obese patients with BMI greater than 40 kg/m^2. UFH dosing in patients is typically 5000 units BID or TID and may increase to 7500 units TID in obese patients with BMI greater than 40 kg/m^2.

Mechanical methods are recommended immediately prior to the onset of surgery and continued postoperatively. There is variation in recommendations for pharmacologic VTE

prophylaxis, but in general, it is recommended 2–12 hours preoperatively. Ongoing postoperative pharmacologic prophylaxis would be initiated 2–72 hours post-procedure depending on the risk of bleeding. However, with neuraxial anesthesia or spinal puncture, the risk of spinal or epidural hematoma is of concern. It is recommended, if undergoing procedures with this type of anesthesia, preoperative pharmacologic VTE prophylaxis should be avoided and should be delayed postoperatively until at least 6–8 hours after catheter removal.

VTE prophylaxis is typically continued until the patient is fully ambulatory or until hospital discharge. Routine extended therapy postoperatively is not recommended in most non-orthopedic surgical patients unless they are undergoing abdominal or pelvic surgery for cancer. In patients undergoing cancer surgery, extending prophylaxis may be recommended for up to 12 weeks postoperatively. VTE risk has been shown to remain elevated during this time. Given this elevated risk and that patients' ambulatory status may vary, there may be justification to extend (10–14 days) therapy for non-cancer patients that have a risk assessment score in the highest risk category [9].

In patients currently anticoagulated, similar to the decision regarding VTE prophylaxis, management of anticoagulant interruption for surgery is dependent on the risk of thromboembolic disease as well as risk of bleeding due to the procedure. There are multiple anticoagulation therapies used at this time including vitamin K antagonist (VKA), such as warfarin, and direct oral anticoagulants (DOAs). Due to their differing half-lives, the recommendations differ on when to stop use prior to surgery. In procedures at low risk for bleeding, there may be no need to stop anticoagulation.

If interruption is recommended due to bleeding risk of the procedure, guidelines of the ACCP can be used [10]: In patients with a mechanical heart valve, atrial fibrillation, or VTE at high risk for thromboembolism, it is recommended to have bridging anticoagulation rather than interruption of VKA therapy. In patients at low risk for VTE, no bridging is recommended and interruption can occur. In patients at moderate risk for VTE, the decision may be individualized and bridging or interruption may occur based on risks. In patients who are receiving bridging anticoagulation with therapeutic-dose IV UFH, it is recommended to stop UFH approximately 4–6 hours before surgery. In patients who are receiving bridging anticoagulation with therapeutic-dose LMWH, it is recommended to have the last preoperative dose of LMWH approximately 24 hours before surgery. In patients who require temporary interruption of a VKA before surgery, it is recommended to stop VKAs approximately 5 days before surgery. In patients who require temporary interruption of a DOA before surgery, it is recommended to stop DOAs approximately 24–48 hours before surgery. Resumption of anticoagulation is recommended beginning approximately 12–24 hours after surgery if there is no concern for bleeding risk. For patients who are undergoing surgery with high risk of bleeding, postoperative anticoagulation may be deferred until 48–72 hours.

Key Teaching Points

- VTE is the leading cause of death in the hospital setting and half occur in association with surgery
- VTE prophylaxis should be chosen based on type of surgery, patient risk factors for thrombosis, and risk of major bleeding
- Risk assessment models aid in the decision but should be individualized
- Methods that are implemented to reduce VTE include early ambulation, mechanical methods, and pharmacologic prophylaxis
- Interruption or bridging of anticoagulation prior to surgery is dependent first on risk of VTE and balanced by risk of bleeding due to the procedure

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