Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Arrhythmias CHF Myocardial ischemia	Palpitations DOE Orthopnea PND Angina	Narrow pulse pressure, pulsus alternans Displaced PMI Systolic murmur (MR), S_3, S_4 JVD, ascites, pedal edema	ECG, EPS ECHO Stress test Coronary angiography
RESP	Pulm edema	Dyspnea	Rales, wheezes	CXR ABG
GI	Hepatic congestion	Abdominal distension	Hepatomegaly	LFTs, PT, albumin
HEME	Coagulopathy	Bruising		PT/ PTT
RENAL	Renal insufficiency	Oliguria		BUN/Cr, FEN_a
CNS	Cerebral infarcts	Stroke	Focal neurologic deficits	CT, MRI

Key References: Maron BJ, Towbin JA, Thiene G, et al.: Contemporary definitions and classification of the cardiomyopathies: an American Heart Association Scientific Statement from the Council on clinical cardiology, heart failure and transplantation committee; quality of care and outcomes research and functional genomics and translational biology interdisciplinary working groups; and Council on epidemiology and prevention, *Circulation* 113(14):1807–1816, 2006; Sumler ML, Andritsos MJ, Blank RS: Anesthetic management of the patient with dilated cardiomyopathy undergoing pulmonary resection surgery: a case-based discussion, *Semin Cardiothorac Vasc Anesth* 17(1):9–27, 2013.

Perioperative Implications

Preoperative Preparation
- Consider cardiology consultation to optimize pt's cardiac condition.

Monitoring
- ECG with ST-segment analysis.
- Arterial line dependent on invasiveness of surgery.
- Consider PA cath if anticipation of large fluid shifts in moderate- to high-risk surgery.
- TEE is the monitor of choice for the assessment of biventricular function and AV valve regurgitation in invasive surgical cases.

Airway
- None

Preinduction and Induction
- Anesthetic principles are based on afterload reduction, preload conservation, and prevention of tachycardia and myocardial depression.

Maintenance
- Higher doses of volatile anesthetic agents are often poorly tolerated; thus a narcotic-based anesthetic with low-dose volatile agents and/or benzodiazepine supplementation may be preferable.
- Fluid management should be conservative to prevent fluid overload and acute CHF exacerbation.
- Inotropic support may be necessary.

Extubation
- Beware of tachycardia and Htn and treat proactively.

Postoperative Period
- Consider ICU admission and mechanical ventilation if major intraop fluid shifts have occurred.

Adjuvants
- Regional anesthesia techniques are not contraindicated in the absence of coagulopathy and provided that hypotension is prevented.
- ICD management precautions should be taken if applicable.
- DCM predisposes to decreased blood flow to liver and kidney, which prolongs action of many drugs; also increased volume of distribution requires drug dose adjustments.

Anticipated Problems/Concerns
- CHF exacerbation, hemodynamic instability, tachydysrhythmias

Diphtheria

Pierre Moine

Risk
- Approximately 0.001 cases per 100,000 population in USA since 1980 (<5 cases a year).
- Endemic in developing countries.
- Still common in countries where mass immunization programs are not enforced.
- After political changes in Eastern Europe and Central Asia at the end of the 20th century, a resurgence in many vaccine-preventable diseases, including diphtheria, was reported across these countries.
- Risk factors for diphtheria outbreaks: older age (they are not up to date with booster immunization against diphtheria), lack of vaccination, alcoholism, low socioeconomic status, crowded living conditions, and Native American background.

