POCKET NOTEBOOK

POCKET ICU

Second Edition

Gyorgy Frendl
Richard D. Urman

BRIGHAM AND WOMEN'S HOSPITAL
A teaching hospital of Harvard Medical School

Wolters Kluwer

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Pocket ICU

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PREFACE

Critical (intensive) care was born and remains a multidisciplinary specialty. This is obvious in two facets of critical care: (a) it integrates knowledge and practices from many medical specialties (trauma, transplant medicine, cardiology, pulmonary medicine, anesthesiology and pain medicine, and many others); and (b) it requires the close collaboration of medical professionals from many specialties (physicians, nurses, physiotherapists, respiratory therapists, nutritionists, pharmacists, etc.). To achieve this, critical care professionals must be masters of communication, team building, management, and possess the most up-to-date clinical knowledge.

Since its inception in the polio era in the 1950s, critical care has grown beyond adolescence and now is considered to be an evidence-based specialty. In the past 15 years, dozens of high-quality clinical trials built a solid scientific foundation for critical care and allowed us to significantly improve both patient survival and the quality of their lives following critical illness. This is obvious as evidenced by the much improved survival from ARDS and sepsis. In this book, our goal was to highlight this extensive body of knowledge for our readers in an easy to view format.

As we reach for personalized (individualized) medicine to custom tailor our management of the patient, provide care for the elderly in their 80s and 90s, treat diseases that were untreatable just years before, the knowledge has to be solid and the commitment firm. Critical care professionals will always put their patients first. The challenges remaining are substantial and will require a well-trained, collaborative, patient-centered, and cost-effective effort from all of us. The era of precision medicine is becoming a reality in cancer care and is expanding to other medical specialties. Critical care is not far behind in this effort.

This significantly updated and reorganized second edition is intended to provide concise, evidence-based information for all critical (intensive) care professionals, as well as for those who are having their first encounter with ICUs and critically ill patients. To accomplish our goals, we solicited contributions from many leading critical care experts, incorporated the most recent evidence, improved the table of contents and the indexing of the book. We are grateful for our authors' clinical insights and for sharing their many years of experience.

The rewards of providing care for the most needy are great. With our book, we invite all of you for a great and satisfying professional journey.

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CONTENTS

EXTRACORPOREAL MEMBRANE OXYGENATION AND VENTRICULAR ASSIST DEVICES

Gaurav Budhrani, James M. Blum

- Introduction to ECMO
- Ventricular Assist Devices
- Minimally Invasive Interventions

HEMATOLOGY, FLUID AND ELECTROLYTE MANAGEMENT

Yasser El Kouatli, Lena M. Napolitano

- Hematology
- Transfusion and Transfusion Triggers in the ICU
- Venous Thromboembolism and Pulmonary Embolism, Prevention Strategies
- Electrolytes
- Fluid Resuscitation and IV Replacement Solutions

INFECTIOUS DISEASE, SEPSIS, AND THE SURVIVING SEPSIS GUIDELINES

David Oxman, Ankit Gupta, Gyorgy Frendl

- Evaluation of New Fever in the Critically Ill Patient
- Nosocomial Infections
- Principles for the Use of Antibiotics in the ICU
- Sepsis and Septic Shock
- Summary of Recommendations—Surviving Sepsis Campaign 2012
- Summary of National Quality Forum/Surviving Sepsis Campaign Management Bundles/Milestones
- Severe Acute Pancreatitis: Pancreatitis with Persistent Organ Failure >48 Hours

ENDOCRINE DISORDERS AND RENAL ISSUES IN THE ICU AND RENAL ISSUES

Ernest I. Mandel, Kenneth B. Christopher

- Hyperglycemia—Diabetic Emergencies
- Glycemic Control
- Adrenal Insufficiency
- Thyroid Disease
- Renal Issues Encountered in the ICU

COMMON ICU PROBLEMS

RAGHU SEETHALA, MD

HYPERKALEMIA (also see Chapter 22)

Serum **K** >**5.0** mmol/l, severe hyperkalemia >**6.0** mmol/l

Causes

Renal insufficiency
Adrenal insufficiency
Insulin deficiency
Tissue damage from rhabdomyolysis, trauma, or burns
Medication related
Acidosis

Clinical Manifestations

Peaked T waves on ECG; hyperkalemia depolarizes the cardiac membrane leading to further ECG changes, like widening of QRS (sinusoidal wave forms) which can progress to asystole or ventricular fibrillation
Muscular effects can include paresthesias, weakness, or flaccid paralysis

Management

Stabilize cardiac membrane

Calcium gluconate (10%) 10 ml IV push over 2–3 min, can repeat q5min

Shift potassium intracellularly

Insulin (regular) 10 U IV push with 25 g of Dextrose IV push (if not hyperglycemic)

Albuterol 15–20 mg (β-agonist) nebulized over 10 min

Sodium bicarbonate 50 mmol IV push or 150 mmol/l IV at a variable rate (only use if pt has a severe met acidosis)

Potassium elimination from body

Furosemide (Lasix) 40–80 mg IV push

Sodium polystyrene sulfonate (Kayexalate) 15–30 g in 15–30 ml (70% sorbitol PO)

Do not administer in ileus or bowel obstruction because of risk of colonic necrosis

Hemodialysis (if hyperkalemia is unresponsive to conservative measures listed above)

Shock

Hypoperfusion causing tissue hypoxia resulting in multiorgan dysfunction (also see Chapter 23 for septic shock).

Differential Diagnosis

Hypovolemic
Hemorrhage (trauma, GI bleed, retroperitoneal bleed)
Dehydration (vomiting, diarrhea, GI fistula)
3rd spacing (burns, malnutrition, sepsis, septic shock)
Cardiogenic
MI
Myocarditis
End-stage cardiomyopathy
Valvular failure
CHF
Arrhythmia
Distributive
Sepsis
Anaphylaxis
Liver failure
Neurogenic
Adrenal insufficiency
Drugs
Obstructive
Tension pneumothorax (PTX)
Cardiac tamponade
Constrictive pericarditis
PE
Aortic coarctation

Clinical Manifestations

Hypotension
Tachycardia
Tachypnea
Mottled skin
Cool extremities
Altered mental status
Decreased urine output

Management

Establish & maintain ABCs (airway, breathing, circulation)
Fluid resuscitation
Blood & blood product transfusion
Vasopressors
Inotropes
Hemodynamic monitoring (CVC, arterial line, PA catheter, echocardiogram)
Consider the following resuscitation endpoints for septic shock (the most common type of shock)
CVP 8–12 mm Hg, 12–15 mm Hg if mechanically ventilated
MAP ≥65 mm Hg
Urine output (UOP) ≥0.5 ml/kg/hr
$ScVO_2$ ≥70% or MVO_2 ≥65%
Lactate clearance
Identification & treatment of underlying problem including source control in septic shock

Sepsis

Life-threatening organ dysfunction caused by a dysregulated host response to infection (also see Chapter 23; Singer M, et al. *JAMA*. 2016;315(8):801–810).

Causes

Pneumonia
Catheter-related blood stream Infxn
Sinusitis
Clostridium difficile
Intra-abd (cholecystitis, abscess, peritonitis)
UTI, pyelonephritis
Meningitis, encephalitis
Cellulitis, necrotizing soft tissue Infxn, wound Infxn
Septic arthritis, osteomyelitis
Endocarditis
Fungemia, fungal abscess

Investigations

CBC, electrolytes, BUN/Cr, PT/INR, LFT
Blood cx, urine cx, site-specific cx
ABG/lactate
Procalcitonin
Imaging studies: CXR, site specific CT scan, US, etc.

Management (Dellinger RP, et al. *Crit Care Med*. 2013;41(2):580–637)

Early identification of sepsis

Early fluid therapy—30 cc/kg bolus of crystalloid if hypotensive

Early abx—broad spectrum IV abx therapy within 1st hour

Source identification & control as rapidly as possible

Repeated assessments to measure volume responsiveness. Can use the following:

Bedside cardiovascular US

Dynamic assessment of fluid responsiveness with passive leg raise or fluid challenge

Once pt judged to be volume replete. Administer vasopressors to maintain MAP ≥65 mm Hg (norepinephrine with or without vasopressin as 1st choice)

Outcomes with protocolized care using early goal directed therapy (EGDT) are similar to usual care. Can use the following EGDT endpoints for guidance:

CVP 8–12 mm Hg, 12–15 mm Hg if mechanically ventilated

MAP ≥65 mm Hg

UOP ≥0.5 ml/kg/hr

$ScVO_2$ ≥70% or MVO_2 ≥65%

Consider inotropic therapy with dobutamine for sepsis induced cardiac dysfunction

May consider corticosteroids when hypotension is not responding to fluid resuscitation & vasopressors (ACTH stimulation test is no longer recommended)

Supportive therapy (ARDSnet ventilation strategy, glycemic control to keep blood glucose in the 140–160 mg/dl range, renal replacement, stress ulcer ppx, DVT ppx)

Arrhythmias (see Chapter 9 for ACLS)

Bradyarrhythmia: HR <60 bpm

Differential Diagnosis

SA node dysfunction
Sinus arrest
SA conduction block
Sick sinus syndrome
AV node dysfunction
1st-degree AV block
2nd-degree AV block Mobitz type I
2nd-degree AV block Mobitz type II
3rd-degree AV block
Junctional escape rhythm
Ventricular escape rhythm
Sinus bradycardia

Management

12-lead ECG
Atropine 0.5 mg IV bolus repeat 3–5 min (maximum 3 mg)
Dopamine IV infusion 2–10 mcg/kg/min
Epinephrine IV infusion 2–10 mcg/min
Transcutaneous pacing (consider pacing for symptomatic bradycardias, 3rd-degree AV block, Mobitz type II 2nd-degree block)
Transvenous pacing
Treat underlying cause

Tachyarrhythmia: HR >100 bpm

Differential Diagnosis

Narrow complex tachycardia
Sinus tachycardia
Focal atrial tachycardia
Atrial fibrillation
Multifocal atrial tachycardia
Atrial flutter
Junctional tachycardia
AV node reentry tachycardia
AV reentry tachycardia
Wide complex tachycardia
Monomorphic VT
Polymorphic VT
SVT with aberrancy
Pre-excitement tachycardia (WPW)

Management

12-lead ECG
If unstable (hypotension, altered mental status, signs of shock) then proceed to synchronized cardioversion
Narrow regular 50–100 J biphasic
Narrow irregular 120–200 J biphasic or 200 J monophasic
Wide regular: 100 J biphasic; if ineffective, increase Joules (J) in a stepwise fashion
Wide irregular: Defibrillation dose (not synchronized)
Vagal maneuvers for SVT
Adenosine 6 mg IV push (if regular) for paroxysmal SVT
β-Blocker—Metoprolol 2.5–5 mg IV
Calcium channel blocker—Diltiazem 0.25 mg/kg IV followed by infusion
Amiodarone 150 mg IV over 10 min (may consider 150 mg IV repeated dose if unresponsive to 1st loading dose), followed by maintenance infusion (1 mg/min for 6 hrs, reduced to 0.5 mg/min after that)
Treat underlying cause

Atrial Fibrillation

Causes

Alcohol intake
Autonomic dysfunction
Cardiac/thoracic surgery
Cardiomyopathy
Electrolyte abnormality
Heart failure
Hyperthyroidism
MI
Pericarditis
Pulmonary dz
Valvular heart dz

Management

If unstable then synchronized cardioversion

120–200 J biphasic

If <48 hrs consider cardioversion (DC or pharmacologic)

Pharmacologic cardioversion—Amiodarone, Sotalol, Ibutilide, Flecainide

If >48 hrs rate control & anticoagulate (if no contraindications)

Rate control

Metoprolol 5 mg IV q5min total of 15 mg
Diltiazem 0.25 mg/kg IV followed by infusion
Digoxin 0.25 mg IV q2h total of 1.5 mg loading dose
Amiodarone 150 mg IV over 10 min (may consider 150 mg IV repeated dose if unresponsive to 1st loading dose), followed by maintenance infusion (1 mg/min for 6 hrs, reduced to 0.5 mg/min after that)

Treat underlying cause

Hypotension

MAP <60 mm Hg, SBP <90 mm Hg, or decrease in SBP by >40 mm Hg from baseline.
MAP = CO × SVR

Differential Diagnosis

Decrease in CO

Decreased preload

Hypovolemia, hemorrhage, 3rd spacing, decreased venous return, excessive PEEP

Decreased contractility

MI, myocarditis, cardiomyopathy, valvular failure, arrhythmia, CHF, drugs, electrolyte imbalance

Obstruction (to inflow or outflow of cardiac pump)

PE, tension PTX, cardiac tamponade

Decrease in SVR

Sepsis, SIRS, anaphylaxis, neurogenic shock, vasodilating drugs, adrenal insufficiency, liver failure due to decreased SVR

Management

Hemodynamic monitoring (CVC, arterial line, PA catheter, echo)

500 ml NS or LR IVF bolus, then reassess hemodynamics (HR, BP, CO, index [CI], stroke volume, CVP) & repeat IVF bolus prn

Review medications, decrease dose of vasodilating drugs & cardiac depressants (sedatives, opioids, etc.)

Vasopressors (norepinephrine, dopamine, phenylephrine, epinephrine)

Inotropes (dobutamine, milrinone, levosimendan)

Assess for & treat underlying cause

Hypoxemia (also see Chapters 18 & 19)

PaO_2 <60 mm Hg or SpO_2 <90%

Differential Diagnosis

Hypoventilation

COPD, asthma, bronchospasm, inappropriate ventilator settings

CNS depression—drug overdose, CNS lesion

Obesity hypoventilation syndrome

Neuromuscular weakness—myasthenia gravis, critical illness polyneuropathy, Guillain–Barré syndrome, hypophosphatemia

V/Q mismatch

Most common cause of hypoxemia in the ICU

Imbalance between lung perfusion & ventilation

Pneumonia, ARDS, pneumonitis, pulmonary edema, PE

Right to left shunt

Intracardiac shunt, pulmonary AVM, hepatopulmonary syndrome

Diffusion impairment (seen rarely in very advanced pulmonary fibrosis, asbestosis)

Usually occurs along with V/Q mismatch

Interstitial lung dz

Reduced inspired FiO_2

High altitude, equipment failure

Investigations

SpO_2

ABG—PaO_2, $PaCO_2$, A-a gradient

PaO_2/FiO_2 ratio

CXR, CT of chest if needed

Management

Initially administer 100% FiO_2, titrate FiO_2 to SpO_2 >90%

Initiate mechanical ventilation if unresponsive to supplemental O_2 therapy

Appropriate ventilator settings (low tidal volume, higher PEEP, adequate RR)

Ensure proper position of ET tube

Bronchoscopy prn (mucous plug, atelectasis, abundant secretions)

Bag mask ventilation if considering equipment failure

Treat underlying cause

Pericardial Tamponade (also see Chapters 25 & 46)

Accumulation of pericardial fluid under pressure compressing all cardiac chambers resulting in cardiovascular collapse.

