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Consultative Medicine

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01 - 490 Approach to Medical Consultation

490 Approach to Medical Consultation

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Approach to Medical Consultation Effective health care requires teams of generalists and specialists with complementary expertise. Many clinical conditions require the input of more than one clinical provider, either because the diagnosis and recommended treatment is uncertain or because the required diagnostic procedure or management lie outside the principal provider's area of expertise. To consult is to seek advice from someone with expertise in a particular area, whereas consultation refers to the meeting or comparable outcome arising from that request. Medical consultation takes several forms. Its most traditional forms include in-hospital consultation, in which physicians provide recommendations, typically recorded in the medical record, or perform procedures for a hospitalized patient, and outpatient consultations, in which patients are seen in the office setting. More contemporary forms of consultation include e-consultations, telemedicine evaluations (see "Consultation Involving Telemedicine," below), and remote medical second opinions. In these forms, the consultant may not actually see the patient but, nonetheless, assumes the responsibility of evaluating the patient's clinical condition, assessing and analyzing pertinent clinical data, and offering a synthesis and appropriate recommendations. While forms of medical consultation evolve, basic responsibilities associated with medical consultation endure. These responsibilities can be divided into those that fall to the requesting physician or non-physician practitioner; the consultant, who provides the consultation; and the health system, hospital, or organization that must support this important medical encounter (Table 490-1).

■ **RESPONSIBILITIES OF THE REQUESTING CLINICIAN** Before requesting a consultation, the physician or other provider should ensure that the patient endorses the purpose of the consultation, understands the role of the consultant, and anticipates the likely outcomes of the encounter. Further responsibilities of the requesting physician include being specific and communicating clearly the reason for the consultation. Vague messages such as "Please evaluate" are not

TABLE 490-1 Stakeholder Responsibilities in the Medical Consultation Process

REFERRING PHYSICIAN OR PROVIDER	CONSULTANT	PHYSICIAN	HEALTH SYSTEM, HOSPITAL, OR CARE ORGANIZATION
• Ensure patient	• Maintain standards of	• Maintain adequate participation and engagement	• Be specific
• Professionalism, including those pertaining to availability, communication, respect, and collegiality	• Appreciate levels of urgency	• Specialty workforce to enable appropriate access	• Support systems

regarding clinical question and desired outcome • Communicate level and respond appropriately • Assemble and develop one's for efficient exchange of clinical information • Develop culture of urgency • Avoid consulting own database • Be specific in synthesis and of collegiality and team-based care for nonclinical purposes recommendations • Understand desired outcomes, including arrangements for follow-up • Communicate with referring provider in whatever manner is mutually desirable

Consultative Medicine PART 19 as helpful as more specific inquiries such as "What is the cause of the declining kidney function?" or "How should this asymptomatic pulmonary nodule be evaluated?" To the extent possible, the requesting physician should provide the relevant clinical information, summarized as succinctly as possible. Urgency should be clearly conveyed, typically with a phone call or other direct communication. The requesting physician should be explicit regarding the intended outcome of the consultation, i.e., is this for a single evaluation or ongoing co-management? Communication between the requesting and the consulting physicians is paramount. Whether this communication includes direct contact is less important than that the relevant information and desired outcome be explicit and clear, regardless of communication medium. Consultations should be requested for clinical purposes and always directed to qualified consultants; they should not be driven by entrepreneurial or relationship-building purposes.

Another responsibility of the referring physician is not to "overconsult." Medical care should be focused on value, not volume. ■ ■ RESPONSIBILITIES OF THE CONSULTANT Just as the referring physician should attend to clear and explicit communication, so too should the consultant follow the precepts of effective interactions between professionals, which include courtesy, availability, and clarity. Particularly on the inpatient service, where consultants may receive several requests each day, it is important that the incoming consultations are triaged and dispatched as clinically appropriate. Consultants also need to determine the requested level of involvement going forward and not assume that long-term co-management is being sought. While consultants can and should make use of available clinical data, they should also assemble independently their own database, including taking a history, performing a physical exam, and reviewing pertinent laboratory, imaging, and pathology studies. Absent that, they may be unable to provide an independent and actionable synthesis. Just as the referring physician needs to be clear and concise, so too should the consultant be specific and focused in the recommendations provided. "Possible malignant ascites" is less helpful than, "I will arrange for paracentesis to exclude the possibility of malignant ascites." For the most part, recommendations to "consider" some diagnosis or test are less helpful than more specific and concrete advice. Some referring physicians wish to be called after a patient is seen; others prefer that communication be handled as part of the medical record. How this communication is handled must also align with the complexity and urgency of the consultation and clinical circumstances. ■ ■ RESPONSIBILITIES OF HEALTH SYSTEMS, HOSPITALS, AND MEDICAL ORGANIZATIONS Health systems, hospitals, and medical organizations also have responsibilities in the consultation process. This responsibility includes ensuring that qualified consultants are accessible and available on the medical staff. Consultations within a single system are aided by common shared electronic medical records, particularly when consultations originate in the hospital, but then also involve care in the outpatient setting. Finally, health care entities should strive to foster a culture of team-based care and collegiality. Reimbursement for consultations varies among payors and may have implications for self-pay or unreimbursed expenses for providers or health systems. While it is important to understand reimbursement models, the clinical needs of the patient should be prioritized. ■ ■ SPECIAL ISSUES IN MEDICAL CONSULTATION

Curbside Consults Curbside consults are requests from one physician to another for an informal and unwritten opinion about a specific patient care matter. They are typically limited in scope, mostly regarding management or questions regarding procedures, and developed from information provided by the consulting physician and perhaps the medical record (such as labs and imaging studies). Although

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often viewed as convenient, efficient, and a common aspect of clinical care, without a comprehensive review of the record or any direct contact with the patient, curbside consults have been found to often be incomplete or even flawed. It is not uncommon for the question being asked to be deemed too complex for a curbside consult or for it not to be the actual or only issue the consultant feels needs to be addressed. As a general rule, curbside consults should be avoided. While medicolegal liability is often cited as a reason to limit curbside consults, the risk is actually negligible as U.S. courts have ruled that curbside consults do not establish a doctor-patient relationship necessary for creating the basis for medical malpractice litigation. An important exception, however, is when a curbside consult is provided by a resident or fellow in training; in this circumstance, the trainee's supervising physician, whether aware of the curbside consult or not, is responsible for the recommendations of the trainee.

Advice Related to curbside consultation, but decidedly different, are instances when one physician reaches out to another, often one in another specialty, for advice. Examples include an internist turning to a radiologist for guidance on what is the most appropriate imaging study to diagnose a deep tissue abscess; a general internist asking a gastroenterologist for advice on management of acute diverticulitis; a hospitalist asking a neurologist for guidance on management of a patient with Parkinson's disease who is NPO; or a nephrologist asking an infectious disease specialist about immunizations in a kidney transplant recipient. PART 19 Consultative Medicine Outreach such as this is typically triggered by a specific patient encounter, but the request is more for general information that the requesting physician may use for the encounter at hand as well as for similar encounters going forward. Thus, reaching out for advice differs from formal consultation and from curbside consultation, which are specific for a particular patient. As such, requests for advice fall within the realm of collegial communication and not necessarily within that of clinical consultation per se. Second Opinions Physicians may find themselves providing consultations requested by patients who have already been evaluated for the same problem by another physician. Not a "consult" in the usual context of one physician referring a patient to another, the service provided by the consultant is, nonetheless, very much aligned with a physician-referred consult. Second opinions, which often are encouraged by the patient's physician, may be sought by patients for reassurance that a diagnosis and treatment recommendation are correct, out of dissatisfaction

with the initial physician, or with the hope of an entirely different opinion and recommendation. The physician providing the second opinion should strive to understand the patient's motivations for seeking the additional opinion. While a second opinion may have been initiated by the patient rather than referral from another physician, it is recommended that the consulting physician communicate with the patient's primary physician, as would be done following a standard consultation, unless the patient insists otherwise. In addition, professional behavior in how the consulting physician refers to the recommendations or actions of previous physicians is important, including when there is disagreement. Likewise, it is important that a transfer of care from the prior physician to the one providing a second opinion be enacted only if specifically requested by the patient or the physician who encouraged the second opinion. Consults Involving Advanced Practice Providers Increasingly, specialist physicians may find themselves being consulted by nurse practitioners and physician assistants rather than other physicians. Whether the quality of the information provided to the consultant physician by these providers is different from physician-to-physician referrals has not been studied. Consulting physicians should know whether they should respond back to the advanced practice provider or to the supervising physician, if there is one. As with physician-to-physician consults, it is also important for the consultant to know whether the individual calling for the consult has an ongoing role in the care of the patient or is simply covering for a limited period of time. Finally, the consultant, if responding back to the advanced practice provider, should make sure that the information provided meets the

needs of that provider and that questions are answered as they would be if responding back to another physician. Consultation Involving Telemedicine and Electronic Health Records (EHRs) Consultations making use of EHRs, patient portals, and various forms of telecommunication technology, including video conferencing or cell phone communication, can improve access to care, reduce cost, and improve outcomes. This is particularly true when employed in geographic areas of health care shortage and when the clinical issues can be handled without direct contact with the patient, i.e., radiology or dermatology. However, the absence of direct contact between patient and consultant introduces special issues related to diagnostic accuracy and physician-patient relationship. Regulatory, liability, security, and confidentiality issues arise as well, as do concerns about disparities related to access to telemedicine technologies and willingness and ability to use them among some patient populations. ■ ■ FURTHER READING Ahmed S et al: Utility, appropriateness, and content of electronic consultations across medical subspecialties. A cohort study. *Ann Intern Med* 172:641, 2020. Pearson SD: Principles of generalist-specialist relationships. *J Gen Intern Med* 14:S13, 1999. Sulmasy DH: Policy recommendations to guide the use of telemedicine in primary care: An American College of Physicians Position Paper. *Ann Intern Med* 163:787, 2015. Sarah Rae Easter, Robert L. Barbieri