Perioperative Risks
- Early (days after exposure): Respiratory compromise; respiratory arrest; airway obstruction and hemorrhage; conduction abnormalities, dysrhythmia, cardiogenic shock, CHF, myocarditis; shock, coma, and death
- Late (2–6 wk): Myocarditis and polyneuritis

Worry About
- Respiratory diphtheria early toxic manifestations: neck edema, pharyngitis, large pseudomembranes, massive swelling of the tonsils, bull-neck diphtheria (with massive edema of the submandibular and paratracheal region and foul breath, thick speech, and stridor), hoarseness, and difficulty breathing are associated with severe advanced disease/poor prognosis and with a significant early risk of total airway obstruction.
- Late toxic manifestations of diphtheria: polyneuropathy (resembles Guillain-Barré syndrome) and myocarditis (cardiac arrhythmias, conduction abnormalities, or CHF).
- Other complications: Septic arthritis, pneumonia, renal failure, endocarditis, encephalitis, cerebral infarction, and pulmonary embolism.
- Fatal pseudomembranous diphtheria typically occurs in pts with nonprotective antibody titers and in unimmunized pts. Death occurs in 5–10% of respiratory cases. Risk factors for death include bull-neck diphtheria, myocarditis with ventricular tachycardia, atrial fibrillation or complete heart block, an age of >60 y or <6 mo, alcoholism, extensive pseudomembrane elongation, and laryngeal, tracheal, or bronchial involvement, and delayed antitoxin administration.

Overview
- Diphtheria is caused by superficial infection of the respiratory tract or skin with toxin-producing strains of *Corynebacterium diphtheriae*. The pathogens multiply locally and produce diphtheria toxin. This results in necrosis of the mucosal cells and production of a thick, gray pseudomembrane containing fibrin, epithelial cells, bacteria, and neutrophils. Diffusion of toxin in the circulation causes toxic neurologic and myocardial complications.
- The major risk factor for *C. diphtheriae* infection continues to be travel to an endemic country (Indian subcontinent, Africa, or South East Asia).
- Prompt consideration of diphtheria: Severe pharyngitis, difficulty swallowing, respiratory compromise, or signs of systemic disease, including myocarditis or generalized weakness, and presence of a pharyngeal pseudomembrane or an extensive exudate.
- Respiratory diphtheria: Sore throat with low-grade fever and a strongly adherent pseudomembrane of the tonsils, pharynx, or nose. Occasionally weakness, dysphagia, headache, and voice change. The diphtheritic pseudomembrane is gray or whitish, sharply demarcated and tightly adherent to the underlying tissues. Respiratory diphtheria can progress to a swollen so-called bull neck, and the pseudomembrane can progress to cause airway obstruction. Attempts to dislodge the membrane may cause bleeding. Respiratory diphtheria remains the most common clinical presentation.
- Systemic toxin-mediated neurologic and cardiac toxicity of diphtheria: Neuritis and polyneuropathy

(cranial nerve involvement, respiratory and abdominal muscle weakness, generalized sensorimotor polyneuropathy and autonomic manifestations), and myocarditis (dysrhythmia of the conduction tract, dilated cardiomyopathy, congestive failure and circulatory collapse).
- Cutaneous diphtheria: Painful infected skin lesions and nonhealing or enlarging skin ulcers which lack a characteristic appearance. Cutaneous diphtheria has a low mortality rate, rarely associated with myocarditis or peripheral neuropathy.
- Invasive disease: Bacteremia, endocarditis, mycotic aneurysms, osteomyelitis, and septic arthritis.