Differential Diagnosis

Massive PE
Acute MI with RV involvement
Constrictive pericarditis
Large pleural effusion
Tension PTX

Causes

Inflammatory—rheumatoid arthritis (RA), SLE
Malignancy
Uremia
Hypothyroidism
MI with free wall rupture
Trauma
Infectious—viral, TB
Cardiac interventions—pacemaker placement, cardiac catheterization, heart surgery

Clinical Findings

Tachycardia, pericardial friction rub
Beck triad—hypotension, JVD, muffled heart sounds
Pulsus paradoxus
Low-voltage QRS, electrical alternans
Equilibration of diastolic pressures in all chambers of the heart CVP = RVEDP = PCWP = LVEDP
Bedside echocardiogram—right atrium systolic collapse, RV diastolic collapse, distended noncompliant inferior vena cava

Management

Dx made with echocardiography

Optimize preload with IVF bolus in hypovolemic pts

Consider dobutamine, though heart is usually at maximum inotropic state via endogenous stimulation

Definitive therapy is drainage via pericardiocentesis

Cases of intrapericardial bleeding (trauma, postop, tumor) usually require surgical intervention

Tension Pneumothorax (also see Chapter 45)

Progressive accumulation of air in the pleural space that compresses the mediastinum kinking off venous return leading to cardiovascular (CV) collapse.

Differential Diagnosis

Pericardial tamponade
Hemothorax

Causes

Thoracic trauma
Iatrogenic—CVC placement, transthoracic needle biopsies
Spontaneous PTX
Secondary PTX
Barotrauma from mechanical ventilation

Clinical Findings

Distended neck veins
Progressive hypotension (often rapidly severe, may lead to CV collapse)
Tracheal deviation to contralateral side
Absent breath sounds
Absent lung sliding on bedside US

Management

Immediate needle decompression with 14–16 gauge needle in the midclavicular line of the 2nd intercostal space of affected side
Followed by chest tube placement for definitive therapy

Acute Mental Status Change

A spectrum of states including confusion, delirium, obtundation, stupor, & coma.

Differential Diagnosis

Stroke/hemorrhage
Seizure
Encephalitis/meningitis
Delirium
Postcardiac arrest brain injury/anoxic encephalopathy
Drugs (illicit or medication overdose)
Alcohol withdrawal
Thiamine deficiency
Hypo/hyperthyroid
Adrenal insufficiency
Hepatic encephalopathy
Hypo/hyperglycemia
Hypoxia/hypercarbia
Electrolyte abnormality (hypo/hypernatremia, hypercalcemia, hypophosphatemia)
Septic encephalopathy

Investigations

Vitals signs
CT head
Labs—electrolytes, BUN, Cr, CBC, LFTs, ammonia, UA, ABG
Lumbar puncture to evaluate for meningitis/encephalitis
EEG to evaluate for nonconvulsive status epilepticus

Management

Establish & maintain ABCs (airway, breathing, circulation)

Thiamine 100 mg IV (prior to dextrose to prevent precipitating acute Wernicke encephalopathy)

Dextrose 50 ml of D50W (25 g IV push)

Naloxone 0.2–0.4 mg by slow (fractioned) IV push if comatose & suspect opioid intoxication

Search for & treat underlying cause

Flumazenil 0.2 mg IV may be repeated 3 more times with a few minute intervals (to reverse the effects of benzodiazepines; beware of the potential seizure after reversal of benzodiazepine effect). Do not use in pts who chronically use benzodiazepines: the potential for intractable Seizure is much higher in this group.

Low Urine Output—Acute Renal Failure (also see Chapter 24)

Oliguria with <400 ml/24 hr.

Differential Diagnosis

Prerenal

Hypovolemia—GI loss, hemorrhage, burns, sepsis, 3rd spacing
Cardiac dysfunction—MI, CHF, cardiomyopathies, arrhythmias
Vasodilatory shock—sepsis, liver failure, anaphylaxis

Renal

Ischemia/ATN—trauma, surgery, sepsis, rhabdomyolysis
Nephrotoxic—radiocontrast, abx (aminoglycosides), NSAIDs
Vascular—Wegener, HSP, PAN
Glomerular—glomerulonephritis
Interstitial—AIN

Postrenal

Malignancy, enlarged prostate
Nephrolithiasis
Obstructed urinary catheter
Papillary necrosis

Investigations

Urine electrolytes
Urinary sediment
Urine osm
Renal US
Cardiovascular evaluation to r/o pump failure or hypovolemia
Measure serum CK & myoglobin to r/o rhabdomyolysis

Management

Flush or change foley bladder catheter
IV fluid bolus to optimize IV volume status & hemodynamics
Maintain MAP >65 mm Hg to ensure renal perfusion
If adequately volume loaded can consider diuretic (furosemide)
Renal replacement therapy—in cases of acidosis, electrolyte abnormality, volume overload, uremia
Eliminate any nephrotoxins

Fever in the ICU

Temp >38.3°C (101.0°F)

Differential Diagnosis

Infectious

Pneumonia

Catheter-related blood stream Infxn

Sinusitis

C. difficile

Intra-abd (cholecystitis, abscess, peritonitis)

UTI, pyelonephritis

Meningitis, encephalitis

Cellulitis, necrotizing soft tissue Infxn, wound Infxn

Septic arthritis, osteomyelitis

Endocarditis

Fungal

Noninfectious

Neuro—seizures, CVA/intracerebral hemorrhage

Pulmonary—PE, ARDS, atelectasis, pneumonitis

Cardio—pericarditis

GI—pancreatitis, acalculous cholecystitis, mesenteric ischemia

Endocrine—adrenal insufficiency, thyrotoxicosis

Inflammatory conditions—SLE, vasculitis, polymyalgia rheumatica

Miscellaneous—alcohol withdrawal/delirium tremens, drug fever, neuroleptic malignant syndrome (NMS), malignant hyperthermia (MH), postoperative fever

Management

Thorough hx & physical exam looking for infectious etiology
Obtain appropriate cx (2 sets of blood cx, urine cx, sputum cx) & imaging studies (CXR, Abd CT, etc)
Source control (incise, drain, remove) of Infxn
If signs of severe sepsis then broad spectrum abx after obtaining cx
Consider noninfectious causes when Infxn site unclear from diagnostic tests
If febrile >48 hrs:
Remove CVC
If diarrhea present evaluate for *C. difficile*
Consider antifungal therapy
US to evaluate for acalculous cholecystitis
IV dantrolene (2.5 mg/kg, more if needed) is the specific acute phase therapy for malignant hyperthermia related to anesthesia

MONITORING

SAMUEL M. GALVAGNO, JR., DO, PhD, FCCM • JONATHAN H. CHOW, MD

Noninvasive Monitoring

Electrocardiogram (ECG) (see www.ecglibrary.com for sample images)

Can detect transmural & subendocardial ischemia when leads are properly positioned

Lead V_5 has been validated & found to detect 75% of ischemic changes seen in other leads

The combination of leads II, V_2, V_3, V_4, & V_5 has been shown to be over 90% sensitive for detecting ischemia

Temperature Monitoring

Core temp is best estimated from the nasopharynx, bladder, esophagus, or rectum

Rectal temp lags behind PA & tympanic temp in cardiac surgical pts during the rewarming period after bypass

The same is true for pts in shock

This is due to decreased splanchnic blood flow

Subjective assessment of skin temp may be misleading in some instances
(Schey BM, et al. *Heart Lung*. 2010;39(1):27–40.)

Pulse Oximetry (SpO_2)

Monitors SpO_2; monitors *oxygenation, not ventilation*

Has the potential to increase vigilance & detect hypoxemia

Based on the Beer–Lambert law

The concentration of a substance can be determined by transmitting a known intensity of light through a solution

Red light (660 nm) & near-infrared light (940 nm) are transmitted through a vascular bed (typically a finger)

Both of these types of light readily penetrate tissue whereas other wavelengths of light are absorbed

660 nm light is absorbed by reduced Hb

940 nm near-infrared light is absorbed preferentially by oxygenated Hb

A photodiode detector measures the amount of light transmitted, & the red/near-infrared ratio is calculated & compared with reference values

The pulse-added component discriminates from venous blood or connective tissue from arterial blood

Limitations:

Nail polish & dark skin may cause variable interference

Hypovolemia, vasoconstriction, or peripheral vascular dz may cause a low signal-to-noise ratio & inaccurate measurements

Extra ambient light & excessive motion may cause artifacts

Dyshemoglobinemias are a well-established cause of optical interference

Both carboxyhemoglobin & methemoglobin absorb light within the red & near-infrared wavelength ranges

A Co-oximeter offers a multiwavelength analysis that takes into account these absorptions

With methemoglobinemia, standard oximeters falsely detect a greater degree of absorption of both Hb & oxyhemoglobin, increasing the absorbance ratio

When the absorbance ratio reaches 1, the calibrated saturation level approaches a plateau of approx. 85%

The SpO_2 reading will remain at 85%

With carboxyhemoglobinemia, red light is falsely absorbed, & the SpO_2 will be falsely high

Despite prevalent usage, there is little evidence that pulse oximetry prevents deaths, complications, or readmissions to the ICU (Niehoff J, et al. *Crit Care Med*. 1988;16(7):701–705; Pedersen T, et al. *Cochrane Database Syst Rev.* 2014;(3):CD002013.)

Nevertheless, monitoring oxygenation with pulse oximetry is a standard of care in the ICU

Capnography (see www.capnography.com for more information)

Refers to the digital display of CO_2 on a digital or analog monitor

Is a standard monitor for noninvasively measuring *ventilation*

Indications in the ICU

Confirmation of ET intubation

Noninvasive monitoring of ventilation (esp. during positional changes)

Assessment of CO (see additional section below)

Prognosis when CPR is required

Prediction of outcome during resuscitation for trauma

Confirmation of needle placement during percutaneous dilatational tracheostomy

Colorimetric CO_2 detection *or* capnography has become the standard of care for confirming that an ETT has been placed correctly (in addition to other clinical determinants)

A purple color corresponds to an $ETCO_2$ level <0.5%, a tan color indicates $ETCO_2$ of 0.5–2%, & a yellow color indicates $ETCO_2$ >2%

Normal $ETCO_2$ is >4%; hence, the device should turn *yellow* when the ETT is inserted in pts with intact circulation

Infrared (IR) spectrography is the most commonly used method for measuring $ETCO_2$

IR rays are absorbed by polyatomic gases such as nitrous oxide, CO_2, & water vapor

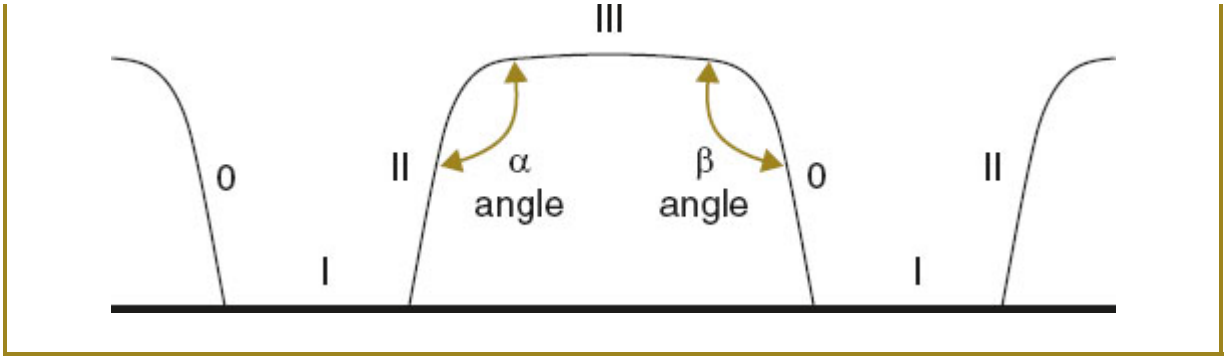
CO_2 selectively absorbs specific wavelengths (4.3 μm) of IR light

The CO_2 concentration measured by the monitor is usually expressed as partial pressure in millimeters of mercury

Some units display % CO_2

Current terminology for capnograms is depicted in Figure 2-1.

Figure 2-1. The Phases of a Capnogram. Phase II Indicates the Beginning of Expiration; Phase 0 Indicates Inspiration. See www.capnography.com for details.



Under normal circumstances, $ETCO_2$ is lower than $PaCO_2$ by 2–5 mm Hg

This gradient is caused by V/Q mismatching in the lungs

This gradient may change in hemodynamically unstable pts or when there are abrupt changes in CO

The $ETCO_2/PaCO_2$ fraction is a measure of alveolar dead space

Provides an indirect measure of V/Q mismatching in the lung

Reductions in $ETCO_2$ also occur with decreased CO & pulmonary blood flow

Causes of increased or decreased $ETCO_2$ are reviewed in the table below.