Medical Disorders

During Pregnancy Each year, ~3.7 million births occur in the United States, and >130 million births occur worldwide. A significant proportion of births are complicated by medical disorders. Advances in medical care and fertility treatment have increased the number of people with serious medical problems seeking pregnancy. Medical problems that interfere with the physiologic adaptations of pregnancy increase the risk for poor pregnancy outcome. Conversely, in some instances, pregnancy events may have implications for an individual's long-term health. HYPERTENSION (See also Chap. 288) Cardiac output increases by 40% in pregnancy, with most of the increase due to an

increase in stroke volume. Heart rate increases by ~10 beats/min during the third trimester. In the second trimester, systemic vascular resistance decreases, and this decline is associated with a fall in blood pressure. A blood pressure of systolic ≥ 140 and/or diastolic ≥ 90 mmHg on two measurements 4 h apart after 20 weeks' gestation is abnormal and is associated with an increase in perinatal morbidity and mortality. Hypertension during pregnancy is classified as preeclampsia, gestational hypertension, or chronic hypertension. These classifications are distinguished based on timing in pregnancy and the presence of associated features (see below). The prevalence of hypertensive disorders in pregnancy (HDP) is rising. The Centers for Disease Control and Prevention (CDC) estimated that in 2019, 16% of deliveries in the United States were complicated by a HDP. ■ ■PREECLAMPSIA Approximately 5–7% of all pregnant women develop preeclampsia, the new onset of hypertension (blood pressure $\geq 140/90$ mmHg) and proteinuria (either a 24-h urinary protein >300 mg/24 h or a

protein-creatinine ratio ≥ 0.3) after 20 weeks of gestation. Preeclampsia can be diagnosed without proteinuria in the presence of symptoms or laboratory abnormalities raising concern for end-organ damage. Specific clinical features qualify as evidence of severe disease, including severe hypertension (blood pressure $\geq 160/110$ mmHg), new-onset symptoms (headache not responsive to medications, visual changes, or unremitting severe epigastric pain), pulmonary edema, or laboratory abnormalities signifying thrombocytopenia (platelets $<100 \times 10^9/L$), renal insufficiency (creatinine >1.1 mg/dL), or liver impairment (elevation of transaminases to twice the normal concentration). Eclampsia is diagnosed when a pregnant person with preeclampsia develops generalized seizures. The HELLP syndrome (hemolysis, elevated liver enzymes, low platelets) is a special subtype of preeclampsia with severe features and is a major cause of morbidity and mortality. Coagulopathy, cerebrovascular accidents (CVAs), hepatic capsule rupture, and placental abruption are additional end-organ complications of preeclampsia. The precise pathophysiology of preeclampsia remains unknown, but chronic uteroplacental ischemia, an exaggerated maternal inflammatory response, and/or imbalance of angiogenic factors likely contribute to the clinical syndrome. In preeclampsia, there is excess production of an antiangiogenesis factor, soluble fms-like tyrosine kinase 1 (sFlt-1), and decreased production of an angiogenic factor, placental growth factor (PlGF). A ratio of circulating sFlt-1/PlGF ≥ 40 is associated with an increased risk of developing preeclampsia with severe features in the 2 weeks following the measurement. Abnormalities of cerebral circulatory autoregulation explain some of the neurologic manifestations of the disease and can increase the risk of stroke at even modestly elevated blood pressures. In the absence of treatment, 1 in 100 cases of preeclampsia may progress to eclampsia—new-onset generalized tonic-clonic seizures in a patient with preeclampsia. Low-dose aspirin initiated between 12 and 14 weeks of gestation reduces the risk in women at high risk of developing preeclampsia. ■ ■GESTATIONAL HYPERTENSION The development of elevated blood pressure after 20 weeks of pregnancy in the absence of preexisting chronic hypertension or proteinuria is referred to as gestational hypertension. Gestational hypertension with severe features of the disease is best classified as preeclampsia. Both gestational hypertension and preeclampsia are associated with an increased risk of developing chronic hypertension, cardiovascular disease, chronic kidney disease, or diabetes mellitus later in life. TREATMENT Preeclampsia The management of preeclampsia is challenging because it requires the clinician to balance the health of the mother with the health of the fetus. The definitive treatment of preeclampsia is delivery of the fetus and placenta, but preterm delivery exposes the fetus to the risks of prematurity. In preeclampsia without severe features, delivery at 37 weeks is recommended. People with preeclampsia without severe features

may be managed expectantly until 37 weeks with close monitoring for development of severe features or laboratory abnormalities, frequent fetal surveillance, and limited physical activity to reduce blood pressure. Expectant management of preeclampsia with severe features remote from term affords some benefits for the fetus but at significant risk to the mother. For women with preeclampsia with severe features, delivery is recommended unless the patient is <34 weeks and eligible for expectant management in a tertiary hospital setting. Indications for delivery prior to 34 weeks include unremitting symptoms, development of laboratory abnormalities, or severe range blood pressures refractory to medical management. The goal of prolonging pregnancy to this gestational age is to improve neonatal outcomes. Therefore, concerns about fetal well-being, such as severe fetal growth restriction or placental abruption, may also prompt delivery before 34 weeks. Timely management of blood pressures $\geq 160/110$ mmHg reduces the risk of CVAs. Labetalol and

hydralazine IV are the first-line agents to manage severe hypertension in preeclampsia with consideration of oral agents once blood pressure is controlled.

Women who have had preeclampsia are at increased risk of cardiovascular disease later in life. Interventions to reduce cardiovascular risk can be initiated in health encounters following birth. ■

■ **CHRONIC HYPERTENSION** Pregnant people with chronic hypertension are at increased risk for superimposed preeclampsia and placental complications such as fetal growth restriction and placental abruption. These complications may necessitate preterm birth, which is associated with newborn respiratory distress syndrome. People with chronic hypertension should have a thorough prepregnancy evaluation to identify remediable causes of hypertension and to transition off antihypertensive agents associated with adverse outcomes in pregnancy. Angiotensin-converting enzyme inhibitors and angiotensin-receptor blockers are contraindicated in pregnancy because of an increased risk of stillbirth and congenital fetal anomalies. Labetalol and extended-release nifedipine are the most commonly used medications for the treatment of chronic hypertension in pregnancy. The optimal target blood pressure is <140/90 mmHg, which reduces the risk of developing preeclampsia and preterm birth. A preconception or early pregnancy assessment for end-organ impacts of hypertension, including the presence of proteinuria, may help differentiate the effects of chronic hypertension from those of superimposed preeclampsia. CHAPTER 491 ■

■ **RENAL DISEASE** Normal pregnancy is characterized by a 40% increase in glomerular filtration rate and creatinine clearance secondary to a rise in renal plasma flow. Patients with underlying renal disease may expect a worsening of existing hypertension or development of preeclampsia during pregnancy. A prepregnancy serum creatinine level ≥ 133 $\mu\text{mol/L}$ (≥ 1.5 mg/dL)

and low C4 levels are associated with adverse pregnancy outcomes. Certain pathologies, such as those associated with glomerular disease, increase the risk of adverse outcomes. Neither hemodialysis nor prior renal transplant is a contraindication to pregnancy, but both require close multidisciplinary management. When renal disease worsens during pregnancy, close collaboration between the internist and the maternal-fetal medicine specialist is essential so that decisions regarding delivery can be weighed to balance the sequelae of prematurity for the neonate versus long-term sequelae for the mother with respect to future renal function. Medical Disorders During Pregnancy

CARDIAC DISEASE Cardiac disease is the leading cause of maternal mortality in the United States. Prepregnancy cardiac disease and cardiac disease caused by pregnancy are both major contributors. Patient education, risk stratification, optimization of hemodynamics, and

multidisciplinary planning with a pregnancy heart team are the tenets of management. Patients with pulmonary hypertension (Chap. 294), severe ventricular dysfunction (ejection fraction <30% or New York Heart Association class III–IV), severe mitral or aortic stenosis, severe aortic dilation, or Fontan circulation with severe complications are at the highest risk of maternal mortality.

Pregnancy is contraindicated in these women, with termination of pregnancy as an option to reduce maternal risk. Risk stratification including a detailed history with attention to symptoms, echocardiography, and cardiopulmonary exercise testing guides monitoring and management for most patients. Contemporary guidelines support continuing most nonteratogenic pre-pregnancy medications and reserving cesarean delivery for obstetric indications with few exceptions. ■

■ **VALVULAR HEART DISEASE** (See also Chaps. 272–279.) **Mitral Stenosis** The pregnancy-induced increase in blood volume, cardiac output, and tachycardia can increase the transmitral pressure gradient and cause pulmonary edema or tachyarrhythmias in

women with mitral stenosis. People with moderate to severe mitral stenosis (mitral valve area ≤ 1.5 cm²) who are planning pregnancy and have either symptomatic disease or pulmonary hypertension should undergo valvuloplasty prior to conception, preferably with percutaneous balloon valvotomy. Careful control of heart rate and avoidance of hypovolemia, especially during labor and delivery, mitigate the risk of tachycardia and reduced ventricular filling times on cardiac function. The immediate postpartum period is a time of particular concern secondary to rapid volume shifts.

Aortic Stenosis People with aortic stenosis, a mean valve gradient <25 mmHg, and normal left ventricular function are likely to tolerate pregnancy. Symptomatic aortic stenosis or severe aortic stenosis with a peak gradient >50 mmHg should be evaluated for correction prior to pregnancy. **Mitral and Aortic Regurgitation** The pregnancy-induced decrease in systemic vascular resistance reduces the risk of cardiac failure with these conditions, especially in those with chronic lesions. As a general rule, regurgitant lesions are well tolerated in pregnancy with acute onset of mitral or aortic regurgitation as an exception. **Mechanical Heart Valves** People with mechanical heart valves are at high risk of valve thrombosis in pregnancy and warrant special consideration. Use of warfarin in pregnancy is limited to this population and avoided in the first trimester due to its association with fetal chondromalacia punctata. The risk of serious neonatal bleeding and associated neurologic injury persists throughout pregnancy, but the superiority of warfarin in preventing valve thrombosis merits its use in the second and third trimesters. Bridging from warfarin to heparin infusion at 36 weeks' gestation minimizes bleeding risk and facilitates neuraxial analgesia at delivery. **PART 19 Consultative Medicine** ■ ■