Etiology

- Corynebacteria are Gram-positive rods (nonsporulating, nonencapsulated, and nonmotile Gram-positive bacillus). Many species from this genus are skin commensals and act only as opportunistic pathogens. Of the many *Corynebacterium* species, three can potentially produce a diphtheria toxin and cause diphtheria or diphtheria-like diseases: *C. diphtheriae*, *C. ulcerans*, and *C. pseudotuberculosis*.
- Historically the most commonly identified causative bacterium is *C. diphtheriae*. Human beings are the reservoir for *C. diphtheriae*, in particular children, and transmission of *C. diphtheriae* occurs from person to person, predominantly from the respiratory tract (via the aerosol route) but occasionally from cutaneous lesions or fomites. The incubation period for respiratory diphtheria is usually 2–5 d but occasionally is longer, with duration of up to 10 d reported.
- Two human isolate phenotypes: Nontoxigenic and toxigenic. *C. diphtheriae*, *C. ulcerans*, and *C. pseudotuberculosis* toxigenic strains express diphtheria exotoxin (mechanism of pathogenesis during human infection) that inhibits protein synthesis and kills susceptible cells. Toxin is produced in the pseudomembranous lesion and distributed to all organ systems through the blood. Toxigenic strains cause pharyngeal/respiratory and cutaneous diphtheria, and systemic diseases. The clinical and epidemiologic significance of nontoxigenic strains remains unclear. Nevertheless, cases caused by nontoxigenic strains have been reported in immunocompromised individuals.
- Laboratory diagnosis is by culture of an isolate of *Corynebacterium* species. qPCR assay identifies *Corynebacterium* species, plus the presence of the *tox* gene (diphtheria exotoxin) in DNA extracts from submitted isolates. If the *tox* gene is detected, the isolate goes to have an Elek test to detect expression of toxin.
- *C. ulcerans* is now more frequently reported and can also cause the same ranges of diphtheria-like illness. By contrast, the *C. ulcerans* reservoir is thought to be animals. It has been reported after consumption of raw dairy products and contact with cattle, pigs, and domestic pets. *C. ulcerans* diphtheria person-to-person transmission is proposed, but is not confirmed. *C. pseudotuberculosis* is also traditionally associated with farm animal contact and dairy products.

Usual Treatment

- Prompt hospitalization in respiratory isolation with close monitoring of cardiac and respiratory function. Cardiac work-up recommended. Airway management might be necessary and should be considered early in the course of disease.
- Determination of toxigenicity status of the strains of *Corynebacterium* is probably the most important aspect of laboratory investigation.
- Start treatments as soon as possible, even before confirmatory tests are completed, due to the high potential for mortality and morbidity.
- Equine DAT, the mainstay of treatment, is available in the USA only through the CDC. DAT neutralizes only non-tissue-bound circulating toxins and should therefore be given early in the course of the disease, on the basis of clinical suspicion rather than laboratory diagnosis. DAT reduces the extent of local disease, as well as the risk of complications of myocarditis and neuropathy. Rapid institution of DAT is associated with a significant reduction in mortality risk. The protective effect is described for both *C. diphtheriae* and *C. ulcerans*. DAT should be promptly administered after testing for sensitivity to DAT and without awaiting lab confirmation. DAT is based on horse serum and therefore severe, immediate anaphylaxis may occur.
- Macrolide antimicrobial therapy: Erythromycin remains the mainstay of therapy (erythromycin 500 mg IV q6h [for children, 40–50 mg/kg per day IV in 2 or 4 divided doses]/PO erythromycin 500 mg q6h daily to complete a 14-d course). Newer macrolides (azithromycin, clarithromycin) have shown minimum inhibitory concentrations similar to that for erythromycin.
- Erythromycin adverse effects include an association with prolonged QT syndrome and a theoretical concern of potentiation of myocarditis sequelae from diphtheria toxin. Therefore the appropriateness of erythromycin should be carefully considered.
- Main alternative therapy: Penicillins (procaine penicillin G 600,000 units [for children, 12,500–25,000 U/kg] IM q12h/PO penicillin V 125–250 mg q6h daily to complete a 14-d course)
- Alternative antimicrobial agents: Rifamycins (rifampin), lincosamides (clindamycin), tetracyclines (doxycycline), fluoroquinolones, third- (cefotaxime and ceftriaxone) and fourth-(cefepime) generation cephalosporins, glycopeptides (vancomycin, teicoplanin), lipopeptides (daptomycin), oxazolidinone (linezolid).
- Few cases of multidrug resistance to first-line antimicrobials have been reported. Antimicrobial susceptibility testing on all diphtheria toxin-producing *Corynebacterium* species is strongly recommended.
- Sustained routine campaigns for vaccination of children and adequate boosting vaccination of adults. Age-appropriate vaccination with diphtheria toxoid vaccines and timely decennial boosters should be encouraged to prevent diseases. Administration of diphtheria vaccine is recommended during convalescence because diphtheria infection does not always confer immunity.
- Respiratory diphtheria remains a notifiable disease in USA (national surveillance through the National Electronic Telecommunications System for Surveillance), whereas cutaneous diphtheria is not.
- Potential surgical debridement in cutaneous diphtheria.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Nasal, faucial or proximal pharyngeal, laryngeal diphtheria	Altered speech, pharyngitis, respiratory distress, croupy cough, hoarseness and stridor, chills, sore throat	Neck edema, fever, pharyngitis, large pseudomembranes, massive swelling of the tonsils, "bull-neck" diphtheria	Gram stain, nasopharyngeal swab, throat swab, culture of throat specimens/"membrane," indirect laryngoscopy
CV	Conduction abnormalities, dysrhythmia, cardiogenic shock, CHF, myocarditis	Dyspnea with minimal exertion, symptoms of CHF, palpitations	Tachycardia, ectopic beats, first-degree heart block, second-degree heart block, third-degree block, bundle branch block, atrial fibrillation, signs of CHF	ECG, CXR, serum troponin I, ECHO
RESP	Tracheobronchial diphtheria	Fever, tachypnea, dyspnea, presence of membrane, enlarged anterior cervical lymph nodes, edema of the surrounding soft tissue, "bull neck" appearance	Progressive respiratory compromise with partial to complete respiratory obstruction	Indirect laryngoscopy
HEME/IMMUNE	Systems compromised dependent on amount of toxin			CBC, blood cultures, PCR assays
GU	Proteinuria			UA
DERM/SOFT TISSUE	Cutaneous ulcers	Vesicles, "rolled edge" ulcers		Cultures, tissue biopsy for histopathologic examination
CNS	Interference with phonation, swallowing, respiration, resembles Guillain-Barré syndrome, peripheral polyneuritis	Symptoms depend on involved nerves: Cranial neuropathies, particularly ocular and bulbar palsies, limb weakness with reduced reflexes, limb paralysis, respiratory failure	Cranial nerves (most often III, VI, VII, X), peripheral nerves (motor >sensory)	Nerve conduction study