Causes of Increased or Decreased $ETCO_2$	
Increased $ETCO_2$	**Decreased $ETCO_2$**
Hypoventilation	Hyperventilation
Hyperthyroidism/thyroid storm	Hypothermia
Malignant hyperthermia	Venous air embolism
Fever/sepsis	PE
Rebreathing	Decreased CO
Other hypermetabolic states	Hypoperfusion

Noninvasive Blood Pressure Measurement

Measured by an electronic pressure transducer that detects oscillating blood flow as the cuff is slowly deflated

If the upper extremity used, the brachial artery is compressed & oscillates as restricted blood flows during systole & diastole

The MAP is generally the most accurate component of this type of noninvasive BP measurement

Some studies have shown that oscillatory measurements are often lower than invasive BP measurements

Use of improperly sized cuffs is a common source of error

Brain Monitoring

Useful when heavy sedation is required with or without the use of muscle relaxants

Awareness under anesthesia is estimated to occur in 0.1–0.2% of all pts undergoing general anesthesia; the risk may be higher for ICU pts who require prolonged sedation with or without muscle relaxation

Awareness during sedation or paralysis in the ICU has not been as thoroughly studied as in the general surgical population

Several brain monitors based on electroencephalographic (EEG) indices are commercially avail.

The Bispectral Index (BIS; Aspect Medical Systems, Norwood, MA) is the best studied & the most widely used brain monitor

A dimensionless index is calculated using a proprietary algorithm derived empirically by recording EEG data from healthy adults undergoing various levels of anesthesia

The index ranges from 0 to 100

BIS values between 45 & 60 are considered ideal for surgical anesthesia

BIS levels <45 have been associated with poor outcomes, including increased morbidity & mortality

Other brain monitors include the Entropy Index, the Cerebral State Index, & the SEDLine monitor (Maisimo Corp, Irving, CA)

Invasive Monitoring

Direct Arterial Pressure Monitoring

Indications:

Continuous BP measurement, need for beat-to-beat BP monitoring

Need for frequent ABG determinations or blood sampling

When noninvasive BP monitoring is not reliable or possible

Common locations for cannulation include the radial, femoral, dorsalis pedis, brachial, & axillary arteries

The radial artery is the most commonly utilized site

The ulnar artery has been reported in some studies to be larger, but is typically avoided due to proximity to the ulnar nerve & the potential for hand ischemia

Although most texts report the ulnar artery to be larger than the radial artery, significant anatomical variation exists (Brzezinski M, et al. *Anesth Analg*. 2009;109(6): 1763–1781.)

The few studies addressing the use of the ulnar artery for cannulation have reported a safety & efficacy profile comparable to radial artery cannulation

Contraindications:

Infxn at the cannulation site

Lack of collateral flow

Can be assessed with the Modified Allen test for radial cannulation:

Pressure is held firmly over the radial & ulnar arteries

The pt clenches his or her fist several times until the palmar skin is blanched

The pt unclenches the fist, & the ulnar artery pressure is released while maintaining pressure on the radial artery

The time for palmar capillary refill is noted; brisk return of skin color indicates adequate collateral circulation as supplied by the ulnar artery

The test is not reliable for predicting hand ischemia after radial artery cannulation

Other assessments include addition of a pulse oximeter during the Allen test, Doppler US, & plethysmography

Lymphatic disruption at the site of insertion

Arterial insufficiency at the site of insertion

Complication rates (radial artery):

Hematoma—14.4%

Catheter-related bacterial colonization—1–22%

Local Infxn—0.72%

Bleeding—0.5%

Sepsis—0.13%

Pseudoaneurysm—0.09%

Permanent hand ischemia—0.09%

Catheter maintenance after placement

Current guidelines from the Centers for Dz Control do not recommend routine replacement of peripheral arterial catheters at fixed intervals to prevent Infxn

Many institutions now suggest that maximum barrier precautions (as used during placement of CVC) should be used for arterial lines since some studies have shown similar Infxn rates (Lucet JC, et al. *Crit Care Med.* 2010;38(4):1030–1035.)

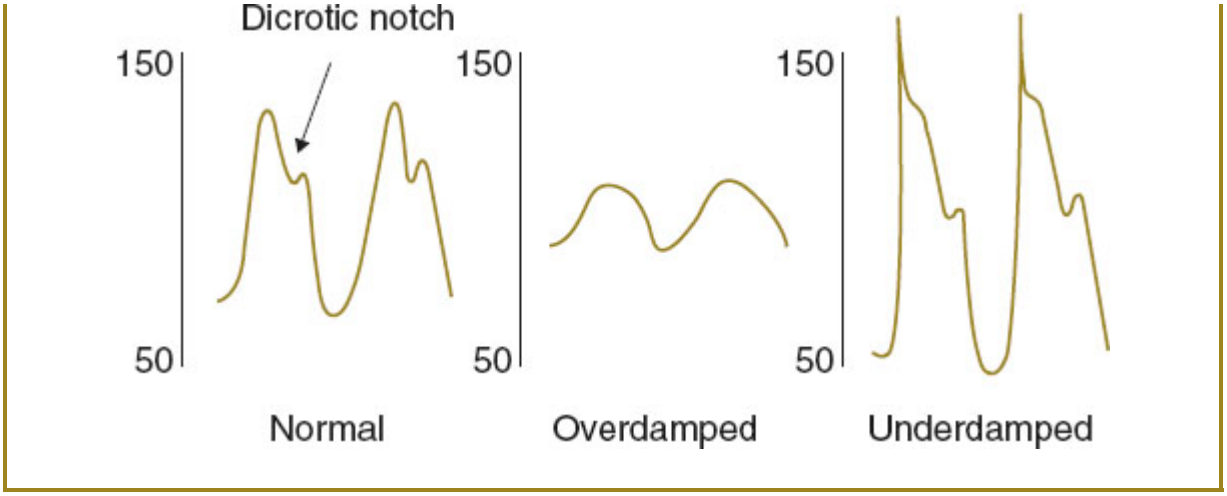
Heparinized solutions are considered to be advantageous by some regarding maintaining catheter patency

Complications from this practice include antibody formation causing heparin-induced thrombocytopenia & altered anticoagulation tests

Interpretation

The dicrotic notch (see Fig. 2-2) indicates closure of the aortic valve, indicating the end of systole or the ejection phase of the heart

Figure 2-2. Examples of Normal, Overdamped, & Underdamped Arterial Waveforms



Systolic pressure increases as the arterial pressure waveform moves away from the aorta toward the peripheral arteries

The systolic pressure may be up to 20 mm Hg greater in the radial or femoral arteries than at the aortic root

The MAP remains the same, regardless of the distance of the catheter from the aorta

The transducer should be leveled at the phlebostatic axis

This corresponds to the right atrium, & may be estimated by locating the 4th intercostal space at the halfway point between the anterior–posterior diameter of the chest

After zeroing, the pressure will be artificially elevated or decreased if the transducer is moved

This is because for every 1 cm movement, pressure may change by 0.7 mm Hg

For example, if the arm is elevated 1 cm above the phlebostatic axis, the pressure will be artificially lower by approx. 0.7 mm Hg

For every cm the arm is lowered below the phlebostatic axis after zeroing, the BP will be artificially elevated by 0.7 mm Hg/cm

Troubleshooting

Waveforms may be overdamped or underdamped (see Fig. 2-2)

Overdamping is usually the result of air bubbles & can be fixed by flushing the system

Underdamping is usually the result of lengthy connector tubing

A flush test can also be used to determine if the system is underdamped or overdamped

If the flush test does not produce any oscillations, the system is likely overdamped

If the flush test produces many postflush oscillations, system is likely underdamped

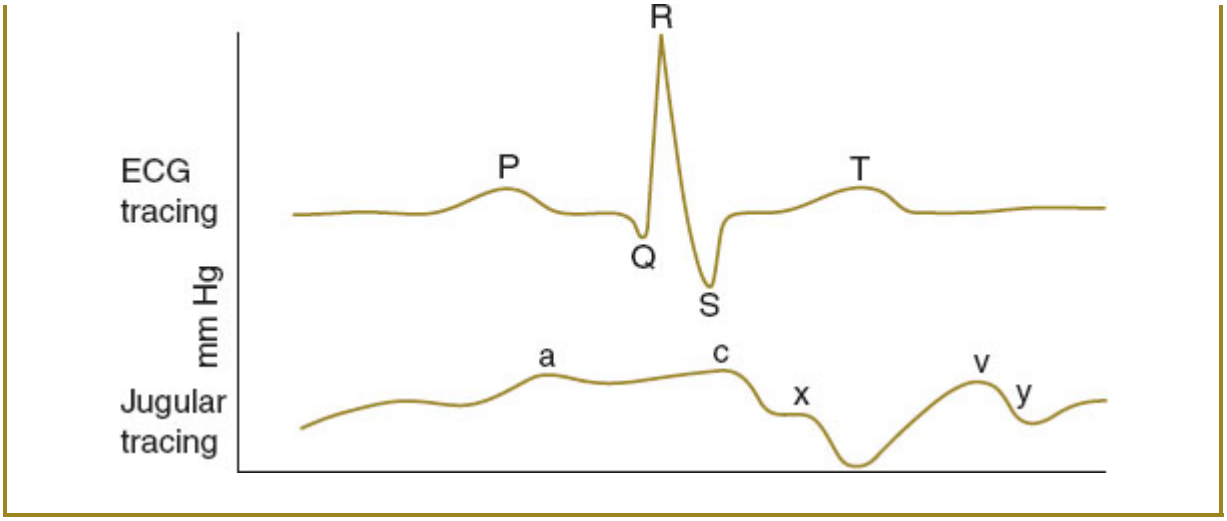
Central Venous Pressure (CVP)

Indications:

Measurement of CVP

Surrogate marker for cardiac preload

Figure 2-3. CVP Waveforms



Measurement of central mixed venous oxygen ($ScVO_2$)

Use for pulse wave analysis/minimally invasive CO determination (e.g., PiCCO system)

Interpretation of CVP waveforms (see Fig. 2-3)

a wave: corresponds to P wave on ECG; indicates atrial contraction

c wave: corresponds to QRS on ECG; indicates elevation of the tricuspid valve into the right atrium during early ventricular contraction

x descent: occurs before the T wave; caused by downward movement of the ventricle during systolic contraction

v wave: corresponds to T wave; reflects the pressure produced when the blood filling the right atrium comes up against a closed tricuspid valve

y descent: occurs when the tricuspid valve opens

CVP waveform anomalies

Absence of a waves: atrial fibrillation

"Cannon a waves": AV dissociation (i.e., heart block or junctional rhythm)

Tricuspid regurgitation: c wave & x descent is replaced by a large positive wave of regurgitation as blood flows back into the right atrium during ventricular contraction

Cardiac tamponade: all pressures are elevated; absent y descent

Problems with CVP interpretation & use in the ICU

CVP does not accurately predict fluid responsiveness since there is a very poor correlation with CVP & blood volume (Marik PE, et al. *Chest*. 2008;134(1):172–178.)

Impaired RV function, severe pulmonary dz, or valvular heart dz affect the CVP reading

CVP does not correlate well with stroke volume (Alhashemi JA, et al. *Curr Heart Fail Rep*. 2010;7(3):116.)

Complications

PTX

Infxn

Hemorrhage

Thrombus/embolism

Dysrhythmias

Pulmonary Artery Catheter

Despite controversy regarding its use, remains the gold standard for CO determination (Fig. 2-4)

Remains a valuable tool when used in selected pts

Provides information on 3 key variables: (1) intrathoracic IV pressures, (2) CO, & (3) mixed venous SvO_2

Thermodilution technique

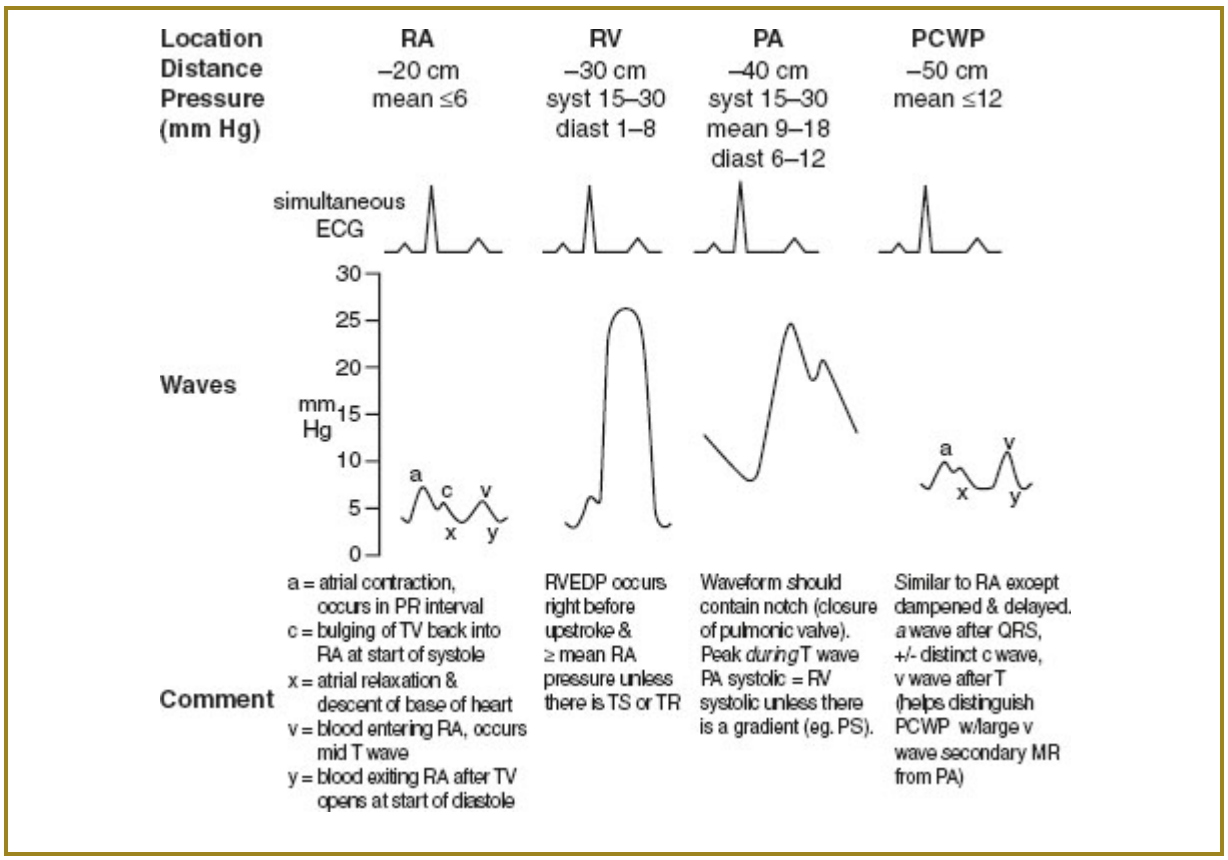
The thermal indicator, typically 10 ml of room temp saline, is injected into the central venous circulation

The resulting temp change is detected in the PA

CO is calculated from the area under the thermodilution curve with the modified Stewart–Hamilton equation

When the area under the curve is *increased,* the CO is low

Figure 2-4. PA Catheter Waveforms



PCWP waveform abnormalities: large a wave → mitral stenosis; large *v* wave → mitral regurgitation; blanted y descent → tamponade; steep *x* & *y* descents → constriction. *Pocket Medicine by Sabatine, 4th ed*, 2011.