■ **CONGENITAL HEART DISEASE** (See also Chap. 280) Reparative surgery has markedly increased the number of adults with congenital heart disease seeking pregnancy with a variety of disease-specific management considerations and outcomes. Repaired septal defects are comparatively low risk, whereas unrepaired septal lesions or repaired complex lesions such as tetralogy of Fallot may warrant additional surveillance by a pregnancy heart team to ensure that pregnancy is tolerated. People with complications in the setting of lower risk disease or with high-risk disease including uncomplicated Fontan circulation, systemic right ventricle, or cyanotic disease require delivery at a tertiary care center with subspecialty expertise. In Eisenmenger's syndrome, i.e., the combination of pulmonary hypertension with right-to-left shunting due to congenital abnormalities (Chap. 280), maternal and fetal deaths occur frequently, informing the recommendation for termination of pregnancy. The presence of a congenital cardiac lesion in the mother increases the risk of congenital cardiac disease in the newborn and is the basis

for the recommendation to screen for fetal congenital heart disease with fetal echocardiography. ■
■**AORTOPATHY** The physiologic cardiovascular adaptations of pregnancy can predispose to aortic dissection, the majority of which occur in people with underlying aortopathies (Chap. 291). Although dissection may occur in the absence of aortic root enlargement in some genetic syndromes, sequential transthoracic echocardiographic (TTE) monitoring during pregnancy for evolution of the aortic root diameter is the mainstay of monitoring those at risk. Aortic magnetic resonance imaging (MRI) without gadolinium is useful to define thoracoabdominal aortic pathology in high-risk diseases. For most diseases, an aortic root diameter <40 mm portends a favorable pregnancy outcome, whereas a diameter >50 mm is an indication for pre-pregnancy repair. Beta blockers are a mainstay of therapy for most patients. A high clinical suspicion for dissection in patients presenting with chest pain is mandatory. Marfan Syndrome (See also Chap. 425) This autosomal dominant disease is associated with an increased risk of aortic dissection and rupture. An aortic root diameter >40 mm is associated with an increased risk of aortic dissection, and an aortic root diameter >45 mm is

an indication for surgical treatment. Operative vaginal delivery to limit the aortic wall stress associated with Valsalva should be considered for women with an aorta of 40–45 mm. Ehlers-Danlos Syndrome (EDS) (See also Chap. 425) Vascular EDS (vEDS, type IV) is an autosomal dominant disease associated with an increased risk of uterine or vascular rupture that may cause death. For people with vEDS, pregnancy is relatively contraindicated because of this risk. ■
■**CARDIAC COMPLICATIONS IN PREGNANCY** Arrhythmias New-onset arrhythmias in healthy patients or patients with cardiac disease are common cardiac complications. Treatment is generally the same as in the nonpregnant patient, and fetal tolerance of medications such as beta blockers, calcium channel blockers, and common antiarrhythmics is acceptable. Pharmacologic or electric cardioversion may be performed to improve cardiac performance and reduce symptoms according to standard indications. Peripartum Cardiomyopathy (PPCM) (Chap. 269) This uncommon but life-threatening condition should be considered in patients presenting in the third trimester or postpartum period with unexplained cardiogenic pulmonary edema. Treatment is directed toward symptomatic relief and improvement of cardiac function. The majority of patients recover completely. The subset of patients with left ventricular ejection fraction $<30\%$ are at high risk of progressive dilated cardiomyopathy. People with a history of PPCM may carry a genetic mutation that influences cardiac function. Approximately 10% of people with a history of PPCM have a truncating mutation in the titin gene encoding the sarcomere protein and experience higher rates of ongoing cardiomyopathy. Recurrence in a subsequent pregnancy is a risk, with a left ventricular ejection fraction of $<50\%$ 12 months post partum as the threshold to advise against another pregnancy. **ENDOCRINE AND METABOLIC DISORDERS** The fetoplacental unit induces major metabolic changes to shunt glucose and amino acids to the fetus while the mother uses ketones and triglycerides to fuel her metabolic needs. The use of glucose by the fetus leads to a maternal state of accelerated ketosis during maternal fasting, characterized by lower glucose concentrations and higher hydroxybutyrate and acetoacetate levels. These metabolic changes are accompanied by maternal insulin resistance that increases during the course of pregnancy caused in part by placental production of steroids, a growth hormone variant, and placental lactogen. ■ ■**DIABETES MELLITUS** (See also Chaps. 415–417) Pregnancy complicated by pregestational diabetes mellitus (pgDM), either type 1 or type 2 diabetes, complicates $\sim 1\%$ of pregnancies and is associated with increased maternal and perinatal morbidity and mortality rates. The prevalence of pgDM is greater among patients who are obese compared to normal weight (2.2 vs 0.5%). The metabolic changes

of pregnancy can precipitate hyperglycemia requiring increased insulin needs, development of diabetic ketoacidosis, or hypoglycemia. Impaired glycemic control during the critical first 5–8 weeks of embryonic growth leads to an increased risk of spontaneous abortion and congenital malformations and highlights the importance of prepregnancy glycemic control. pgDM increases the risk of stillbirth, preeclampsia, and large for gestational age infants. Macrosomia increases the risk of shoulder dystocia and birth trauma, including brachial plexus injury and obstetric lacerations. Neonates are at risk of hypoglycemia, hyperbilirubinemia, polycythemia, and respiratory distress. An assessment of end-organ complications of pgDM including nephropathy, retinopathy, and neuropathy is essential to understanding the patient's risk profile. ■

■ **GESTATIONAL DIABETES** Gestational diabetes mellitus (GDM) occurs in ~8% of pregnancies, and screening for GDM is a routine part of prenatal care, recommended by the U.S. Preventive Services Task Force with a B recommendation. The typical two-step strategy to diagnose GDM is performed at 24–28 weeks of

gestation and involves the initial administration of a 50-g oral glucose challenge with a single serum glucose measurement at 60 min. Plasma glucose >7.2 mmol/L (>130 mg/dL) warrants administration of a 100-g oral glucose tolerance test (GTT) with plasma glucose measurements obtained in the fasting state and at 1, 2, and 3 h. Normal plasma glucose concentrations at these time points are <5.3 mmol/L (<95 mg/dL), <10 mmol/L (<180 mg/dL), <8.6 mmol/L (<155 mg/dL), and <7.8 mmol/L (<140 mg/dL) as the upper norms. Two elevated glucose values indicate a positive GTT diagnostic of GDM. GDM increases the risks of maternal and neonatal complications similar to those seen with pregestational diabetes. Treating GDM reduces the risk of preeclampsia, birth weight >4000 g, and shoulder dystocia. **TREATMENT** Diabetes Mellitus in Pregnancy Preconception counseling to optimize glycemic control and assess for end-organ complications of pgDM is a cost-effective and evidence-based intervention. Guidelines encourage people with pgDM considering pregnancy to initiate insulin prior to pregnancy, targeting a preconception hemoglobin A1c $<6\%$ to reduce the risk of fetal congenital malformation. Insulin is the preferred medical therapy for pgDM in pregnancy due to its safety profile and lower rates of treatment failure compared to oral hypoglycemic medications. Once pregnancy is established, glucose control should be managed more intensively than in the nonpregnant state with assessment of blood glucose when fasting and either 1 or 2 h after a meal at a minimum. Fasting blood glucose levels should be maintained at <5.3 mmol/L (<95 mg/dL), with postprandial targets of <7.8 mmol/L (140 mg/dL) or <6.7 mmol/L (120 mg/dL) at 1 and 2 h, respectively. Continuous glucose monitoring is an evidence-based intervention to improve neonatal outcomes in type 1 diabetes. Sequential measurement of hemoglobin A1c is of minimal utility for monitoring glucose control during pregnancy because of the higher rate of red blood cell turnover during pregnancy and resultant falsely low values. Average daily insulin needs increase from 0.7–0.8 units/kg in the first trimester to 0.8–1 units/kg in the second trimester and 0.9–1.2 units/kg in the third trimester. Most management strategies utilize a combination of basal insulin with short-acting insulin at mealtime or continued use of a prepregnancy insulin pump in appropriately selected patients. Glycemic control may become more difficult to achieve as pregnancy progresses due to an increase in insulin resistance. Attention to glycemic control and frequent fetal surveillance including ultrasounds are mainstays of management in the third trimester. Ultrasound identification of a large for gestational age fetus or polyhydramnios on antenatal ultrasound can be indicators of suboptimal glycemic control. Tight glycemic control at delivery minimizes the risk of neonatal hypoglycemia due to fetal hyperinsulinemia caused by elevated maternal glucose levels. Infants of

mothers with pgDM have higher rates of preterm birth, although preterm delivery is generally reserved for poor glycemic control, worsening maternal renal disease, or active proliferative retinopathy in addition to the usual obstetric indications. Induction of labor may be recommended in the early term period of 37–39 weeks of gestation. Cesarean delivery is reserved for cases of suspected macrosomia based on an estimated fetal weight of 4500 g or greater to minimize the risk of shoulder dystocia and associated birth trauma. **TREATMENT** Gestational Diabetes Treatment of GDM begins with nutritional therapy to optimize normoglycemia and gestational weight gain, which is effective in the majority of women. Insulin is the preferred therapy for patients who exceed the aforementioned targets despite nutritional therapy. Metformin and glyburide are alternatives for patients who decline

or cannot reliably take insulin. Contemporary data demonstrate lower mean birth weights, gestational weight gain, and rates of pre-eclampsia with metformin compared to both glyburide and insulin. The unknown long-term developmental and metabolic effects of metformin, including higher adiposity measurements in children exposed to metformin in utero, inform the preference for insulin.

GDM confers a 7- to 10-fold increase in the risk of developing type 2 diabetes later in life, with a 10% risk within 5 years of delivery. All people with GDM should have a 2-h 75-g GTT to screen for diabetes or impaired glucose tolerance 4–12 weeks following birth. The increased long-term risks of diabetes and cardiovascular disease and the need for regular follow-up with a primary care provider should be emphasized for all people with GDM. Following birth, exercise, weight loss, and treatment with metformin reduce the risk of developing diabetes in these at-risk patients. ■

■ **OBESITY** (See also Chap. 414) Pregnant people who are obese have an increased risk for GDM, preeclampsia, cesarean delivery, congenital malformations, stillbirth, and neonatal death. A growing body of literature suggests the in utero effects of excess adipose tissue may cause changes in fetal metabolic programming that lead to adverse health outcomes in adult life. People contemplating pregnancy should attempt to attain a healthy weight prior to conception, recognizing that even a 10% reduction in weight may significantly reduce many of these risks. Those undergoing bariatric surgery should be counseled to avoid conception for 12–18 months after surgery until weight stabilizes. Bariatric surgery reduces the risks for some complications but requires increased laboratory surveillance for micronutrient deficiencies in pregnancy with appropriate supplementation. All women should be counseled to avoid weight gain in excess of the National Academy of Medicine guidelines (25–35 lb for normal weight, 15–25 lb for overweight, and 11–20 lb for obese women) with the knowledge that excess gestational weight gain increases the risk of macrosomia and cesarean delivery, independent of the presence of comorbid diabetes.