Key References: MacGregor RR: *Corynebacterium diphtheria* (Diphtheria). In Bennett JE, Dolin R, Blaser MJ, editors: *Mandell, Douglas, and Bennett's principles and practice of infectious diseases,* updated ed 8, Philadelphia, PA, 2015, Elsevier, pp 2366–2372; Moore LS, Leslie A, Meltzer M, et al.: *Corynebacterium ulcerans* cutaneous diphtheria, *Lancet Infect Dis* 15(9):1100–1107, 2015.

Perioperative Implications

Preoperative Preparation

- Initiate prompt treatments with diphtheria antitoxin and antimicrobial therapy.
- Assessment of respiratory distress/airway compromise.
- Assessment of cardiac toxicity (for early detection of rhythm abnormalities. Initiate electrical pacing for clinically significant conduction disturbance and provide pharmacologic intervention for arrhythmias or for heart failure).
- Assessment of neurologic toxicity.
- Assessment of immunization status of exposed healthcare workers.

Monitoring

- Maintain close monitoring of cardiac activity for early detection of rhythm abnormalities.
- Provide two large-bore IVs for pts with a toxic appearance; provide invasive monitoring and aggressive resuscitation for pts with septicemia.
- Initiate electrical pacing for clinically significant conduction disturbance and provide pharmacologic intervention for arrhythmias or for heart failure.
- Consider PA cath/noninvasive cardiac output monitoring or transesophageal echocardiography to assess degree of myocardial involvement.

Airway

- Secure definite airway for pts with impending respiratory compromise or the presence of laryngeal membrane (careful manipulation as membrane will bleed if manipulated).
- Early airway management allows access for mechanical removal of tracheobronchial membranes and prevents the risk of sudden asphyxia through aspiration.

Induction and Maintenance

- Compensate for problems of exotoxin shock and possible CHF, as well as cardiac arrhythmia.

Extubation

- Early: May need prolonged ventilation.
- Late: Cardiogenic shock/extensive polyneuritis may necessitate prolonged ventilatory support.

Adjuvants

- Cardiac pacemaker for arrhythmia control/complete heart block.
- Minimize use of sedative-hypnotics because development of respiratory difficulties may be obscured.