When the area under the curve is *decreased,* the CO is high

Conditions that affect CO (see table below):

Conditions That May Effect Thermodilution-Derived Measurements of Cardiac Output			
Overestimate	**Underestimate**	**No Change**	**Impossible to Predict**
Left → right or right → left intracardiac shunts	Use of >10 ml of injectate	Mitral regurgitation	Looping of the catheter
Use of <10 ml of injectate	Use of colder than room temp injectate	Tricuspid regurgitation	Choice of an incorrect constant ('K' in the Stewart–Hamilton equation) for the particular catheter
Infusion of warm blood or fluids through a side port	Presence of infusions running simultaneously through an infusion port on the catheter	Cold ambient temp	
Encapsulation of the thermistor around a clot			

Indications

Differentiation of types of shock

Assessment of pulmonary edema (ARDS vs. cardiogenic)

Dx & monitoring of pulmonary HTN

Dx of valvular dz, intracardiac shunts, cardiac tamponade, PE

Assessment of hemodynamic response to therapies

Esp. in instances when other conventional therapeutic endpoints are not feasible or reliable (e.g., lack of UOP in a pt with renal failure)

Monitoring & management for pts with heart failure or significant cardiac dysfunction

Contraindications

Coagulopathy

Prosthetic right heart valves

Endocardial pacemaker/defibrillator (relative contraindication)

Left bundle branch block (may precipitate complete heart block)

Right-sided endocarditis

Poorly controlled dysrhythmias

RV thrombus

Technique for insertion (see typical PA pressures & waveforms in Fig. 2-4)

The catheter is inserted into the introducer port of a large-bore single-lumen CVC (typically an 8, 8.5, 9, or 10 French cordis introducer) placed in the subclavian or IJ vein

The catheter is advanced past the length of the introducer port

Pressure is monitored continuously during insertion

The balloon is inflated with no more than 1.5 ml of air once in the superior vena cava

The catheter is advanced with the balloon inflated, & the position in the heart is determined by the pressure tracings

The PA occlusion pressure (PAOP) is a venous-type pressure waveform with the same value as the pulmonary diastolic pressure (Fig. 2-4)

This pressure reflects a static column of pressure from the left atrium & reflects left ventricular end-diastolic pressure

A normal PAOP is 6–12 mm Hg

The pulmonary capillary wedge pressure (PCWP) if often regarded as a synonym for the PAOP

Technically, the PCWP is reached when the catheter is "wedged" as distally as possible in the PA as opposed to the PAOP which is the 1st pressure measured when the artery is occluded

Once the PAOP appears the balloon is deflated, & the catheter is either locked in place or withdrawn slightly

PA waveforms should appear again (PA in previous figure)

Some pearls & pitfalls for successful placement & interpretation

When inserted from the right jugular vein, the right atrium should be encountered within 20 cm from skin entry of the catheter

From the right atrium, the RV should be encountered within 20 cm

From the RV, the PA should be encountered within 20 cm (typically <60 cm from the site of skin insertion)

The PAOP should be measured at end expiration

At this point in the breathing cycle, average transmural pressure is best estimated

Correct measurement is imperative (Vincent JL, et al. *Crit Care Med.* 2008;36(11):3093–3096.)

Zeroing, calibration, & elimination of artifacts is mandatory

Many errors are made in data collection when these tasks are not accomplished

Newer catheters can provide continuous measurements of parameters

Complications

PTX (during placement of introducer line; 1–2%)

Right bundle branch block (0.1–5%)

Dysrhythmias (often self-limiting)

PA rupture (0.2%)

CVC associated bloodstream Infxn

Thrombosis

Endocarditis

Knotting of catheter

Interpretation

The reader is referred to a free educational reference for PA catheter waveform & data interpretation at http://www.pacep.org

Interpretation of Pulmonary Artery Catheter Findings			
Condition/Type of Shock	**PAOP/PADP**	**CO/CI**	**SVR**
Distributive shock (sepsis, anaphylaxis, neurogenic)	Normal/↑	↑	↓
Cardiogenic	↑	↓	↑
Hypovolemic	↓	↓	↑
Obstructive (tension PTX)	↑	↓	↑
PE	Normal/↑	↓	↓
Pericardial tamponade*	= CVP	↓	↓

*Classic finding: near equalization of right atrial, central venous, & PA diastolic pressures. PADP, pulmonary artery diastolic pressure; CO, cardiac output; CI, cardiac index; SVR, systemic vascular index.

Minimally Invasive Hemodynamic Monitoring

Pulse wave analysis (LiDCO; LiDCO Ltd, Cambridge, UK)

Transpulmonary indicator dilution is performed using small doses of lithium (<1% of levels used pharmacologically)

Serves to calibrate the system

Based on principle of mass/power conservation

A linear relationship between net power & net flow is assumed in the vascular system

Pulse wave is analyzed by a complex mathematical function

Requires only an arterial line; a CVC is not required

Reliably estimates continuous CO in hemodynamically stable pts

Calculates stroke volume variation (SVV) & pulse pressure variation (PPV)

Principal indication is stroke volume optimization in the perioperative setting

Results may be altered by high doses of muscle relaxants, electrolyte disorders, vasoactive medications, & changes in hematocrit

Cannot be used in pts taking lithium

Esophageal Doppler

CO is calculated based on the diameter of the aorta, the distribution of CO to the descending aorta, & the measured blood flow velocity in the aorta

Limitations

Assumes constant aortic cross-sectional area; this is often dynamic & varies among pts

Accurate measurements are highly dependent on correct positioning of the probe; 10–12 probe insertions are recommended to attain competency (Lefrant JY, et al. *Intensive Care Med.* 1998;24:347–352.)

Cannot reliably produce continuous CO measurements

Has demonstrated modest correlation with PA catheter thermodilution techniques

Plethysmography/thoracic electrical bioimpedance

Electrical resistance (impedance) across the chest is measured

The lower the fluid content, the higher the resistance (fluid conducts electricity)

With newer devices, correlation between this technique & traditional thermodilution techniques with a PA catheter is improving

Echocardiography (see also Chapter 20)

Applications of bedside transthoracic echocardiography in the ICU

Dx of cardiac tamponade

CO & stroke volume assessment

Assessment of left ventricular function by measurement of ejection fraction, E/A ratio, E/E′ ratio, & tissue Doppler imaging (TDI) of lateral mitral valve annulus

Assessment of RV function by measurement of transannular plane systolic excursion (TAPSE)

Intracavitary pressure measurements

Assessment of fluid responsiveness

Transesophageal echocardiography (TEE) is a minimally invasive technique that provides a rapid, real-time assessment of cardiac anatomy & functional status

Bedside lung US may be used to evaluate pleural effusion, PTX, ARDS, pulmonary edema, or lung consolidation (Lichtenstein DA. *Chest.* 2015;147(6):1659–1670.)

Arterial Pressure Waveform Analysis Not Requiring External Calibration (FloTrac/Vigileo; Edwards Lifesciences, Irvine, CA)

Analyzes arterial pressure waveform in conjunction with pt demographic data to calculate CO

Pt wt, ht, & age are entered

Algorithm is based on the principle that the pulse pressure is proportional to stroke volume & inversely proportional to aortic compliance

Requires placement of an arterial catheter pressure sensor

Provides continuous CO & SVV

SVV > 10% may be an indicator of fluid responsiveness (Benes J, et al. *Crit Care*. 2010;14(3): R118.)

Acceptable agreement has been found when compared with conventional thermodilution techniques (PA catheter)

Pts with arrhythmias, on vasopressors, & tidal volume <8 ml/kg may not have reliable measurements (De Backer D, et al. *Intensive Care Med.* 2005;31(4):517–523.)

Systolic Pulse Contour Analysis with Transpulmonary Thermodilution Calibration (PiCCO; Pulsion Medical Systems, Munich, Germany)

Uses a dedicated thermistor-tipped catheter which is usually placed in the femoral artery

Tracks changes in stroke volume on a beat-to-beat basis

Radial or brachial thermistor-tipped catheters may be used as well

A central venous line is required to perform CO determination with transpulmonary thermodilution

Device calibration is required every 8 hrs in hemodynamically stable pts

Calibration needs to be done more frequently in unstable pts

Several studies have validated the PiCCO system by comparing it with conventional thermodilution techniques (PA catheter)

In addition to CO, estimates static preload variables such as global end-diastolic volume (GEDV) & extravascular lung water (EVLW)

Calculates functional variables such as PPV & SVV

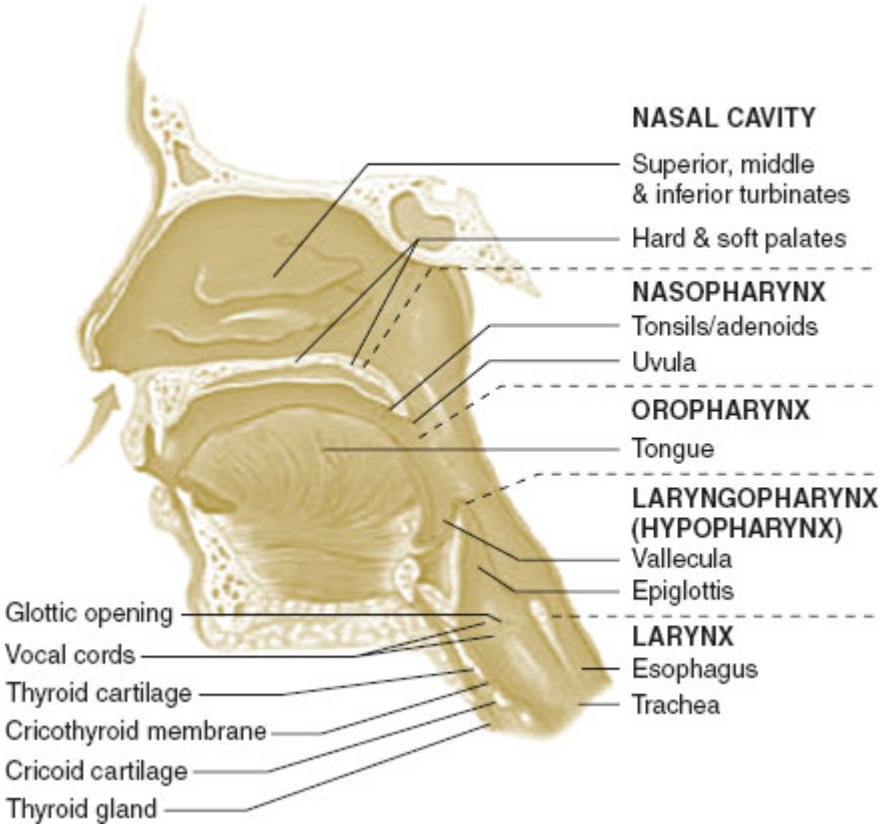
Intra-abdominal Pressure Monitoring: see Chapter 41

AIRWAY MANAGEMENT

TARUN BHALLA, MD • TENSING MAA, MD • AMOD SAWARDEKAR, MD

Airway Innervation—Sensory	
Glossopharyngeal nerve (= CN IX)	Posterior 1/3 of tongue, oropharynx from nasopharyngeal surface to junction of pharynx & epiglottis, including vallecula; tonsillar area; gag reflex
Superior laryngeal nerve, internal branch (off CN X/vagus)	Mucosa from epiglottis to vocal cords (sensory innervation of larynx above vocal cords), including base of tongue, supraglottic mucosa, cricothyroid joint
Superior laryngeal nerve, external branch (off CN X/vagus)	Anterior subglottic mucosa
RLN (off CN X/vagus)	Subglottic mucosa, muscle spindles
Trigeminal nerve (= CN V)	Nares & nasopharynx

Figure 3-1. Anatomy of the Upper Airway.



Airway Innervation—Motor	
Superior laryngeal nerve, external branch (off CN X/vagus)	Cricothyroid muscles tensing of vocal cords, inferior pharyngeal constrictors
RLN (off CN X/vagus)	All other intrinsic muscles of larynx: thyroarytenoid, lateral cricoarytenoid, interarytenoid, posterior cricoarytenoid
Glossopharyngeal (CN IX) & superior laryngeal, internal branch (off CN X/vagus)	No motor innervation contribution

Note: All laryngeal motor innervation is by 2 branches of vagus: superior laryngeal nerve RLN.