CHAPTER 491 Medical Disorders During Pregnancy ■ ■ **THYROID DISEASE** (See also Chap. 394) The estrogen-induced increase in thyroxine-binding globulin increases circulating levels of total T3 and total T4 in pregnancy. Placental human chorionic gonadotropin (hCG) directly stimulates the thyroid, causing an increase in free T3 and T4, especially in the first trimester. Interpretation of the measurement of free T4, free T3, and thyroid-stimulating hormone (TSH) should use trimester-specific ranges. People with a history of Graves' disease have an increased risk of fetal goiter and neonatal Graves' disease independent of treatment status due to the transplacental passage of thyroid-stimulating antibodies and stimulation of the fetal thyroid. **TREATMENT** Hyperthyroidism Options for the treatment of symptomatic hyperthyroidism in pregnancy include beta blockers, propylthiouracil, and methimazole. Methimazole crosses the placenta to a greater degree than

propylthiouracil and has been associated with fetal aplasia cutis. Propylthiouracil can be associated with maternal liver failure. Some experts recommend propylthiouracil in the first trimester and the option of continuing propylthiouracil or switching to methimazole thereafter. Radioiodine should not be used during pregnancy, either for scanning or for treatment, because of effects on the fetal thyroid. **TREATMENT Hypothyroidism** The goal of therapy for hypothyroidism is to maintain the serum TSH in the normal range, and thyroxine is the drug of choice. The dose of thyroxine required to keep the TSH in the normal range

rises during pregnancy. Since the increased thyroxine requirement occurs as early as the fifth week of pregnancy, one approach is to increase the thyroxine dose by 30% (two additional pills weekly) as soon as pregnancy is diagnosed and then adjust the dose according to TSH.

HEMATOLOGIC DISORDERS Pregnancy has been described as a state of physiologic anemia. Red blood cell mass increases in pregnancy but to a lesser degree than plasma volume. This differential increase results in a lower hemoglobin concentration and so-called dilutional anemia. However, iron, folate, and vitamin B12 deficiencies are common causes of correctable anemia during pregnancy. Transfer of iron to the fetal compartment may explain why iron deficiency anemia is detected in ~11% of pregnant people in the third trimester. Screening for anemia is recommended in the first trimester and at 24 to 28 weeks' gestation. Measurement of ferritin can help detect iron deficiency before anemia is diagnosed. Iron replacement therapy is recommended in pregnancy. Hemoglobinopathy screening is recommended for all pregnant women with testing of mean corpuscular volume, mean corpuscular hemoglobin, ferritin, and hemoglobin analysis (Chap. 103). Hemoglobinopathies can be associated with increased maternal and fetal morbidity and mortality, with sickle cell disease as a particularly high-risk entity in pregnancy. Management is tailored to the specific hemoglobinopathy and is generally the same for both pregnant and nonpregnant women. Prenatal diagnosis of hemoglobinopathies in the fetus is readily available and should be discussed with prospective parents either prior to or early in pregnancy. **PART 19 Consultative Medicine** Thrombocytopenia occurs in 5–10% of pregnancies. The majority of cases are benign gestational thrombocytopenias, but the differential diagnosis should include immune thrombocytopenia (Chap. 120), preeclampsia, and thrombotic thrombocytopenic purpura. Benign gestational thrombocytopenia is unlikely if the platelet count is $<100,000/\mu\text{L}$. ■ ■ **DEEP VENOUS THROMBOSIS AND**

PULMONARY EMBOLISM (See also Chap. 290) Pregnancy is associated with venous stasis, endothelial injury, and a hypercoagulable state. During pregnancy, circulating coagulation factors II, VII, VIII, IX, X, and XII, fibrinogen, and von Willebrand factor increase, and protein S and antithrombin III decrease. Inherited thrombophilias and the presence of antiphospholipid antibodies increase the risk of venous thromboembolism (VTE) in pregnancy and often require prophylactic anticoagulation during pregnancy and the postpartum period to mitigate risk. Deep venous thrombosis (DVT) or pulmonary embolism (PE) occurs in about

1 in 500 pregnancies, with the highest risk in the postpartum state. In general, all diagnostic and therapeutic modalities afforded to the non pregnant patient should be utilized in pregnancy.

TREATMENT Venous Thromboembolism Aggressive diagnosis and management of suspected DVT or PE optimize outcomes for both patient and fetus. Anticoagulant therapy with low-molecular-weight heparin (LMWH) or unfractionated heparin is indicated in pregnant people with VTE.

Anticoagulants increase the risk of epidural hematoma in the setting of neuraxial analgesia (e.g., epidural or spinal anesthesia) in labor and must be withheld prior to placement. To ensure patient access to neuraxial analgesia in labor, prophylactic LMWH can be stopped 12 h before placement of an epidural catheter, whereas therapeutic LMWH can be discontinued for a full 24 h. Transition to unfractionated heparin as delivery approaches can shorten the time between anticoagulant administration and epidural placement. Unfractionated heparin can be used with an epidural catheter in place in those at highest risk of worsening thromboembolic disease.

■ ■ **NEOPLASIA** Cancer complicates ~1 in 1400 pregnancies. The four cancers that occur most commonly in pregnancy are cervical cancer, breast cancer, melanoma, and lymphoma. Also, cancer rates in pregnancy vary across the globe depending on local medical practices and exposures. In addition to cancers developing in other organs, gestational trophoblastic tumors can arise from the placenta. Pregnancy has relatively little or no impact on the natural history of malignancies, despite the hormonal influences. People with a history of active or treated hormonally responsive breast cancer who choose to pursue pregnancy have similar rates of cancer-related events as those who do not. Spread of the cancer to the fetus (so-called vertical transmission) is exceedingly rare. However, managing cancer in a pregnant person is complex, with competing interests for mother and fetus. Generally, the management that optimizes maternal physiology is also best for the fetus. The best way to approach management of a pregnant woman with cancer is to ask, “What would one do in this clinical situation if she was not pregnant? Then, which, if any, aspect of those plans needs to be modified because she is pregnant?”

TREATMENT

Malignancy Exposure of the developing fetus to therapeutic doses of ionizing radiation may cause adverse effects and is generally avoided during pregnancy. Chemotherapy is associated with adverse fetal effects, but the significance of these depends on the specific agent and gestational age. Cytotoxic chemotherapy should virtually never be given in the first trimester due to risk of spontaneous abortion or malformation. If avoiding chemotherapy during this vulnerable time period could compromise maternal health, patients should be counseled about the role of therapeutic abortion to avoid serious neonatal sequelae. A variety of single agents and combinations have been administered in the second and third trimesters, without a high frequency of toxic effects to the pregnancy or the fetus. Whether the association between chemotherapy and outcomes such as fetal growth restriction is due to the therapy or underlying malignancy is unknown. Literature supporting the short- and long-term neonatal safety of common agents is growing. For malignancies diagnosed closer to term or slowly progressive malignancies, delaying treatment until after delivery to avoid fetal exposure to chemotherapy may be desirable. If delaying therapy may compromise maternal prognosis, then treatment might be initiated after the first trimester of pregnancy with plans to deliver the fetus preterm to avoid excess cumulative exposure to chemotherapy. Neonatal prognosis is most closely linked to gestational age at delivery. Decisions regarding timing of delivery should contextualize this within the natural history of the disease, safety of the proposed treatment, and the person’s goals of care.

NEUROLOGIC DISORDERS

Neurologic complaints such as headaches or neuropathies are common in pregnancy, and differentiating bothersome symptoms from life-threatening pathology is challenging (Chap. 437). While most complaints are benign, cerebrovascular accidents (CVAs) should be high on the differential diagnosis and evaluated with MRI without gadolinium or a head computed tomography (CT) in cases of suspected stroke. Noncontrast MRI is more sensitive than CT in identifying early and small infarcts and cerebral venous thrombosis. Exclusion of preeclampsia is important for any patient presenting with a headache after 20 weeks of gestation with a low threshold to assess for

CVA due to the comparatively high prevalence in this population. Headache in preeclampsia can be associated with the posterior reversible encephalopathy syndrome (PRES), which is on the spectrum of reversible cerebral vasoconstriction syndromes (RCVS) that can present in pregnancy or the postpartum period with neurologic complaints. Peripheral nerve disorders associated with pregnancy include

Bell's palsy (idiopathic facial paralysis) (Chap. 452), carpal tunnel syndrome (median nerve entrapment), or meralgia paresthetica (lateral femoral cutaneous nerve entrapment). Restless leg syndrome (RLS) is the most common peripheral nerve and movement disorder in pregnancy, affecting up to 20% of patients. If serum ferritin is low, oral iron supplementation is a first-line treatment option. Pregnancy is safe for most people with neurologic disorders, with management considerations focusing on medication safety, the impact of pregnancy on the disease, and potential neonatal consequences. For those with epilepsy planning pregnancy, lamotrigine and levetiracetam are first-line monotherapies due to the abundance of safety data. Valproate is known to be associated with congenital malformations and should be discontinued in favor of another medication for people planning to conceive. Folic acid supplementation of 4 mg daily is recommended for those taking antiepileptic drugs (AEDs). Escalating doses of AEDs may be required due to increased clearance in pregnancy and guided by monthly monitoring of AED levels. Patients with preexisting multiple sclerosis (Chap. 455) experience a gradual decrease in the risk of relapses as pregnancy progresses and, conversely, an increase in attack risk during the postpartum period. Prior to conception, disease-modifying therapies (DMTs) should be used to gain control of the disease. DMTs are typically withheld in pregnancy due to the decreased risk of relapse alongside limited neonatal safety data. Relapses should be treated with glucocorticoids, which may be given prophylactically after birth to reduce the risk of postpartum relapse. Finally, certain tumors, particularly pituitary adenoma (Chap. 392) and meningioma, may manifest during pregnancy because of accelerated growth, possibly driven by hormonal factors. Neuroimaging with noncontrast MRI may be required for women with a history of central nervous system (CNS) tumors to facilitate neuraxial analgesia.