Postoperative Period

- Careful observation for respiratory, cardiac, and neurologic compromises

Anticipated Problems/Concerns

- Airway obstruction requiring tracheostomy/intubation
- Myocardial conduction problems that may necessitate electrical pacing
- Cardiogenic shock/CHF
- Neuritis that can present as a Guillain-Barré-like syndrome

Disseminated Intravascular Coagulation

Adrian Hendrickse

Risk

- Most common coagulopathy in the ICU.
- 1% of all hospital admissions.
- Evidence of a coagulopathy in the DIC spectrum approaches 90% in cases of severe sepsis.
- The most important initiator of DIC is sepsis, along with trauma (hypovolemic shock, extensive tissue damage, fat embolism, head injury); surgery (neurosurgery, CPB); obstetric emergencies (hemorrhage, preeclampsia, retained products, amniotic fluid embolism); malignancy (acute promyelocytic leukemia, disseminated metastases); and severe liver disease. Vascular abnormalities, immunologic reactions, toxins, and drugs can also cause DIC.
- Mortality: Dependent on the underlying condition and the severity of the coagulopathy.

Perioperative Risks

- Existing coagulopathy
- Organ failure

Worry About

- Excessive bleeding from surgical and anesthetic access sites
- Organ dysfunction and the need for supportive measures
- Coordinating the management of the coagulopathy

Overview

- DIC is a syndrome characterized by the pathologic imbalance of the coagulation, anticoagulation, and fibrinolytic processes, leading to systemic intravascular thrombosis and the deposition of fibrin in the microcirculation. DIC exists as a spectrum of clotting disorders, the two ends being acute (life-threatening) and chronic (subclinical).
- Acute DIC exists when there is a rapid activation of the coagulation system resulting in the consumption of platelets and the depletion of clotting factors at a rate greater than the body can compensate for, which can lead to excessive hemorrhage. Chronic DIC is a slower affair where the rate of consumption of platelets and clotting factors can be compensated for and where the clinical picture is generally that of microvascular thrombosis.
- Dx: There are no specific laboratory tests for DIC. DIC can be diagnosed clinically on the basis of the presence of a suitable risk factor, along with a selection of laboratory findings: a rapidly falling platelet count or a count $<100{,}000/mm^3$; prolongation of clotting times (APTT, PTT, INR); the presence of FDPs; a reduction in plasma concentration of coagulation inhibitors (ATIII, protein C); TEG analysis of clot formation and lysis.
- Serial testing showing temporal trends are invaluable.

Etiology

- DIC is initiated in one of two ways:
  - Systemic inflammatory response resulting in the activation of the complement pathway and the release of cytokines leading to systemic coagulation.
  - Activation of the extrinsic pathway of coagulation by the presence of increased concentrations of tissue factor.
- An impairment of fibrinolysis, which normally keeps coagulation localized, also plays its part in the progression of the syndrome.

Usual Treatment

- Primary goal is to treat the underlying condition.
- Mechanical ventilation, invasive monitoring, and hemodynamic support are often required.
- Surgery intended to remove the cause of DIC should not be delayed.
- Early involvement of a hematologist, serial coagulation testing, and communication with the transfusion laboratory to guide the use of blood products is recommended.
- Blood products:
  - PRBCs for significant hemorrhage.
  - FFP for clotting factor deficiencies.
  - Cryoprecipitate infusions to maintain fibrinogen >100 mg/dL.
  - Platelet infusions to keep level $>20{,}000/mm^3$ (in the absence of hemorrhage) or $>50{,}000/mm^3$ (with active bleeding or prior to surgery).
- Pharmacologic agents (limited, mixed, or poor evidence):
  - Heparin may be of benefit in cases in which thrombosis predominates but should be used in the critical care environment for venous thromboembolism prophylaxis .
  - ATIII, activated protein C, and thrombomodulin (if available) have all been used in the care of specific subgroups of hematologic and septic DIC cases with some success.
  - Antifibrinolytic agents (ε-aminocaproic acid, tranexamic acid, aprotinin) are generally not recommended but may be considered in pts with DIC who continue to bleed.