Injury of superior laryngeal nerve (SLN) (external branch) → hoarseness

Injury of RLN: unilateral paralysis → paralysis of ipsilateral vocal cord → hoarse voice; bilateral paralysis → stridor & respiratory distress

Airway Assessment

Hx

Adverse events related to prior airway management

Radiation/surgical hx

Burns/swelling/tumor/masses/facial or airway trauma

Obstructive sleep apnea (snoring)

TMJ dysfunction

Dysphagia

Problems with phonation

C-spine dz (disk dz, osteoarthritis, rheumatoid arthritis, Down syndrome, ankylosing spondylitis)

Congenital syndrome (Trisomy 21, Pierre Robin, Treacher Collins)

Physical examination

Position of comfort (tripoding)

Level of consciousness

Respiratory mechanics: RR & regularity, head bobbing, grunting, flaring, accessory muscle use, wheeze or prolonged exhalation

Edema, upper airway trauma

Mallampati score

Symmetry of mouth opening (3 finger breadths)

Loose/missing/cracked/implanted teeth

Macroglossia (associated with difficult laryngoscopy)

High arched palate (associated with difficulty visualizing larynx)

Mandible size:

Thyromental distance <3 fingerbreadths suggests poor laryngeal visualization

Neck examination

Cervical spine injury or instability

Prior surgeries/tracheostomy scars

Abnormal masses (hematoma, abscess, goiter, tumor) or tracheal deviation

Neck circumference & length

Range of motion (flexion/extension/rotation)

Mnemonic for Airway Evaluation (LEMON)		
Physical Signs	**Signs of a Potentially Difficult Airway**	
Look externally	• Abnormal face shape • Sunken cheeks • Edentulous • "Buck teeth"	• Narrow mouth • Obesity • Receding mandible • Facial/neck pathology
Evaluate the 3-3-2 rule	• Mouth opening <3 fingerbreadths • Hyoid–chin distance <3 finger-breadths	• Thyroid cartilage–mouth floor distance <2 fingerbreadths
Mallampati	• Classes III & IV	
Obstruction	• Pathology around upper airway (peritonsillar abscess)	
Neck mobility	• Limited range of motion	

Airway Devices

Oral & nasal airways

Typically inserted to relieve upper airway obstruction due to loss of upper airway muscle tone in obtunded/semiconscious patients (Pt) → usually caused by tongue or epiglottis falling against posterior pharynx wall

Size of oral airway estimated by measuring from corner of mouth to angle of the mandible

Length of nasal airway estimated by measuring from nares to tragus of ear

Use extreme caution with insertion in pt on anticoagulation or with basilar skull fx

Mask airway

Facilitate O_2 delivery using airtight seal

Hold mask with left hand, while right hand generates positive pressure ventilation → (use <20 cm H_2O to avoid gastric inflation). Confirm that mask ventilation is effective by checking for chest rise and/or by confirming breath sound with auscultation

Single person, "E-C clamp" technique

Fit snugly around bridge of nose to below bottom lip

Elicit downward pressure with left thumb & index finger ("C"), have the middle & ring fingers grasp the mandible, while the 5th finger is placed under angle of jaw to thrust anteriorly ("E")

Difficult Mask Ventilation: Maneuvers to Maintain Airway Patency

Call for additional help to assist with 2-person bag mask ventilation (have someone else squeeze bag)
Insert oral and/or nasal airways
Extend neck & rotate head (note: this is contraindicated for spine fx)
Perform jaw thrust

Independent Risk Factors for Difficult Mask Ventilation

- Presence of a beard
- Body mass index >26 kg/m^2
- Lack of teeth
- Age >55
- H/o snoring

(Langeron O, et al. *Anesthesiology.* 2000;92(5):1229–1236.)

Supraglottic airways (laryngeal mask airways or LMAs)

Insertion technique

Pt placed in sniffing position

Deflated LMA is lubricated & inserted blindly into hypopharynx (note that many operators insert the LMA while it is inflated, finding it easier to displace the tongue & soft tissues with an inflated LMA)

Cuff is inflated to create a seal around entrance to larynx (*tip rests over upper esophageal sphincter, the cuff's upper border rests against the base of tongue, sides lying over pyriform fossae*)

Indications

Alternative to ET intubation (not as a replacement) or mask ventilation

Rescue device in expected/unexpected difficult airway

Conduit for intubating stylet, flexible fiberoptic bronchoscopy/intubation (FOB), or small diameter ETT

Contraindications

Pharyngeal pathology, obstruction, high aspiration risk, low pulmonary compliance (need PIP >20 cm H_2O), long surgeries

Disadvantages: does not protect the airway, can become dislodged

ETTs

Modified for a variety of specialized applications

Flexible, spiral wound, wire-reinforced (armored), rubber, microlaryngeal, oral/nasal RAE™ (preformed), double lumen tubes

Airflow resistance depends on tube diameter, curvature, length

All ETTs have an imprinted line that is opaque on radiographs

Oral Tracheal Tube Sizing		
Age	**Internal Diameter (mm)**	**Tube Length at Lip (cm)**
Full-term infant	3.5	12
Child	4 + age/4	14 + age/2 or 3 × ETT diameter
Adult: Female Male	7.0–7.5 7.5–8.5	20 22

Rigid laryngoscopes: used to examine larynx & facilitate tracheal intubation

Macintosh blade (curved): tip inserted into vallecula; use size 3 blade for most adults

Miller blade (straight): tip inserted beneath laryngeal surface of epiglottis; use size 2 blade for most adults

Modified laryngoscopes: Wu, Bullard, & Glidescope for use in difficult airways

Flexible fiberoptic bronchoscopes

Indications: potentially difficult laryngoscopy/mask ventilation, unstable cervical spines, poor cervical range of motion, TMJ dysfunction, congenital/acquired upper airway anomalies

Light wand

Malleable stylet with light emanating from distal tip, over which ETT is inserted

Dim lights in OR & advance wand blindly

C-MAC: newly avail. direct video-laryngoscopes using fiberoptics with larger display screens & slightly different configuration of blades are improving the visualization of airway for pt who are otherwise difficult to intubate

Glow in lateral neck → tip in piriform fossa

Glow in the anterior neck → correctly positioned in trachea

Glow diminishes significantly → tip likely in esophagus

Retrograde tracheal intubation

Performed in awake & spontaneously ventilating pt

Puncture cricothyroid membrane with 18G needle

Introduce guide wire & advance cephalad

Visual wire with direct laryngoscopy & guide ETT through vocal cords

Airway bougie

Solid or hollow, semimalleable stylets usually passed blindly into trachea

ETT is threaded over bougie into trachea; can feel “clicking” as passes over tracheal rings

May have internal lumen to allow for insufflation of O_2 & detection of CO_2

The Aintree catheter (Cook Medical), is a special Bougie. It is hollow on the inside & accommodates a pediatric fiberoptic bronchoscope so it can be

placed into the trachea under direct fiberoptic visualization. Then, subsequently, it can be used as a tube guidance device (Bougie) to place the ETT over it. It can also be used for temporary emergency ventilation via the hollow inside either by ventilator with high flow or with a jet-ventilation device (both adapters are supplied with the catheter).

Required Equipment for Intubation
O_2, positive pressure ventilation source (ventilator), & back-ups (bag-valve mask)
Face masks, oropharyngeal & nasopharyngeal airways
ETTs (cuffed & uncuffed, 1 size up & 1 size down) & stylets
Syringe for tracheal tube cuff inflation (10 ml)
Suction
Laryngoscope handles & blades (with functioning lights)
Towel, blanket for pt positioning
Stethoscope, capnograph, or $ETCO_2$ detector

Indications for Tracheal Intubation

Upper airway obstruction
Emergency drug delivery in cardiac arrest (epinephrine, atropine, lidocaine, naloxone)
Respiratory failure
Shock or hemodynamic instability
Neuromuscular weakness with progressive respiratory compromise
Absent protective airway reflexes (cough, gag)
Inadequate respiratory drive
Need to maintain normocarbia in pt with increased ICP
GCS <8 for trauma pt

Drugs

Local anesthetics

1–4% lidocaine, cocaine solution, phenylephrine + lidocaine for vasoconstriction, & anesthesia prior to nasal intubations

Analgesia

Fentanyl, morphine

Synergistic effects on respiratory depression when given with a benzodiazepine

Sedation

Benzodiazepines

Midazolam, lorazepam

Synergistic effects on respiratory depression when given with an opiate

Barbiturates

Thiopental (not avail. in US)—decreases cerebral oxygen consumption & reduces ICP, also negative inotropy, hypotension

Etomidate—decreases cerebral oxygen consumption & reduces ICP, few cardiovascular side effects, adrenal suppression, lowers seizure threshold

Propofol—negative inotropy, vasodilation

Dissociative anesthesia (Ketamine)—analgesia & amnesia

Muscle relaxants

Succinylcholine—a depolarizing muscle relaxant, may cause bradycardia in infants, due to its effects on the muscarinic acetylcholine receptors; contraindicated in hyperkalemia, h/o trauma, burns, crush injuries, neuromuscular dz (may cause or worsen hyperkalemia), caution in acute renal failure or chronic renal insufficiency if K is elevated, causes temporary elevation of intracerebral & intraoccular pressures (avoid if elevated ICP or globe injury; can trigger malignant hyperthermia)

Nondepolarizing agents (rocuronium, vecuronium, cisatracurium, pancuronium)

Preinduction Agents			
Agent	**Indication**	**Dose (IV)**	**Comments**
Atropine	Prevents bradycardia during laryngoscopy	0.01–0.02 mg/kg (min 0.1 mg)	For children <1 yr
Glycopyrrolate	Prevents bradycardia & ↓ oral secretions	3–5 mcg/kg	
Lidocaine (IV or via ETT)	Blunts HTN & ICP response with laryngoscopy & bronchospasm due to insertion of ETT	1–1.5 mg/kg	Give 3–4 min prior to laryngoscopy
Fentanyl	Analgesia, blunts ↑ HR & BP during laryngoscopy	2–3 mcg/kg	Rigid chest syndrome, rarely bradycardia
Esmolol	Blunts ↑ HR & BP during laryngoscopy	2 mg/kg	Caution in hemodynamically unstable pt

Induction Agents			
Agent	**Dose (IV)**	**Indications**	**Precautions**
Thiopental (not avail. in US)	3–5 mg/kg	Status epilepticus, elevated ICP	Bronchospasm, hypotension
Etomidate	0.15–0.3 mg/kg	Trauma, hemodynamic instability	Adrenal suppression, lowers seizure threshold
Ketamine	1–2 mg/kg	Status asthmaticus, hemodynamic instability	May ↑ ICP, apnea, laryngospasm, hypersalivation
Propofol	2–4 mg/kg	Elevated ICP	hypotension
Midazolam	0.1–0.2 mg/kg	Amnesia, sedation	hypotension
Fentanyl	5–10 mcg/kg	Analgesia, hemodynamic instability	Rigid chest syndrome
Morphine	0.1 mg/kg	Analgesia	Histamine release, hypotension

Neuromuscular Blockade			
Agent	**Class**	**Dose (IV)**	**Comments**
Succinylcholine	DNMB	1–1.5 mg/kg	See above
Rocuronium	NDNMB	1–1.2 mg/kg	Hepatobiliary excretion
Cisatracurium	NDNMB	0.1 mg/kg	Hoffman degradation
Vecuronium	NDNMB	0.1 mg/kg	Hepatobiliary excretion

DNMB, depolarizing neuromuscular blocker; NDNMB, nondepolarizing neuromuscular blocker.

Airway Management: Orotracheal Intubation

Gather all anticipated equipment & drugs including bolus IVF (hypotension associated with changes in intrathoracic pressure in critically ill pt)

Elevate ht of bed to laryngoscopists xyphoid process

Place pt in *Sniffing Position:* neck flexion, head extension; aligns oral, pharyngeal, & laryngeal axes to provide the straightest view from lips to glottis

Preoxygenation with 100% O_2 (a true denitrogenation step, replacing nitrogen with 100% oxygen) to increase the safe apnea period

Induce anesthesia

Hold laryngoscope in left hand, scissoring mouth open with right thumb & index finger

Insert laryngoscope in right side of mouth, sweeping tongue to left

Advance until glottis appears in view

Do not use laryngoscope as a lever in a pivoting maneuver (instead lift "up & away")

Using the right hand pass the tip of the ETT through vocal cords under direct visualization

Inflate ETT cuff with least amount of air necessary to create seal during positive pressure ventilation

Confirm correct placement of ETT with:
(1) chest auscultation, (2) $ETCO_2$, (3) palpate ETT cuff in sternal notch, (4) may use FOB to confirm ET placement of ETT *Earliest manifestation of bronchial intubation is increased peak pressure (R. mainstem bronchus common)*

For trauma airway management, see Trauma & Bedside Procedures (Chapters 41 & 46)

Rapid sequence intubation

Indication: pt at high risk for aspiration

Full stomach, pregnant, GERD, morbidly obese, bowel obstruction, delayed gastric emptying—pain/diabetic gastroparesis

Use rapid paralyzing agent: succinylcholine (1–1.5 mg/kg) or rocuronium (0.6–1.2 mg/kg)

Place cricoid pressure (Sellick Maneuver) as pt is induced

Protect regurgitation of gastric contents to oropharynx

Help visualize vocal cords during laryngoscopy

Proper cricoid pressure should be performed with "BURP" technique:

Displace larynx **(B)**ackward, **(U)**pward, **(R)**ight, with **(P)**ressure

Intubate pt once paralytic takes effect (30–60 s); do **not** mask ventilate pt

Release cricoid pressure once ETT placement into airway is confirmed

Airway Management: Nasotracheal Intubation

Indications: intraoral, facial/mandibular procedures

Contraindications: basilar skull fx, nasal fx, polyps or tumors, underlying coagulopathies, upper airway foreign body obstruction

Prep: anesthetize & vasoconstrict mucosa with lidocaine/phenylephrine mix or cocaine → select nares that pt can breathe through most easily

Lubricated ETT is advanced perpendicular to face below inferior turbinate via selected nares → direct bevel laterally away from turbinates

Advance ETT until able to visualize tip in oropharynx under direct laryngoscopy → use Magill forcep with right hand to advance/direct through vocal cords

Airway Management: Awake Flexible Fiberoptic Intubation

Equipment: Ovassapian/Williams/Luomanen airway, topical anesthetics, vasoconstrictors, antisialagogues, suction, fiberoptic scope with lubricated ETT