GASTROINTESTINAL AND LIVER DISEASE Up to 90% of pregnant people experience nausea and vomiting during the first trimester of pregnancy. Hyperemesis gravidarum (HG) is a severe form that prevents adequate fluid and nutritional intake and may require hospitalization to prevent dehydration and malnutrition. GDF15, which is produced by the placenta and is known to suppress appetite, may be involved in the pathogenesis of HG. Thiamine and folate supplementation and monitoring of electrolytes for evidence of refeeding syndrome should be considered in severe cases with evaluation for supplemental enteral nutrition in refractory disease. Exacerbation of inflammatory bowel disease is common, and medical management, including the use of anti-tumor necrosis factor agents, parallels the nonpregnant state (Chap. 337). Pregnancy is a risk factor for development or worsening of gallbladder disease such as cholelithiasis. This aggravation may be due to pregnancy-induced alteration in the metabolism of bile and fatty acids. Intrahepatic cholestasis of pregnancy is generally a third-trimester event presenting with profound pruritus and confirmed with an elevated level of bile acids with or without transaminitis. The association between cholestasis and stillbirth merits increased fetal surveillance and delivery before term. Symptoms can be improved with the use of ursodiol. Acute fatty liver is a rare complication of pregnancy on the spectrum with HELLP syndrome and preeclampsia. Acute fatty liver of pregnancy is generally distinguished by markedly increased serum levels of bilirubin and ammonia and by hypoglycemia. Management of acute fatty liver of pregnancy includes delivery accompanied by supportive care. Most people recover within

7–10 days after delivery, but reports of fulminant liver failure requiring transplant underscore the importance of prompt diagnosis and management. The association between acute fatty liver in pregnancy and long-chain 3-hydroxyacyl CoA dehydrogenase (LCHAD) deficiency in the fetus informs the recommendation for close monitoring in the newborn with consideration of genetic testing. All pregnant people should be screened for hepatitis B virus with HBsAg testing and hepatitis C virus (Chap. 350). All infants receive hepatitis B vaccine, but infants born to mothers who are carriers of hepatitis B surface antigen should also receive hepatitis B immune

globulin as soon after birth as possible to decrease the risk of vertical transmission. The presence of the hepatitis B E antigen in the mother and high viral load increase the risk of vertical transmission. Strategies to decrease vertical transmission of hepatitis C are limited to avoiding procedures (i.e., amniocentesis) that increase the risk. Postpartum referral to a specialist for consideration of potentially curative therapy is indicated.

INFECTIONS ■ ■ BACTERIAL INFECTIONS All pregnant patients are screened prenatally for syphilis, gonorrhea, and chlamydial infections, and the detection of any of these should result in prompt evaluation and treatment (Chaps. 161, 187, and 194). Other than bacterial vaginosis, the most common bacterial infections during pregnancy involve the urinary tract (Chap. 140). All pregnant people should be screened with a urine culture for asymptomatic bacteriuria at the first prenatal visit. Pregnancy is an indication for treatment of asymptomatic bacteriuria to avoid pyelonephritis. Progesterone-mediated ureteral and bladder smooth muscle relaxation, coupled with compression effects of the enlarging uterus, promote stasis and increase the risk of these conditions. Pregnant women who develop pyelonephritis should be treated with inpatient IV antibiotic administration due to the elevated risk of urosepsis and acute respiratory distress syndrome in pregnancy-associated pyelonephritis. Pregnant people with recurrent urinary tract infections or one episode of pyelonephritis should receive daily antibiotic suppressive treatment throughout the remainder of their pregnancy. Options for suppressive treatment include nitrofurantoin (50 or 100 mg at bedtime) or cephalexin (250 or 500 mg at bedtime).

CHAPTER 491 Medical Disorders During Pregnancy ■ ■ VIRAL INFECTIONS All pregnant people should be screened for hepatitis B virus, hepatitis C virus, and HIV as well as immunity to rubella and varicella. Screening for varicella immunity begins with obtaining a history of varicella immunization or infection. Testing for antibodies to varicella is reserved for cases where there is no history of prior immunization or infection, because the available varicella antibody test has low sensitivity and does not reliably detect antibodies in people who have been immunized. Influenza (See also Chap. 206) Pregnant people with influenza are at increased risk of serious complications and death. All people who are pregnant or plan to become pregnant in the near future should receive inactivated influenza vaccine. The prompt initiation of antiviral treatment is recommended for pregnant people in whom influenza is suspected. Treatment can be reconsidered once the results of high-sensitivity tests are available. Prompt initiation of treatment lowers the risk of admission to an intensive care unit and death. COVID-19 Pregnancy is a risk factor for severe COVID-19 infection. All unvaccinated people planning pregnancy or who are pregnant should receive a COVID-19 vaccine. Cytomegalovirus Infection The most common cause of congenital viral infection in the United States is cytomegalovirus (CMV) (Chap. 200). As many as 50–90% of women of childbearing age have antibodies to CMV, but only rarely does CMV reactivation result in neonatal infection. More commonly, primary CMV infection during pregnancy creates a risk of congenital CMV. No currently accepted treatment of CMV infection during pregnancy has been demonstrated to protect the fetus

effectively. Severe CMV disease in the newborn is characterized most often by petechiae, hepatosplenomegaly, and jaundice. Chorioretinitis, microcephaly, intracranial calcifications, hepatitis, hemolytic anemia, and purpura may also develop. CNS involvement can result in the development of psychomotor, ocular, auditory, and dental abnormalities over time. People with a primary CMV infection should delay conception for 6 months. Herpesvirus Infection (See also Chap. 197) The acquisition of genital herpes during pregnancy is associated with spontaneous

abortion, prematurity, and congenital and neonatal herpes. Disseminated neonatal herpes carries with it high mortality and morbidity rates from CNS involvement. A cohort study of pregnant people with no evidence of previous herpesvirus infection demonstrated that ~2% acquired a new herpesvirus infection during the pregnancy and ~60% of the newly infected women had no clinical symptoms. The risk of transmission was increased in those with infections closer to delivery. The risk of active genital herpes lesions at term can be reduced by prescribing acyclovir (400 mg three times daily) for the last 4 weeks of pregnancy to all people who had an episode of genital herpes during the pregnancy. Those with active genital herpes lesions at the time of presentation in labor should be delivered by cesarean section.

Rubella (See also Chap. 212) Rubella virus is a known teratogen; first-trimester rubella carries a high risk of fetal malformations, although the risk significantly decreases later in pregnancy. Congenital rubella infection may be diagnosed by percutaneous umbilical-blood sampling with the detection of IgM antibodies in fetal blood. All pregnant people or those considering pregnancy should be tested for their immune status to rubella. Parvovirus Infection (See also Chap. 202) Infection with human parvovirus B19 may occur during pregnancy with the possibility of fetal transmission in the absence of immunity. It rarely causes significant maternal sequelae but can lead to erythroid aplasia in the fetus with resultant anemia, fetal hydrops, and death. Management includes screening for fetal anemia with Doppler assessment of the middle cerebral artery and consideration of intrauterine transfusion of red blood cells to the fetus to avoid the physiologic consequences of anemia while awaiting recovery of the fetal bone marrow. PART 19 Consultative Medicine HIV Infection (See also Chap. 208) The predominant cause of HIV infection in children is transmission of the virus from mother to newborn during the perinatal period. All pregnant women should be screened for HIV infection. Factors that increase the risk of mother-to-newborn transmission include high maternal viral load, low maternal CD4+ T-cell count, prolonged labor, prolonged duration of membrane rupture, and the presence of other genital tract infections, such as syphilis or herpes. Antiretroviral therapy (ART) has decreased the rate of perinatal transmission from 20% to ~1%. For those receiving antepartum ART, viral load guides the decision for vaginal versus cesarean delivery and need for adjunct intrapartum zidovudine. People with an undetectable viral load are at the lowest risk of transmission and require no additional therapy, whereas those without antepartum ART exposure or with viral loads >1000 copies/mL at delivery require IV zidovudine and a prelabor cesarean delivery, typically scheduled at 38 weeks. Cesarean delivery should be reserved for obstetric indications for women with ≥ 50 but ≤ 1000 copies/mL, and intrapartum zidovudine can be considered. Zika Virus Zika virus (ZIKV) can be transmitted from mother to fetus throughout gestation and often results in severe microcephaly, CNS malformations, and fetal death. Symptomatic pregnant people with relevant epidemiologic exposure within 2 weeks of symptom onset should have serum and urine tested for ZIKV and dengue nucleic acids by nucleic acid amplification test and IgM serology. Sequential obstetrical ultrasound is recommended to assess for fetal growth and anomalies. Couples considering

pregnancy should avoid travel to areas with known mosquito transmission of ZIKV. ■

■ **VACCINATIONS** (See also Chap. 129) For rubella-nonimmune individuals contemplating pregnancy, measles-mumps-rubella vaccine should be administered, ideally at least 3 months prior to conception, but otherwise in the immediate postpartum period. All pregnant people should be vaccinated against influenza and COVID-19. Administration of one dose of the tetanus, diphtheria, and pertussis (Tdap) vaccine between 27 and 36 weeks of gestation is recommended to promote maternal IgG production and reduce the risk of neonatal pertussis due to transplacental passage of IgG.

MATERNAL MORTALITY Maternal death is defined as death occurring during pregnancy or within 42 days of completion of pregnancy from a cause related to or aggravated by pregnancy, but not due to accident or incidental causes. The maternal mortality rate is the number of maternal deaths per 100,000 live births. From 1935 to 2007, the U.S. maternal mortality rate decreased from nearly 600/100,000 births to 12.7/100,000 births, rising thereafter. In 2021, the U.S. maternal mortality rate was 32.9/100,000 births. An increasingly complex patient population, with multiple comorbidities, and the COVID-19 pandemic likely contributed to the high rate of maternal death in 2021. There are significant racial and ethnic disparities in the maternal mortality rate, with a nearly fourfold increased risk of death for non-Hispanic black women compared to non-Hispanic white women (69.9 vs 26.6 deaths per 100,000 live births, respectively) (Chap. 11). Women over 40 years of age had a maternal mortality rate of 139 per 100,000 live births. Pregnancy-related death is defined as the death of a person while pregnant or within 1 year of the end of pregnancy from any cause related to or aggravated by pregnancy. Cardiovascular disease, including cardiomyopathy, accounted for nearly a third of pregnancy-related deaths from 2014 to 2017 followed by infection, noncardiovascular medical conditions, hemorrhage, and thrombotic events. The relative contribution of medical disease to pregnancy-related death, coupled with knowledge that one in three pregnancy-related deaths occur 1 week to 1 year after delivery, highlights the role of the specialist in internal medicine in reducing maternal mortality. In some countries in sub-Saharan Africa and southern Asia, the maternal mortality rate is >500/100,000 live births. The most common causes of maternal death in these countries are maternal hemorrhage, hypertensive disorders, infection, obstructed labor, and complications from unsafe pregnancy termination. The health interventions that have the greatest impact on maternal health include improving the following components of the health system: (1) access to contraceptive services in order to space births and limit total family size; (2) access to safe pregnancy termination; (3) presence of trained birth attendants at all deliveries; and (4) transportation to emergency obstetrical centers that can provide intensive medical and surgical services, including cesarean delivery. Maternal death is a global public health tragedy that could be mitigated with the application of modest resources.