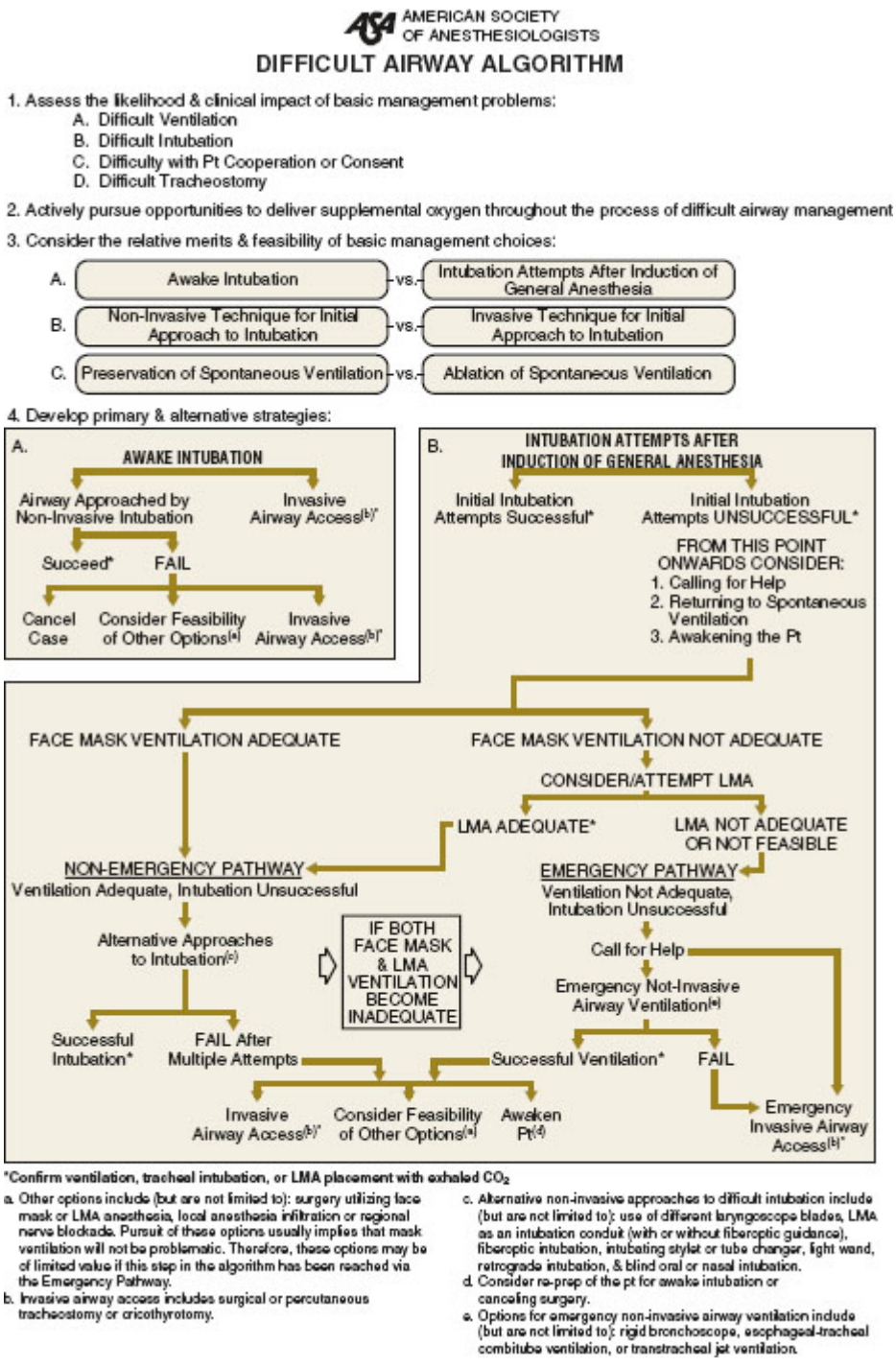
Indications: cervical spine pathology, obesity, head & neck tumors, hx of a difficult airway, presence of anterior mediastinal mass

Premedication: sedation (midazolam, fentanyl, dexmedetomidine, ketamine)

Technique: 1. Take time to topicalize airway while continuing to preoxygenate

2. Place special oral airway or grab tongue with gauze
3. Keep fiberoptic scope in midline while advancing until epiglottis appears
4. Advance scope beneath epiglottis using antero/retroflexion prn
5. Once vocal cords are visualized, advanced scope into trachea
6. Stabilized scope while ETT is advanced off scope into trachea → if resistance is encountered, rotate ETT tube 90°
7. After insertion, visualize carina with scope to avoid endobronchial intubation

ASA Difficult Airway Algorithm



(Reproduced with permission from the American Society of Anesthesiologists.)

Practical Approach to Unanticipated Difficult Airway	
Plan A	• Standard laryngoscopy with blade of choice • If unable to intubate → make 2nd attempt with a different blade • Make no more than 2 attempts (avoid high risk of oral bleeding, secretions, & edema)
Plan B	• Direct laryngoscopy & insertion of bougie or intubating catheter • Confirm placement by: 1. Using hand on anterior neck to palpating catheter advancement through glottis 2. After 40-cm catheter should reach carina & provide resistance (no resistance will be encountered if in esophagus) 3. If using intubating catheter, may attach to $ETCO_2$ monitor
Plan C	• Insertion of LMA (disposable, Fastrach, Proseal) • 5.0 or 6.0 ETT will fit through disposable LMA (± fiberoptic assistance)
Plan D	If intubation attempts are unsuccessful & it is safe to do so: • Terminate anesthetic & awaken pt • Perform awake fiberoptic intubation • Perform surgical airway (i.e., tracheostomy)
Plan E	If intubation attempts are unsuccessful & the pt cannot be safely woken up from anesthesia have a qualified person (usually surgeon) perform a tracheostomy or cricothyroidotomy to secure the airway

(Modified from Morgan EG, et al. *Clinical Anesthesiology*. 4th ed. McGraw-Hill;2006.)

Transtracheal Procedures

Indications: emergency tracheal access when an airway cannot be secured via nasal/oral route

Percutaneous transtracheal jet ventilation

Simple & relatively safe means to sustain a pt during a critical situation

Attach 12-, 14-, or 16G IV catheter to 10-cc syringe with partially filled saline

Advance needle through cricothyroid membrane with constant aspiration, until air returns

Advance angiocatheter, disconnect syringe, attach oxygen source

High pressure O_2 (25–30 psi), insufflation of 1–2 s, 12/min with 16G → will deliver ~400–700 ml

Low pressure O_2 (bag-valve mask 6 psi, common gas outlet 20 psi)

Cricothyroidotomy (must be performed by a qualified practitioner experienced with the procedure)

Contraindications: pt <6 yr old (upper part of trachea not fully developed) → incision through cricothyroid membrane increase the risk of subglottic stenosis

Sterilize skin

Identify cricothyroid membrane

Transverse incision with #11 blade ≈1 cm on each side of midline

Turn blade 90° to create space to pass ETT

Insert ETT caudally, inflate cuff, confirm breath sounds

TRACHEOTOMY (must be performed by a qualified practitioner experienced with the procedure)

Indications: prolonged tracheal intubation, neurologic impairment, congenital airway malformations, craniofacial syndromes, vocal cord paralysis

Complications:

Immediate postop: tube occlusion, accidental decannulation, false passage, pneumomediastinum, PTX

Late: laryngeal stenosis, tracheal stenosis, stomal granuloma formation, stomal bleeding, tube occlusion, Infxn, innominate artery erosion

Complications of Laryngoscopy and Intubation (most common)

Postintubation stridor in children secondary to tracheal/laryngeal edema, treat with dexamethasone preextubation & racemic epinephrine postextubation, heliox, humidified oxygen

Acquired subglottic stenosis in children from incorrect tracheal tube size, traumatic or multiple intubations, inadequate sedation/analgesia resulting in excessive ETT movement & trauma to airway

Recurrent laryngeal nerve damage from ETT cuff compression → vocal cord paralysis

Laryngospasm from stimulation of superior laryngeal nerve

Involuntary/uncontrolled muscular contraction of laryngeal cords

Caused by pharyngeal secretions or direct stimulation of ETT during extubation

Treat with:
1. gentle positive pressure ventilation
2. laryngospasm maneuver—apply firm pressure posterior to mandibular ramus near the earlobe
3. succinylcholine 0.25–1 mg/kg to relax laryngeal muscles

Nosocomial Infxn (ventilator-associated pneumonia [see Chapters 18 & 23])

Extubation

Extubation readiness pt factors:

Resolution of initial indication for intubation

Adequate gas exchange capacity

Airway protective reflexes (cough, gag)

Respiratory muscle strength (NIF, VC), spontaneous breathing trial

Sedatives weaned for adequate respiratory drive & muscle relaxants reversed

Adequate cardiac function to tolerate increase in LV afterload

Pt's airway should be aggressively suctioned while on 100% O_2 prior to extubation

Consider *cuff leak test:* deflate cuff & listen for air leak to r/o glottic swelling & to decrease chance of postextubation stridor (note: reliability of this test is controversial)

Consider delaying extubation if no leak

Untape ETT, deflate cuff, remove ETT while providing small amount of positive pressure (remove secretions at distal end of ETT)

Place mask on pt with 100% O_2 while verifying spontaneous & adequate ventilation

Negative pressure pulmonary edema (postobstructive pulmonary edema [POPE])

Type 1—can occur during strong inspiratory effort caused by large negative intrathoracic pressure gradient against closed vocal cords

Type 2—can occur with relief of upper airway obstruction

Treatment: maintain airway, provide O_2, consider PEEP/reintubation, diuretics are used but are not very effective

ACID–BASE DISTURBANCES

SAMUEL CLARK BERNGARD, MD • MARY B. RICE, MD, MPH • ATUL MALHOTRA, MD

Definitions

Acidemia pH <7.36, alkalemia pH >7.44

pH is determined by $PaCO_2$ & HCO_3^-

Henderson equation: $H^+ = 24 \times PaCO_2/HCO_3^-$

Normal $H^+ = 40$ nM, $PaCO_2 = 40$ mm Hg & $HCO_3^- = 24$ mEq, 40 = 40 for internal consistency

Carbonic acid equilibrium: $H_2O + CO_2 \longleftrightarrow H_2CO_3 \longleftrightarrow H^+ + HCO_3^-$

Anion gap (AG) represents unmeasured ions in serum or urine, normal AG = 8–12, or 2.5 × albumin

Anion Gap Metabolic Acidosis (AGMA) represents an increase in unmeasured serum anions causing a high AG & acidosis

Lungs regulate $PaCO_2$ & kidneys regulate HCO_3^- to control pH

Acidemia vs. acidosis

Acidemia: low blood pH

Acidosis: a disturbance causing proton production

Workup

Check pH, $PaCO_2$, electrolytes, albumin to identify primary disorder

Assess if disorder is simple or mixed by checking if the response is as expected

If HCO_3^- (in respiratory disorder) or $PaCO_2$ (in metabolic disorder) is not the expected value, there is >1 primary acid–base disorder

Calculate AG, if >18 a primary AGMA exists regardless of pH or bicarb

Pneumonic for the expected response of the lungs/kidneys to primary disturbance: **"1 for 1, 10 for 7, 1, 4, 2, 5"**

Numbers represent expected response in alphabetical order: **M**etabolic before **R**espiratory, **A**cidosis before **Alk**alosis, **A**cute before **C**hronic

Primary Acid–Base Disturbances

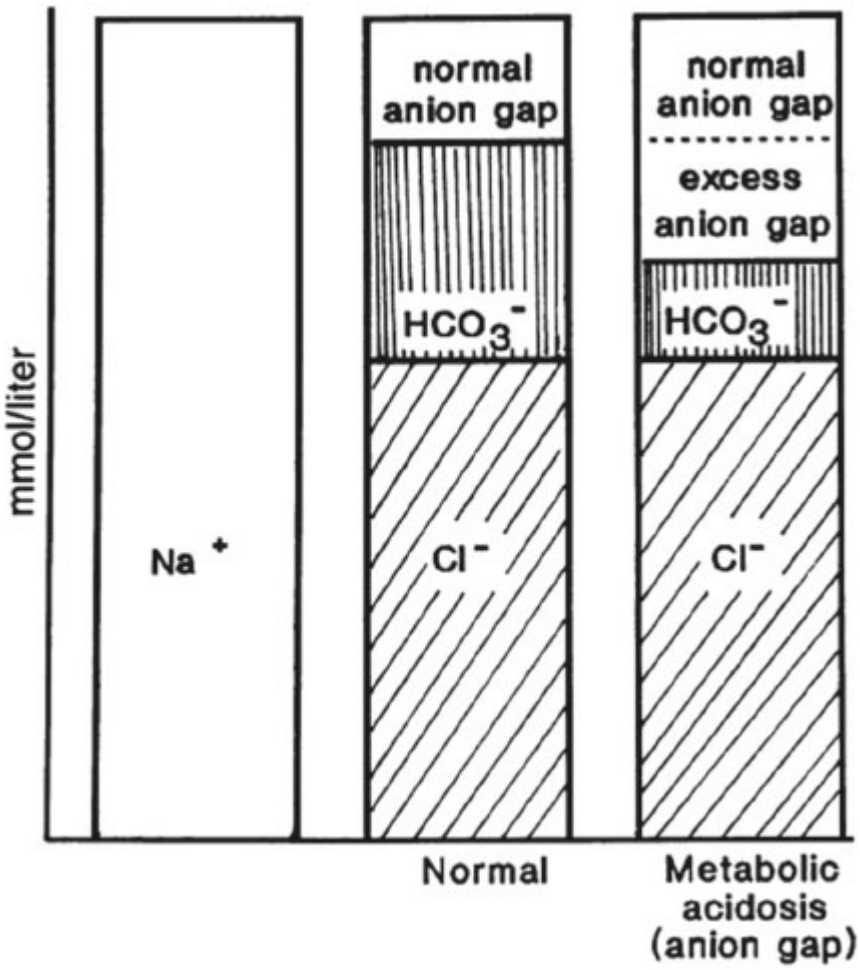
Primary Disorder	Recommended Pneumonic	Other Formulas to Predict Response	Example
Met **A**cidosis	**"1 for 1"** Every 1 ↓ in HCO_3^- → 1 ↓ $PaCO_2$	$PaCO_2 = 1.5 \times HCO_3^- + 8$ (+/–2) (Winter Formula) $PaCO_2$ = last 2 digits of pH	pH = 7.30, $PaCO_2$ = 31, HCO_3^- = 15 → HCO_3^- ↓ by 9, $PaCO_2$ ↓ by 9
Met **Alk**alosis	**"10 for 7"** Every 10 ↑ in HCO_3^- → 7 ↑ $PaCO_2$	$PaCO_2 = 0.9 \times HCO_3^- + 16$	pH = 7.47, $PaCO_2$ = 47, HCO_3^- = 34 → HCO_3^- ↑ by 10, $PaCO_2$ ↑ by 7
Acute **R**espiratory **A**cidosis	**"1"** Every 10 ↑ $PaCO_2$ → 1 ↑ HCO_3^-	Every 10 ↑ $PaCO_2$ → 0.08 ↓ pH	pH = 7.25, $PaCO_2$ = 60, HCO_3^- 26 → $PaCO_2$ ↑ by 20, HCO_3^- ↑ by 2
Chronic **R**espiratory **A**cidosis	**"4"** Every 10 ↑ $PaCO_2$ → 4 ↑ HCO_3^-	Every 10 ↑ $PaCO_2$ → 0.03 ↓ pH	pH = 7.35, $PaCO_2$ = 60, HCO_3^- = 32 → P_aCO_2 ↑ by 20, HCO_3^- ↑ by 8
Acute **R**espiratory **Alk**alosis	**"2"** Every 10 ↓ $PaCO_2$ → 2 ↓ HCO_3^-	Every 10 ↓ $PaCO_2$ → 0.08 ↑ pH[a]	pH = 7.62, $PaCO_2$ = 20, HCO_3^- 20 → $PaCO_2$ ↓ by 20, HCO_3^- ↓ by 4
Chronic **R**espiratory **Alk**alosis	**"5"** Every 10 ↓ $PaCO_2$ → 5 ↓ HCO_3^-	Every 10 ↓ $PaCO_2$ → 0.03 ↑ pH[a]	pH = 7.45, $PaCO_2$ = 25, HCO_3^- = 17 → $PaCO_2$ ↓ by 15, HCO_3^- ↓ by <8

[a]pH changes are less predictable in respiratory alkalosis compared to acidosis.

Strong ion difference (Stewart Approach Figure 4-1) = an alternative approach to acid–base chemistry based on conservation of mass & electrochemical neutrality Figure 4-1.

Conceptually useful but less practical for bedside acid–base analysis.

Figure 4-1. Gamblegram Depicting Strong Ion Difference in AGMA



Source: Haber RJ. *West J Med.* 1991;155(2):146–151.

Management of Severe Acid–Base Disturbances in Critical Illness

Systemic Effects of Acidemia

Cardiovascular: ↓ CO, arterial dilation (hypotension), venoconstriction, reentrant arrhythmias, ↓ threshold for VF, ↓ response to catecholamines/pressors

Respiratory: respiratory muscle fatigue, dyspnea

Metabolic: ↑ metabolic demands, inhibition of anaerobic glycolysis, ↓ ATP synthesis, ↑ K+, insulin resistance

Cerebral: inhibition of cell volume regulation → coma

Treatment of Severe Acidemia

(Adrogue HJ, et al. *N Engl J Med*. 1998;338(1):26–34; Kraut JA, et al. *Nat Rev Nephrol*. 2012;8(10):589–601.)

Treat underlying cause

Base therapy until pH ≤7.10 or ≤7.20 if cardiovascular compromise & HCO_3^- reaches 8–10 mmol/l

For $NaHCO_3$ therapy, assume HCO_3^- space of 50% body wt, e.g., to ↑ HCO_3^- from 4 to 8 mmol/l in 70-kg pt give 140 mmol HCO_3^- (4 mmol/l × 50% × 70 kg)

Infuse $NaHCO_3$ in isotonic solution (e.g., 3 amps $NaHCO_3$ in D5W, 150 mmol HCO_3^-/l) over min–hr (bolus occasionally effective but ACLS no longer recommended)

Consider IV Ca+ therapy after $NaHCO_3$ to prevent hypoCa+

If intubated, consider increasing minute ventilation

THAM is an alternative in pts with hypercarbia & academia

0.3 M THAM requirement (ml) = body dry wt (kg) × base deficit (mEq/l) × 1.1, base deficit = desired serum [HCO_3^-] – actual serum [HCO_3^-]

Oral therapy not reliable in critical illness

Hemodialysis (HD) can rapidly correct acidemia

Problems encountered in treatment of acidemia

"Overshoot" alkalosis, esp. if underlying condition (e.g., DKA) resolves

Buffering of H+ by HCO_3^-—causes ↑ PCO_2 in cells. If no pulmonary reserve or undergoing CPR, paradoxical intracellular or even extracellular acidosis may occur if ↑ PCO_2 >> ↑ HCO_3^-

Systemic Effects of Alkalemia

Cardiovascular: arteriolar constriction (esp. respiratory alkalosis), angina, ↑ SVT, ↑ VT/VF

Respiratory: ↓ ventilation → hypoxemia, reversal of hypoxic pulmonary vasoconstriction → worse V/Q matching

Metabolic: anaerobic glycolysis, ↑ lactate, ketones → ↑ AG, ↓ K+, iCa^{2+}, Mg^{2+}, PO_4

Cerebral: ↓ cerebral blood flow, cerebral vasoconstriction, tetany, seizure, lethargy, delirium, stupor

Treatment of Severe Alkalemia

(Adrogue HJ, et al. *N Engl J Med.* 1998;338(2):107–111, *NEJM*. 2002;346(1):43–53.)

Treat underlying cause: antiemetics for N/V, H_2 blockers if NGT suction required, ↓ loop/thiazide diuresis, add K+-sparing diuretic or acetazolamide, IVF if volume depleted (e.g., NS + KCl)

Correct until HCO_3^- <40 mmol/l (~pH <7.55)

Severe alkalemia is usually chloride responsive. Correcting Na+, Cl−, K+ deficits often → bicarbonaturia

IV HCl if rapid correction needed: 100–200 mmol (0.1–0.2 N) HCl/l of D5W via central line, max rate 0.2 mmol/kg/hr

Arginine HCl & NH_4Cl are occasionally used but reports of hyperkalemia & encephalopathy

HD can rapidly correct alkalemia

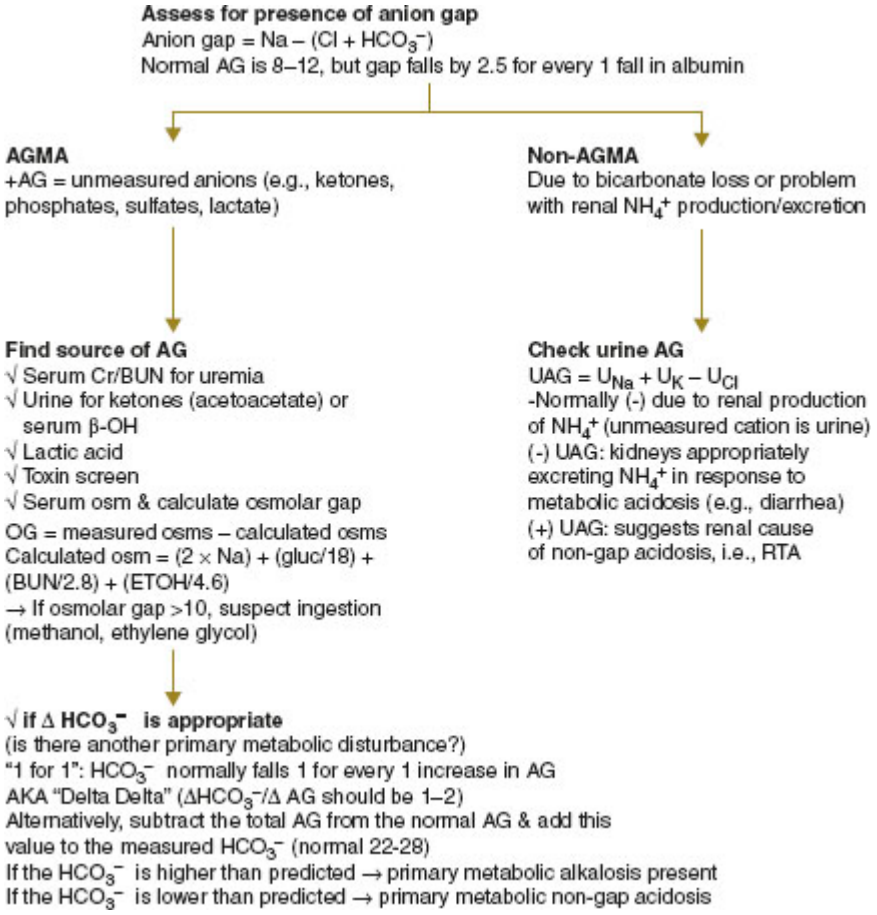
If saline-resistant alkalemia (i.e., mineralocorticoid excess), aggressively replete KCl

Fluid overload is a common complication of alkalemia treatment (esp. in cardiac/renal failure)

Metabolic Acidosis

Approach to Metabolic Acidosis

Figure 4-2. Differential Diagnosis of Acidosis



Causes of AGMA ("KUSMALE")	
Ketones	β-OH & acetoacetate (AcAc), due to DKA, alcoholic ketoacidosis (AKA), starvation ketoacidosis. Urine & blood ketones measure AcAc +/– acetone, not β-OH (unless specific blood test sent). Compared to DKA, AKA mainly ↑ β-OH & may have negative ketone tests
Uremia	Due to accumulation of phosphates, sulfates
Salicylates	Causes met acidosis from lactate & ketones & respiratory alkalosis due to CNS stimulation
Methanol	Due to formate accumulation. Causes blurry vision + osmolar gap
Alcohols	EtOH, Isopropyl alcohol. Alcohols metabolize to organic acids. Early + osmolar gap no AG → late + AG, no osmolar gap
Lactate	↑ due to overproduction by anaerobic metabolism & underuse Type A: impaired tissue oxygenation (e.g., sepsis, ischemic bowel, CO, Seizure) Type B: no impairment in oxygenation (e.g., malignancy, liver failure, thiamine deficiency, medications: NRTIs, metformin, linezolid) D-lactate: byproduct of bacterial metabolism, may → AG in short-gut syndrome, pts with h/o gastric bypass, small-bowel resection
Ethylene Glycol	Ethylene glycol → altered MS, renal failure, cardiopulmonary failure. + osmolar gap. Calcium oxalate crystals in urine; glycolate in serum

Less common causes: propylene glycol, paraldehyde, phenformin, ASA, cyanide, Fe, INH, toluene. ↓ AG consider unmeasured cations (↓ albumin, Li, Ca, Ig from multiple myeloma, Mg, halide intoxication)

Causes of Non-AGMA ("USED CARS")[a]	
Ureterosigmoidostomy	Colonic Cl^-/HCO_3^- exchange
Saline	Large volume crystalloid resuscitation e.g., early goal directed therapy with saline or in DKA
Early renal failure	Due to impaired HCO_3^- generation
Diarrhea	GI loss of HCO_3^- (also pancreatic fistula)
Carbonic anhydrase inhibitors	Causes renal H^+ retention, HCO_3^- excretion
Amino Acids	Arginine HCl, lysine
RTA	See table below
Supplements	TPN (excess chloride vs. acetate)

[a]Recent (resolved) respiratory alkalosis can cause persistent met acidosis as kidneys need time to readjust.

Types of RTAs				
Type of RTA	**Problem**	**UAG**	**Urine pH**	**Serum K**
I (Distal)	Impaired H^+ (i.e., NH_4^+) excretion in collecting tubules	+	>5.3	↓
II (Proximal)	HCO_3^- loss, usually Fanconi syndrome of prox tubule with loss of glucose, phosphates, protein in prox tubule (causes: MM, acetazolamide, ifosfamide)	+ or –	<5.3 (except if receiving bicarb load)	↓
IV (↓ Aldosterone)	Aldosterone deficiency (e.g., from low renin in diabetic nephropathy, adrenal insuff) or tubular resistance to aldosterone (e.g., K-sparing diuretics)	+	<5.3	↑

Case Examples of Metabolic Acidosis		
Case	**Interpretation**	**Diagnosis + Possible Scenario**
pH 7.2, $PaCO_2$ 26, Na^+ 132, Cl^- 97, HCO_3^- 10	pH low, so acidemia. $PaCO_2$ low, so metabolic. HCO_3^- ↓ by 14, $PaCO_2$ ↓ by 14, expected response. AG 25 (↑ by 15) & HCO_3^- ↓ by 14, so only 1 metabolic disorder	**AGMA** DKA
pH 7.35, $PaCO_2$ 35, Na^+ 140, Cl^- 100, HCO_3^- 19	pH low, so acidemia. $PaCO_2$ low, so metabolic. HCO_3^- ↓ by 5, $PaCO_2$ ↓ by 5 (expected). AG 21 (↑ by 11) & HCO_3^- ↓ by only 5 → HCO_3^- higher than expected, so met alkalosis present	**AGMA & met alkalosis** Lactic acidosis + severe vomiting
pH 7.47, $PaCO_2$ 20, Na^+ 140, Cl^- 106, HCO_3^- 14	pH high, so alkalemia. $PaCO_2$ low, so respiratory. $PaCO_2$ ↓ by 20, HCO_3^- ↓ by 10 (more than the 4 expected for acute), so met acidosis present since AG 20	**AGMA & respiratory alkalosis** ASA intoxication

Metabolic Alkalosis

Metabolic Alkalosis Is Associated with ä Mortality due to

Cardiac arrhythmias
Inhibition of hypoxic pulmonary vasoconstriction (worse V/Q matching)
Depression of ventilation

Approach to Metabolic Alkalosis

Determine if saline-responsive or resistant

Urine chloride is best indicator of volume status in setting of alkalemia (urine Na+ not reliable due to obligate cation losses when HCO_3^- is elevated)

Urine Cl− <20 suggests saline-responsive

Urine Cl− >20 suggests saline-resistant (unless pt is on diuretics)

Correct met alkalosis according to cause

Saline for hypovolemia

KCl if euvolemic (or less commonly HCl, arginine HCl, NH_4Cl). See treatment of severe alkalemia

Acetazolamide if hypervolemic (e.g., contraction alkalosis with CHF)

Dialysis for severe, life-threatening alkalemia

Causes of Metabolic Alkalosis

Saline-Responsive	Saline-Resistant (Steroid excess)
Volume depletion • Due to vomiting, NGT, villous adenoma **Diuretic use/"contraction alkalosis"** Diuresis → loss of HCO_3^- poor fluid → extracellular fluid "contracts" around fixed amount of HCO_3^- → ↑ $[HCO_3^-]$ **Posthypercapnea** • Recent respiratory acidosis, kidneys have not completely readjusted	**Hypertensive:** • Hyperaldosteronism • Cushing's • Liddle dz • Exogenous mineralocorticoids **Normotensive:** • Hypokalemia (severe) • Milk alkali syndrome (exogenous alkali) • Bartter/Gitelman syndrome