SUMMARY With improved diagnostic and therapeutic modalities as well as advances in the treatment of infertility, more patients with serious medical complications will be seeking to become pregnant and will require complex obstetric care. Improved outcomes of pregnancy in these people will be best attained by a multidisciplinary team of internists, maternal-fetal medicine (high-risk obstetrics) specialists, pediatricians, and anesthesiologists assembled to counsel these patients about the risks of pregnancy and to optimize interconception care. The importance of preconception counseling and the impact of events of pregnancy on lifelong disease cannot be overstated. It is the responsibility of all physicians caring for women in the reproductive age group to assess their patients' reproductive plans as part of their overall health evaluation and to integrate pregnancy-related diagnoses into their assessment of future risk for cardiovascular

disease. ■ ■FURTHER READING Crisafulli F et al: Variations of C3 and C4 before and during pregnancy in systemic lupus erythematosus: Association with disease flares and obstetric outcomes. *J Rheumatol* 50:1296, 2023. Ford ND et al: Hypertensive disorders in pregnancy and mortality at delivery hospitalization-United States, 2017-2019. *Morb Mortal Week Report* 71:585, 2022. Fu J et al: Increased risk of major congenital malformations in early pregnancy uses of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers: A meta-analysis. *Diabetes Metab Res Rev* 37:e3453, 2021. Hoyert DL: Maternal mortality rates in the United States, 2021. *NCHS Health E-Stats*. 2023. DOI: <https://dx.doi.org/10.15620/cdc:124678>.

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Parikh NI et al: Adverse pregnancy outcomes and cardiovascular disease risk: Unique opportunities for cardiovascular disease prevention in women: A scientific statement from the American Heart Association. *Circulation* 143:e902, 2021. Regitz-Zagrosek V et al: 2018 ESC guidelines for the management of cardiovascular diseases during pregnancy. *Eur Heart J* 39:3165, 2018. Tita AT et al: Treatment for mild chronic hypertension during pregnancy. *N Engl J Med* 386:1781, 2022. Verlohren S et al: Clinical interpretation and implementation of the sFlt-1/PlGF ratio in prediction, diagnosis and management of pre eclampsia. *Pregnancy Hypertens* 27:42, 2022. Prashant Vaishnava, David I. Sahar, Kim A. Eagle

Medical Evaluation of

the Patient Undergoing Noncardiac Surgery Cardiovascular and pulmonary complications continue to account for major morbidity and mortality in patients undergoing noncardiac surgery. Emerging evidence-based practices dictate that the internist should perform an individualized evaluation of the surgical patient to provide an accurate preoperative risk assessment and stratification that will guide optimal perioperative risk-reduction strategies. This chapter reviews cardiovascular and pulmonary preoperative risk assessment, emphasizing the goal-directed management of patients at elevated risk for adverse cardiovascular outcomes in the perioperative period. In addition, perioperative management of diabetes mellitus and prophylaxis of endocarditis and for venous thromboembolism are reviewed. EVALUATION OF INTERMEDIATE- AND HIGH-RISK PATIENTS Simple, standardized preoperative screening questionnaires, such as the one shown in Table 492-1, have been developed for the purpose of identifying patients at intermediate or high risk who may benefit from a more detailed clinical evaluation. Evaluation of such patients for surgery should always begin with a thorough history and physical examination and with a 12-lead resting

electrocardiogram, in accordance with the American College of Cardiology/American Heart Association guidelines. The history should focus on symptoms of occult cardiac or pulmonary disease. The urgency of the surgery should be determined, as true emergency procedures are associated with unavoidably higher morbidity and mortality risk. Preoperative laboratory testing should be carried out only for specific clinical conditions, as noted during clinical examination. Thus, healthy patients of any age who are undergoing elective surgical procedures without coexisting medical conditions should not require any testing unless the degree of surgical stress may result in unusual changes from the baseline state.

PREOPERATIVE CARDIAC RISK ASSESSMENT

A stepwise approach to cardiac risk assessment and stratification in patients undergoing noncardiac surgery is illustrated in Fig. 492-1. The evaluation begins with characterization of the combined surgical and clinical risk into categories of low (<1%) and elevated risk for major adverse cardiovascular events (MACEs). Select surgeries are associated with very low risk for MACE; these surgeries and procedures include select ophthalmologic surgeries (e.g., cataract surgery), select endoscopic procedures, and select superficial procedures. Patients undergoing these low-risk procedures should proceed to surgery without

TABLE 492-1 Standardized Preoperative Questionnaire

1. Age, weight, height
 2. Are you: Female and 55 years of age or older or male and 45 years of age or older? If yes, are you 70 years of age or older?
 3. Do you take anticoagulant medications ("blood thinners")?
 4. Do you have or have you had any of the following heart-related conditions? Heart disease
Heart attack within the last 6 months Angina (chest pain) Irregular heartbeat Heart failure
 5. Do you have or have you ever had any of the following? Rheumatoid arthritis Kidney disease Liver disease Diabetes
 6. Do you get short of breath when you lie flat?
 7. Are you currently on oxygen treatment?
 8. Do you have a chronic cough that produces any discharge or fluid?
 9. Do you have lung problems or diseases?
 10. Have you or any blood member of your family ever had a problem other than CHAPTER 492 nausea with any anesthesia? If yes, describe:
 11. If female, is it possible that you are pregnant? Pregnancy test: Please list date of last menstrual period: Medical Evaluation of the Patient Undergoing Noncardiac Surgery
- aUniversity of Michigan Health System patient information report. Patients who answer yes to any of questions 2–9 should receive a more detailed clinical evaluation. Source: Reproduced with permission from KK Tremper, P Benedict: Paper "Preoperative Computer." *Anesthesiology* 92:1212, 2000. further testing. Clinical risk may be estimated with the American College of Surgeons' National Surgical Quality Improvement Program (NSQIP) risk calculator (<http://www.riskcalculator.facs.org>) or with calculation of the Revised Cardiac Risk Index (RCRI). Additional tools include the Surgical Outcome Risk Tool (SORT) or the American University of Beirut (AUB)-HAS2 Cardiovascular Risk Index. The former is based, in part, on the American Society of Anesthesiologists Physical Status (ASA-PS) grade; the latter provides for estimation of 30-day death, myocardial infarction (MI), or stroke risk. Previous studies have compared several cardiac risk indices. The American College of Surgeons' NSQIP prospective database has identified five predictors

of perioperative MI and cardiac arrest based on increasing age, American Society of Anesthesiologists class, type of surgery, dependent functional status, and abnormal serum creatinine level. However, given its accuracy and simplicity, the RCRI (Table 492-2) is often the favored risk index. The RCRI relies on the presence or absence of six identifiable predictive factors: high-risk surgery, ischemic heart disease, congestive heart failure, cerebrovascular disease, diabetes mellitus treated with insulin, and renal insufficiency with a creatinine >2.0 mg/dL. Each of these predictors is assigned one point. The risk of major cardiac events—defined as MI, pulmonary edema, ventricular fibrillation or primary cardiac arrest, and complete heart block—can then be predicted. Based on the presence of none, one, two, three, or more of these clinical predictors, the rate of development of one of these four major cardiac events is estimated to be 0.4%, 0.9%, 7%, and 11%, respectively (Fig. 492-2). The clinical utility of the RCRI is to identify patients with three or more predictors who are at very high risk ($\geq 11\%$) for cardiac complications and who may benefit from further risk stratification with noninvasive cardiac testing, initiation of preoperative preventive medical management, or avoidance of surgery. For patients at elevated combined clinical and surgical risk for MACE, the stepwise perioperative cardiac assessment for coronary

Patient Needs emergency noncardiac surgery Needs elective noncardiac surgery Exhibits evidence of acute coronary syndrome Perioperative risk for MACE* <1% Perioperative risk for MACE* >1% PART 19 Consultative Medicine Consider noninvasive testing if results would change management Proceed to surgery Proceed to ACS evaluation Proceed to surgery Proceed to surgery Proceed to surgery PERIOPERATIVE MEDICAL INTERVENTION WHEN CONSIDERING NONCARDIAC SURGERY Beta-blockers Statin Alpha agonist • Start in intermediate- to high-risk patients • Should not start on day of surgery • Should not be withdrawn if taking chronically • Continued if on chronically • Start in vascular surgery patients • Considered in patients with clinical indications, undergoing elevated-risk procedures Initiation not recommended prior to noncardiac surgery FIGURE 492-1 Composite algorithm for cardiac risk assessment and stratification in patients undergoing noncardiac surgery. Preoperative evaluation involves a stepwise clinical evaluation. Those individuals requiring emergency surgery should proceed without further risk stratification. Acute coronary syndrome (step 2) should be evaluated and treated according to goal-directed medical therapy. For patients awaiting nonemergent surgeries and without acute coronary syndrome, perioperative risk is a combination of clinical and surgical risk. Select procedures and surgeries (e.g., select endoscopic procedures) are associated with low (<1%) perioperative risk, and no further clinical testing is generally necessary. For those procedures associated with elevated risk, an assessment of functional capacity informs the decision for further testing. Those individuals with moderate or greater functional capacity do not require further testing and should proceed to surgery. Individuals with poor or unknown functional capacity may require pharmacologic stress testing if it would change decision-making or perioperative care. ACE, angiotensin-converting enzyme; ACS, acute coronary syndrome; MACE, major adverse cardiovascular event. (Reproduced with permission from AY Patel et al: Cardiac risk of noncardiac surgery. J Am Coll Cardiol 66:2140, 2015.) artery disease (CAD) proceeds with consideration of functional capacity. Participation in activities of daily living offers an expression of functional capacity, often expressed in terms of metabolic equivalents (METs). For predicting perioperative events, poor exercise tolerance has been defined as the inability to walk four blocks or climb two flights of stairs at a normal pace or to meet a MET level of 4 (e.g., carrying objects of 15–20 lb. or playing golf or doubles tennis) because

of the development of dyspnea, angina, or excessive fatigue (Table 492-3). Patients with moderate or greater (≥ 4 METs) functional capacity (e.g., climbing up a flight of stairs, walking up a hill, or walking on level ground at 4 mph) generally should not undergo further noninvasive cardiac testing prior to elective noncardiac surgery. Those patients with poor (< 4 METs) or unknown functional capacity should undergo pharmacologic stress

- Estimate major adverse cardiac event risk using: • American College of Surgeons National Surgical Quality Improvement Program Surgical Risk Calculator • Revised Cardiac Risk Index, which takes into consideration these factors:

- High-risk surgery
 - History of ischemic heart disease
 - History of congestive heart failure
 - History of cerebrovascular disease
 - Preoperative treatment with insulin
 - Preoperative creatinine > 2 mg/dL
- No evidence of ongoing ACS Functional capacity: Unknown Functional capacity: Excellent Functional capacity: Moderate – Good Functional capacity: Poor Consider noninvasive testing if results would change management ACE inhibitor Aspirin Continued, or if held before surgery, restart postoperatively as soon as clinically feasible Continued when the risk of increased cardiac events outweighs the risk of increased bleeding testing if the results of such testing would impact decision-making or perioperative care. ■ ■ PREOPERATIVE NONINVASIVE CARDIAC TESTING FOR RISK STRATIFICATION There is little evidence to support widespread application of preoperative noninvasive cardiac testing for all patients undergoing major surgery. The current paradigm to guide the need for noninvasive cardiac testing is to perform such testing in patients with poor or unknown capacity if it would alter clinical management or modify perioperative care. Options for pharmacologic stress testing include dobutamine stress echocardiography or myocardial perfusion imaging with coronary vasodilator stress (dipyridamole, adenosine, or regadenoson) with thallium-201 and/or technetium-99m. Similarly, there is a limited

TABLE 492-2 Clinical Markers Included in the Revised Cardiac Risk Index High-Risk Surgical Procedures Vascular surgery (except carotid endarterectomy) Major intraperitoneal or intrathoracic procedures Ischemic Heart Disease History of myocardial infarction Current angina considered to be ischemic Requirement for sublingual nitroglycerin Positive exercise test Pathological Q waves on ECG History of PCI and/or CABG with current angina considered to be ischemic Congestive Heart Failure Left ventricular failure by physical examination History of paroxysmal nocturnal dyspnea History of pulmonary edema S3 gallop on cardiac auscultation Bilateral rales on pulmonary auscultation Pulmonary edema on chest x-ray Cerebrovascular Disease History of transient ischemic attack History of cerebrovascular accident Diabetes Mellitus Treatment with insulin Chronic Renal Insufficiency Serum creatinine > 2 mg/dL Abbreviations: CABG, coronary artery bypass grafting; ECG, electrocardiogram; PCI, percutaneous coronary intervention. Source: Adapted from TH Lee et al: Circulation 100:1043, 1999. role for perioperative coronary computed tomography angiography (CCTA) in patients undergoing noncardiac surgery. While some investigators have shown in observational studies that CCTA may improve prediction of MACEs perioperatively when compared to RCRI, there are few data to demonstrate that such improved

prognostication translates to improved outcomes. Furthermore, coronary revascularization before noncardiac surgery is not recommended for the express purpose of reducing perioperative cardiac events. That said, revascularization before noncardiac surgery should be considered in patients if it would RCRI

≥3 Event Rate 0.50% 1.30% 6.00% 11% Std Dev

0.45% 1.10% 5.30% 10.00% 15% Risk stratification Risk of cardiac events 10% 4–7 5% 0.9–1.3

0.4–0.5 0% Low risk Intermediate risk High risk

≥3 Revised Cardiac Risk Index (RCRI) FIGURE 492-2 Risk stratification based on the Revised Cardiac Risk Index; derivation and prospective validation of a simple index for prediction of cardiac risk in patients undergoing major noncardiac surgery. Cardiac events include myocardial infarction, pulmonary edema, ventricular fibrillation, cardiac asystole, and complete heart block. (Adapted from TH Lee et al: *Circulation* 100:1043, 1999.)

TABLE 492-3 Assessment of Cardiac Risk by Functional Status Higher • Has difficulty with adult activities of daily living • Cannot walk four blocks or up two flights of stairs or does not meet a MET level of 4 • Is inactive but has no limitations • Is active: easily does vigorous tasks Risk Lower • Performs regular vigorous exercises Abbreviation: MET, metabolic equivalent. Source: From LA Fleisher et al: *Circulation* 116:1971, 2007. be indicated regardless of the surgery planned and instead according to clinical practice guidelines. In the Coronary Artery Revascularization Prophylaxis trial, there were no differences in perioperative and longterm cardiac outcomes with or without preoperative coronary revascularization; of note, patients with left main disease were excluded. ■ ■RISK MODIFICATION: PREVENTIVE STRATEGIES TO REDUCE CARDIAC RISK Perioperative Coronary Revascularization Prophylactic coronary revascularization with either coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI) provides no short- or mid-term survival benefit for patients without left main CAD or three-vessel CAD in the presence of poor left ventricular systolic function and is not recommended for patients with stable CAD before noncardiac surgery. Although PCI is associated with lower procedural risk than is CABG in the perioperative setting, the placement of a coronary artery stent soon before noncardiac surgery may increase the risk of bleeding during surgery if dual antiplatelet therapy (DAPT) (aspirin and P2Y12) is administered; moreover, stent placement shortly before noncardiac surgery increases the perioperative risk of MI and cardiac death due to stent thrombosis if such therapy is withdrawn prematurely (Chap. 287). It is recommended that, if possible, elective noncardiac surgery be delayed for 6 months after elective PCI and 12 months after acute coronary syndrome. Contemporary stent platforms allow for greater flexibility in the earlier interruption of DAPT; accordingly, time sensitive noncardiac surgery could be a consideration as soon as 1 month of treatment with DAPT has passed. For patients who must undergo noncardiac surgery early (>14 days) after PCI, balloon angioplasty without stent placement appears to be a reasonable alternative because DAPT is not necessary in such patients. CHAPTER 492 Medical Evaluation of the Patient Undergoing Noncardiac Surgery PERIOPERATIVE PREVENTIVE MEDICAL THERAPIES The goal of perioperative preventive medical therapies with β-adrenergic antagonists, hydroxymethylglutaryl-coenzyme A (HMG-CoA) reductase inhibitors (statins), and antiplatelet agents is to reduce perioperative adrenergic stimulation, ischemia, and inflammation, all of which are heightened during the perioperative period. α-ADRENERGIC ANTAGONISTS The use of perioperative beta blockade should be based on a thorough assessment of a patient's

perioperative clinical and surgery-specific cardiac risk (e.g., as with the RCRI). The paradigm for beta blockade in the perioperative period has shifted in recent years owing, first, to the publication of the PeriOperative Ischemic Evaluation (POISE) trial demonstrating that, while perioperative beta blockade reduces the perioperative risk for MI, this is at the expense of increased death and stroke. Regarding POISE, this trial has been scrutinized for the use of an excessive dose of beta blocker in the perioperative period and one that may not be reflective of clinical practice, nor one that was titrated in the days or weeks preceding the procedure or surgery. Second, research misconduct has discredited the Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography (DECREASE) family of studies, which previously contributed to the bedrock of data supporting the use of perioperative beta blockade but have now been retracted. 9–11

Current guidelines emphasize the following key points:

1. Continuation of beta blockade in patients undergoing surgery and who have been receiving such therapy chronically.
 2. Avoidance of beta-blocker withdrawal or initiation on the day of surgery.
 3. Consideration of initiation of beta-blocker therapy perioperatively (ideally far enough in advance to assess safety and tolerability) in very select high-risk patients, namely, those with intermediate- or high-risk ischemia or three or more RCRI risk factors.
- HMG-COA REDUCTASE INHIBITORS (STATINS)** A number of prospective and retrospective studies support the perioperative prophylactic use of statins for reduction of cardiac complications in patients with established atherosclerosis. For patients undergoing noncardiac surgery and currently taking statins, statin therapy should be continued to reduce perioperative cardiac risk. Initiation of statin therapy is reasonable for patients undergoing vascular surgery independent of clinical risk. There is equipoise about the perioperative initiation of statin therapy in patients undergoing other elevated-risk procedures. In the Lowering the Risk of Operative Complications Using Atorvastatin Loading Dose (LOAD) randomized, placebo-controlled trial, the use of 80 mg of atorvastatin within 18 h before surgery and then followed by 40 mg daily for 7 days in statin-naïve patients (24% of whom had a history of cardiovascular disease) did not reduce the risk of major adverse events.
- PART 19 Consultative Medicine ANGIOTENSIN-CONVERTING ENZYME (ACE) INHIBITORS** It is important to maintain continuity of therapy with inhibitors of the reninangiotensin-aldosterone system (when such therapy is used for the treatment of heart failure or hypertension).
- ORAL ANTIPLATELET AGENTS** The 4- to 6-week period following implantation of an intracoronary stent (bare metal or drug eluting) constitutes the period of time of greatest risk for the development of stent thrombosis. If possible, noncardiac surgery should be avoided in this vulnerable period. The duration of DAPT thereafter is dictated by the circumstances in which PCI was performed and whether the indication was stable ischemic heart disease or acute coronary syndrome. For the former among patients treated with a drug-eluting stent (DES), DAPT should be given for at least 6 months. For the latter, DAPT should be given for at least 12 months. However, DAPT may be interrupted to allow for noncardiac surgery 30 days after bare metal stent (BMS) and 6 months after DES, respectively. Elective, noncardiac surgery should be delayed for 5 days since the last dose of clopidogrel; 7 days since the last dose of prasugrel; and 3–5 days since the last dose of ticagrelor. The use of cangrelor, an intravenous reversible P2Y₁₂ receptor antagonist, may be an appealing bridging strategy, although studies of its use in

those undergoing cardiac and noncardiac surgery are limited. If P2Y₁₂ inhibitor therapy (clopidogrel, prasugrel, or ticagrelor) is interrupted or discontinued in patients who have received intracoronary stents, aspirin should be continued perioperatively (save select circumstances where the risk of bleeding may be catastrophic as in neurosurgical or spinal procedures) and the P2Y₁₂ receptor inhibitor should be restarted as soon as possible postoperatively. Decisions surrounding antiplatelet management in the perioperative setting among patients who have received intracoronary stents are complex and should involve multidisciplinary decision-making.

α₂ AGONISTS Based on the results of POISE-2 (a large multicenter, international, blinded randomized clinical trial of aspirin and clonidine), α₂ agonists for prevention of cardiac events are not recommended in patients who are undergoing noncardiac surgery. In this trial, clonidine increased the rate of nonfatal cardiac arrest and clinically important hypotension, while reducing the rate of death or nonfatal MI.

CALCIUM CHANNEL BLOCKERS Evidence is lacking to support the use of calcium channel blockers as a prophylactic strategy to decrease perioperative risk in major noncardiac surgery.

SODIUM-GLUCOSE COTRANSPORTER 2 INHIBITORS The use of sodium-glucose cotransporter 2 (SGLT-2) inhibitors has grown in

TABLE 492-4 Gradation of Mortality Risk of Common Noncardiac Surgical Procedures

Higher	• Emergent major operations, especially in the elderly	• Aortic and other noncarotid major vascular surgery (endovascular and nonendovascular)	• Prolonged surgery associated with large fluid shift and/or blood loss
Intermediate	• Major thoracic surgery	• Major abdominal surgery	• Carotid endarterectomy surgery
	• Head/neck surgery	• Orthopedic surgery	• Prostate surgery
Lower	• Eye, skin, and superficial surgery	• Endoscopic procedures	

Source: Reproduced with permission from LA Fleisher et al: ACC/AHA 2007 Guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery. *Circulation* 116:1971, 2007.

recent years owing to their beneficial impact in patients with and without type 2 diabetes mellitus and with heart failure with either reduced or preserved ejection fraction. However, euglycemic diabetic ketoacidosis is a known, but rare, complication with this therapy and one that may be precipitated by changes in fasting in the perioperative state. Accordingly, SGLT-2 inhibitor therapy should be interrupted for at least 3–4 days prior to scheduled noncardiac surgery.

ANESTHETICS Mortality risk is low with safe delivery of modern anesthesia, especially among low-risk patients undergoing low-risk surgery (Table 492-4). Inhaled anesthetics have predictable circulatory and respiratory effects: all decrease arterial pressure in a dose-dependent manner by reducing sympathetic tone and causing systemic vasodilation, myocardial depression, and decreased cardiac output. Inhaled anesthetics also cause respiratory depression, with diminished responses to both hypercapnia and hypoxemia, in a dose-dependent manner; in addition, these agents have a variable effect on heart rate. Prolonged residual neuromuscular blockade also increases the risk of postoperative pulmonary complications due to reduction in functional residual lung capacity, loss of diaphragmatic and intercostal muscle function, atelectasis, and arterial hypoxemia from ventilation-perfusion mismatch. Several meta-analyses have shown that rates of pneumonia and respiratory failure are lower among patients receiving neuroaxial anesthesia (epidural or spinal) rather than general anesthesia. However, there were no significant differences in cardiac events between the two approaches. Evidence from a meta-analysis of randomized controlled trials supports postoperative epidural analgesia for >24 h for the purpose of pain relief. However, the risk of epidural hematoma in the setting of systemic anticoagulation for venous thromboembolism prophylaxis (see below) and postoperative epidural catheterization must be considered.

PREOPERATIVE PULMONARY RISK ASSESSMENT Perioperative

pulmonary complications occur frequently and lead to significant morbidity and mortality. Clinical practice guidelines recommend the following:

1. All patients undergoing noncardiac surgery should be assessed for risk of pulmonary complications (Table 492-5).
2. While select studies have suggested that quitting smoking shortly before surgery increases the risk for postoperative complications through increased sputum production and/or decreased cough, meta-analysis of the available data has challenged this, and all patients should be advised of the imperative to stop smoking presurgically.
3. Patients undergoing emergency or prolonged (3–4 h) surgery; aortic aneurysm repair; vascular surgery; major abdominal, thoracic, neurologic, head, or neck surgery; and general anesthesia should

TABLE 492-5 Predisposing Risk Factors for Pulmonary Complications

1. Upper respiratory tract infection: cough, dyspnea
2. Age >60 years
3. Chronic obstructive pulmonary disease
4. Cigarette use
5. American Society of Anesthesiologists Class ≥ 2
6. Functional dependence
7. Congestive heart failure
8. Serum albumin <3.5 g/dL
9. Obstructive sleep apnea
10. Impaired sensorium (confusion, delirium, or mental status changes)
11. Abnormal findings on chest examination
12. Alcohol use
13. Weight loss
14. Spirometry threshold before lung resection a. FEV1 <2 L b. MVV <50% of predicted c. PEF <100 L or 50% predicted value d. PCO₂ ≥ 45 mmHg e. PO₂ ≤ 50 mmHg Abbreviations: FEV1, forced expiratory volume in 1 s; MVV, maximal voluntary ventilation; PCO₂, partial pressure of carbon dioxide; PEF, peak expiratory flow rate; PO₂, partial pressure of oxygen. Source: A Qaseem et al: Ann Intern Med 144:575, 2006. Modified from GW Smetana et al: Ann Intern Med 144:581, 2006, and from DN Mohr et al: Postgrad Med 100:247,
15. be considered to be at elevated risk for postoperative pulmonary complications. 4. Patients at higher risk of pulmonary complications should undergo incentive spirometry, deep breathing exercises, cough encouragement, postural drainage, percussion and vibration, suctioning and ambulation, intermittent positive-pressure breathing, continuous positive airway pressure, and selective use of a nasogastric tube for postoperative nausea, vomiting, or symptomatic abdominal distention to reduce postoperative risk. Multiple pulmonary risk indices are available to estimate the postoperative risk of respiratory failure, pneumonia, and other pulmonary complications; among these is the ARISCAT risk index, which accounts for the following seven risk factors: age, low preoperative oxygen saturation, respiratory infection within the preceding month, upper abdominal or thoracic surgery, surgery lasting >2 h, hemoglobin <10 g/dL, and emergency surgery

(Table 492-6). 5. Preoperative spirometry and chest radiography should not be used routinely for predicting risk of postoperative pulmonary complications but may be appropriate for patients with chronic obstructive pulmonary disease or asthma. 6. Spirometry is of value before lung resection in determining candidacy for coronary artery bypass; however, it does not provide a spirometric threshold for extrathoracic surgery below which the risks of surgery are unacceptable. 7. Pulmonary artery catheterization, administration of total parenteral nutrition (as opposed to no supplementation), or total enteral nutrition has no consistent benefit in reducing postoperative pulmonary complications.

PERIOPERATIVE MANAGEMENT AND PROPHYLAXIS ■ ■ DIABETES MELLITUS (See also Chaps. 415-417) Many patients with diabetes mellitus have significant symptomatic or asymptomatic CAD and may have silent myocardial ischemia due to autonomic dysfunction. Intensive (vs lenient) glycemic control in the perioperative period is generally not associated with improved outcomes and may increase the risk of hypoglycemia. Practice guidelines advocate a target glucose range of 100–180 mg/dL in the perioperative period. Oral hypoglycemic

TABLE 492-6 Risk Modification to Reduce Perioperative Pulmonary Complications

Preoperatively • Smoking cessation • Training in proper lung expansion techniques • Inhalation bronchodilator and/or steroid therapy, when indicated • Control of infection and secretion, when indicated • Weight reduction, when appropriate

Intraoperatively • Limited duration of anesthesia • Avoidance of long-acting neuromuscular blocking drugs, when indicated • Prevention of aspiration and maintenance of optimal bronchodilation

Postoperatively • Optimization of inspiratory capacity maneuvers, with attention to: • Mobilization of secretions • Early ambulation • Encouragement of coughing • Selective use of a nasogastric tube • Adequate pain control without excessive narcotics

CHAPTER 492 Source: From VA Lawrence et al: *Ann Intern Med* 144:596, 2006, and WF Dunn, PD Scanlon: *Mayo Clin Proc* 68:371, 1993.

agonists should not be given on the morning of surgery. Perioperative hyperglycemia should be treated with IV infusion of short-acting insulin or subcutaneous sliding-scale insulin. Patients whose diabetes is diet controlled may proceed to surgery with close postoperative monitoring.

Medical Evaluation of the Patient Undergoing Noncardiac Surgery ■ ■ INFECTIVE ENDOCARDITIS (See also Chap. 133) Prophylactic antibiotics should be administered to the following patients before dental procedures that involve manipulation of gingival tissue, manipulation of the periapical region of teeth, or perforation of the oral mucosa: those with prosthetic cardiac valves (including transcatheter prosthetic valves); prosthetic material used in valve repair (annuloplasty ring or artificial chord); previous infective endocarditis; cardiac transplant recipients with valvular regurgitation from a structurally abnormal valve; and unrepaired cyanotic congenital heart disease or repaired congenital heart disease, with residual shunts or valvular regurgitation at the site adjacent to the site of a prosthetic patch or prosthetic device.

■ ■ AORTIC STENOSIS Previous American College of Cardiology/American Heart Association guidelines have cautioned against surgery in patients with severe aortic stenosis, citing a 10% mortality risk. More recent guidance, rooted in contemporary data, offers greater latitude for noncardiac surgery in appropriately selected patients with severe aortic stenosis. In an analysis of patients undergoing moderate- or high-risk surgery at the Mayo Clinic from 2000 to 2010, there was no significant difference in 30-day mortality between those with severe aortic stenosis and matched controls (5.9 vs 3.1%, $p = .13$); however, those with severe aortic stenosis had more MACEs (18.8 vs 10.5%, $p = .01$), mainly due to heart failure. In sum, severe aortic stenosis is associated with adverse outcomes in patients undergoing noncardiac surgery; however, in contemporary cohorts, this risk is less than has previously been stated. Patients with severe symptomatic aortic stenosis should generally undergo aortic valve intervention (surgical aortic

valve replacement or transcatheter aortic valve implantation) if noncardiac surgery can be deferred. Asymptomatic patients with severe aortic stenosis and preserved ejection fraction can generally safely undergo low- or intermediate-risk noncardiac surgery. Balloon valvotomy is usually not recommended but may serve a role in the minority of patients who need “bridging” to a necessary surgery or procedure. ■ ■ **VENOUS THROMBOEMBOLISM** (See also Chap. 290) Perioperative prophylaxis of venous thromboembolism should follow established guidelines of the American College of

Chest Physicians. Aspirin is not supported as a single agent for thromboprophylaxis. Low-dose unfractionated heparin (≤ 5000 units SC bid), low-molecular-weight heparin (e.g., enoxaparin, 30 mg bid or 40 mg qd), or a pentasaccharide (fondaparinux, 2.5 mg qd) is appropriate for patients at moderate risk; unfractionated heparin (5000 units SC tid) is appropriate for patients at high risk. The use of direct oral anticoagulants may be an alternative to the use of prophylactic doses of low-dose unfractionated heparin and low-molecular-weight heparin; among patients immobilized after nonmajor orthopedic surgery, rivaroxaban 10 mg once daily when compared to enoxaparin was associated with a decrease in venous thromboembolic events, without a significant change in bleeding. Graduated compression stockings and pneumatic compression devices are useful supplements to anticoagulant therapy or as alternatives to anticoagulant therapy in patients at excessive bleeding risk.

■ ■ **FURTHER READING** Eagle KA et al: Perioperative cardiovascular care for patients undergoing noncardiac surgical intervention. *JAMA Intern Med* 175:835, 2015. Fleisher LA et al: 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: A report of the American College of Cardiology/ American Heart Association Task Force on Practice Guidelines. *Circulation* 130:e278, 2014. PART 19 Consultative Medicine

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