Case Examples of Metabolic Alkalosis		
Case	**Interpretation**	**Diagnosis + Possible Scenario**
pH 7.43, $PaCO_2$ 52, HCO_3^- 34	pH high, so alkalemia. $PaCO_2$ high, so metabolic. HCO_3^- ↑ by 10, $PaCO_2$ ↑ by 12 (>7 so ↑ $PaCO_2$ due to respiratory acidosis)	**Met alkalosis & respiratory acidosis** N/V & received opioid for Abd pain
pH 7.48, $PaCO_2$ 47, Na^+ 142 Cl^- 98, HCO_3^- 34, U_{Cl} 29	pH high, so alkalemia. $PaCO_2$ high, so metabolic. HCO_3^- ↑ by 10, $PaCO_2$ ↑ by 7 (expected "10 for 7"). U_{Cl} >20, so not saline-responsive	**Simple met alkalosis, not saline-responsive** Hyperaldosteronism or Cushing dz

Respiratory Acidosis

$PaCO_2$ reflects balance between CO_2 production (VCO_2) & alveolar ventilation (VA):

$PaCO_2 \sim VCO_2/VA$

VE (minute ventilation) = VA + VD (dead space ventilation), so therefore

$PaCO_2 \sim VCO_2/(VE - VD)$

Hypercapnia results from:

↓ VE due to ↓ VT and/or ↓ RR

↑ VD

Rarely, ↑ VCO_2 (e.g., ↑ carb intake, exercise, fever) with all other things equal

Causes of Respiratory Acidosis			
1. "Won't Breathe"			
	Mechanism	**Etiologies**	**Management**
CNS Depression	↓ RR	Sedatives, head injury, brainstem stroke, CNS Infxn, response to met alkalosis, hypothyroidism	Stop/reverse sedatives (Naloxone 0.4 mg q2min prn, Flumazenil 0.2 IV q1min up to 0.8 mg) Head CT if concerns for intracranial process Intubate & ventilate
2. "Can't Breathe"			
	Mechanism	**Etiologies**	**Management**
Neuromuscular Weakness	↓VT, neg insp force (NIF) or mean insp pressure (MIP) weaker than –25 cm H_2O	Neuropathies: ALS, polio, Guillain–Barre NM Junction: myasthenia gravis, botulism Myopathies: diaphragm weakness, PM/DM, muscular dystrophy, ↓↓ phosphate	√fluoroscopic "sniff test" for paradoxical elevation of paralyzed diaphragm Treat underlying disorder, PT, nutrition, BiPap or ventilator support prn
Parenchymal or Airway Dz	↓VT and/or ↑ VD/VT (e.g., rapid shallow breathing)	Pneumonia, CHF, restrictive lung dz, ILD, COPD (usually FEV1 <1 L), Asthma	NIPPV can ↓ intubation in COPD, CHF (Plant PK, Owen JL, Elliott MW. Early use of non-invasive ventilation for acute exacerbations of COPD on general respiratory wards: a multicenter randomized controlled trial. *Lancet.* 2000;355:1931–1935; Peter JV, Moran JL, Phillips-Hughes J, et al. Effect of non-invasive positive pressure ventilation (NIPPV) on mortality in pt with acute cardiogenic pulmonary oedema: a meta-analysis. *Lancet.* 2006;367:1155–1163.)
Thoracic Abnormalities	↓VT due to ↓ compliance	Chest wall: kyphosis, scoliosis, flail chest, obesity (likely also ↓ central drive) Pleura: effusions, pleural fibrosis, PTX	Treat underlying disorder if possible Avoid causes of further ↓ ventilation (opioids, contraction alkalosis)

NM junction, neuromuscular junction; PM/DM, polymyositis/dermatomyositis; ILD, interstitial lung dz; NIPPV, noninvasive positive pressure ventilation.

Respiratory stimulants (e.g., theophylline, medroxyprogesterone, acetazolamide) have not been shown to work except for naloxone in opioid overdose

In COPD, O_2 therapy may → hypercapnia via ↑ O_2 in poorly ventilated lung units → ↓ hypoxic vasoconstriction → ↑ dead space → ↑ $PaCO_2$ (Malhotra A, et al. *Lancet*. 2001;357:884–885.)

Permissive hypercapnia in ARDS: little evidence of harm: HR, CO, PVR transiently ↑, & some evidence of benefit: ↓ shunt, improved CO, better O_2 unloading by Hb, ↓ capillary leak (Carvalho CR, et al. *Am J Respir Crit Care Med*. 1997;156:1458–1466; Kavanagh BP, et al. *Minerva Anesthesiol*. 2006;72(6):567–576.)

Avoid hypercapnia if ↑ ICP, right heart failure (may not tolerate pulmonary vasoconstriction) (Jaber BL, et al. *Am J Kidney Dis*. 1997;30:561–567.), renal failure (unable to buffer pH)

Case Examples of Respiratory Acidosis		
Case	**Interpretation**	**Diagnosis + Possible Scenario**
pH 7.27, $PaCO_2$ 60, HCO_3^- 27	pH low, so acidemia. $PaCO_2$ high, so respiratory acidosis. $PaCO_2$ ↑ by 20, HCO_3^- ↑ by 3 (close to 2, expected in acute respiratory acidosis)	**Acute respiratory acidosis** Pulmonary edema with hypoventilation
pH 7.3, $PaCO_2$ 60, HCO_3^- 29 Na^+ 132 Cl^- 95	pH low, so acidemia. $PaCO_2$ high, so respiratory acidosis. $PaCO_2$ ↑ by 20, HCO_3^- ↑ by 5, which is more than the 2 expected for acute respiratory acidosis but <8 expected for chronic respiratory acidosis, so metabolic disorder may be present OR Chronic respiratory acidosis, but HCO_3^- ↑ by less than the expected change of 8, so met acidosis also present. AG is normal. OR Chronic respiratory acidosis at baseline ($PaCO_2$ 50, HCO_3^- of 28), now with acute ↑ of $PaCO_2$ 50 → 60 & an expected ↑ of HCO_3^- by 1	**Acute respiratory acidosis & met alkalosis** ↓ RR due to opioids in a pt with pancreatitis & severe N/V OR **Chronic respiratory acidosis & non-AGMA** COPD pt with chronic CO_2 retention & early renal failure OR **Acute on Chronic respiratory acidosis** COPD pt with CO_2 retention having an exacerbation
pH 7.22, $PaCO_2$ 48, HCO_3^- 19 Na^+ 135 Cl^- 100	pH low, so acidemia. $PaCO_2$ high so respiratory acidosis. $PaCO_2$ ↑ by 8, HCO_3^- ↓ by 5. HCO_3^- should ↑ for acute or chronic respiratory acidosis, so met acidosis present. AG 16.	**Respiratory acidosis & AGMA** Pneumonia with hypoventilation & sepsis with lactic acidosis

Respiratory Alkalosis

Respiratory alkalosis has more cellular effects at given pH than metabolic alkalosis because $PaCO_2$ equilibrates faster. (Laffey JG, et al. *NEJM*. 2002;347(1):43–53.)

Resp alkalosis is a poor prognostic sign in critical illness, associated with higher mortality. (Cohen JJ, et al. Acid-base. 1982.)

Induced hypocapnia will transiently ↓ ICP by decreasing cerebral blood flow & volume, but will also ↓ O_2 delivery & may cause ischemia (Laffey JG, et al. *NEJM*. 2002;347(1):43–53.)

Hyperventilation & resp alkalosis → bronchospasm & direct lung injury (Laffey JG, et al. *NEJM*. 2002;347(1):43–53.)

Causes of Respiratory Alkalosis

Primary Hyperventilation	Secondary Hyperventilation (due to hypoxemia or pulmonary problem)
Pain, anxiety, fever CNS disorders affecting respiratory drive Drugs: ASA, progesterone, theophylline, β-agonists Pregnancy, sepsis, liver failure, mechanical ventilation	Asthma Pneumonia PE (can also → ↑ $PaCO_2$ with large ↑ dead space with massive PE) Restrictive lung dz CHF (early)

Case Examples of Respiratory Alkalosis

Case	Interpretation	Diagnosis + Possible Scenario
pH 7.72, $PaCO_2$ 20, HCO_3^- 25, Na^+ 135, Cl^- 97	pH high, so alkalemia. $PaCO_2$ low so respiratory. $PaCO_2$ ↓ by 20, HCO_3^- ↑ by 1 (HCO_3^- should ↓ for respiratory alkalosis, so met alkalosis also present)	**Respiratory alkalosis & met alkalosis** Pneumonia with dyspnea, fever, tachypnea & continuing to take diuretic
pH 7.60, $PaCO_2$ 25, HCO_3^- 24, Na^+ 148, Cl^- 95	pH high, so alkalemia. $PaCO_2$ low so respiratory. $PaCO_2$ ↓ by 15, HCO_3^- ↓ by 0 (should be lower, so met alkalosis present). Also AG 29, so AGMA present.	**Respiratory alkalosis, AGMA, & non-AGMA** DKA with N/V & aspiration causing respiratory distress

Assessing Oxygenation by Arterial Blood Gas

Most oxygen in the blood is bound to Hb & a small fraction is dissolved gas. O_2 Content = Hgb × 1.36 × SaO_2 + 0.003 × PaO_2

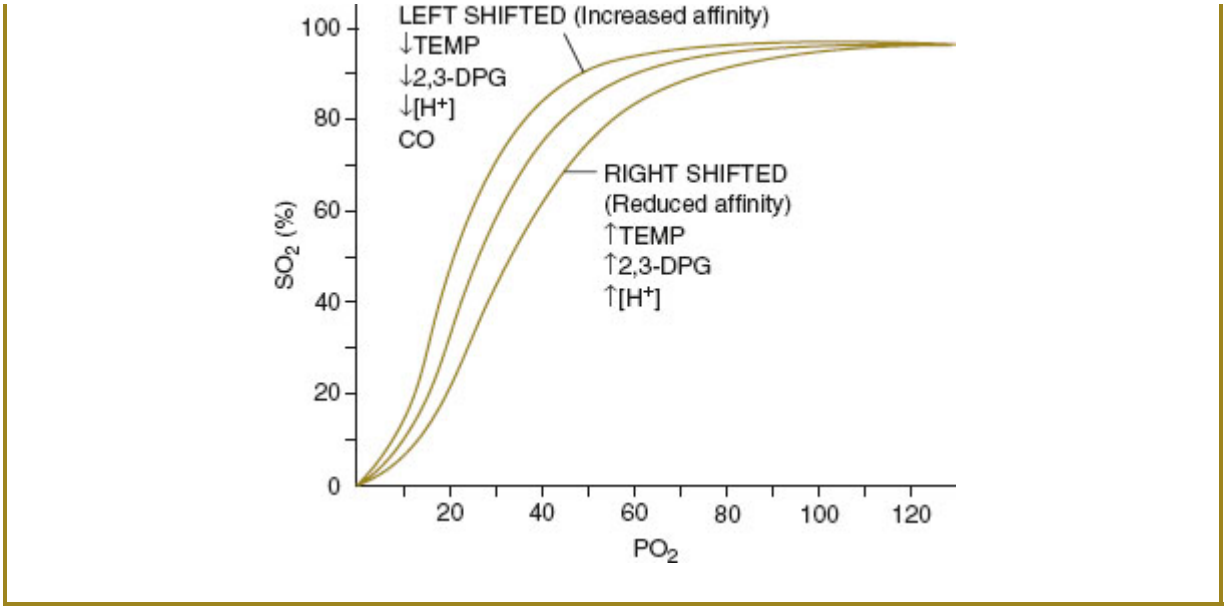
A-a Gradient: difference between PAO_2 & PaO_2, measure of alveolar–capillary gas exchange (abnormal in shunt, V/Q mismatch & diffusion defect)

Calculate PAO_2 from alveolar gas equation: $PAO_2 = FiO_2 \times (P_{atm} - P_{H2O}) - PaCO_2/R$

Normal A-a gradient is age/4 + 4

Oxygenation can be assessed by pulse oximetry (Hgb saturation) or PaO_2. The relationship between O_2 saturation & dissolved O_2 is determined by the oxyhemoglobin dissociation curve (Fig. 4-3)

Figure 4-3. Oxygen–Hemoglobin Dissociation Curve



Source: Walker HK, et al., (eds.). *Arterial Blood Gases in Clinical Methods: The History, Physical, and Laboratory Examinations*. 3rd ed. 1990.

Acidemia, increased T, increased 2,3-DPG will shift the curve to the right & facilitate O_2 unloading to the tissues

Alkalemia, low T, low 2,3-DPG (e.g., due to massive transfusions of stored blood, hypophosphatemia) & CO poisoning will increase the affinity of Hb to O_2 & shift curve to the left. This can lead to false reassurance from pulse oximetry.

CO binds Hb tightly to form CO-Hb which does not carry O_2 (e.g., if COHb is 25% & Hb is 12, effective Hb is 9 & max SaO_2 is 75%). Pulse oximeter will falsely read 100% because COHb is red in color (classic "cherry red" pt). PaO2 will be normal. Diagnose by measuring CO level. Treat with 100% FiO_2 or hyperbaric O_2 to displace CO.

Cyanide decreases peripheral O_2 extraction → increased SvO_2, SaO_2. PaO_2 will be normal. Pt is not cyanotic despite tissue hypoxia.

PAIN, AGITATION, AND DELIRIUM IN THE ICU

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General Principles

Provide comfort, control pain & agitation without over-sedation

Consequences of **undertreating:** pt suffering, device removal, ventilator dyssynchrony, myocardial ischemia

Consequences of **overtreating:** delirium, difficulty assessing neurologic function, prolonged mechanical ventilation (MV), immobility, ventilator-associated pneumonia (VAP), increased hospital & ICU length of stay (LOS), adverse psychological outcomes (e.g., posttraumatic stress disorder)

Interdisciplinary approach best (Sessler CN, et al. *Chest.* 2008;133:552–565.)

Nursing bedside experience & frequent assessments

Pharmacist knowledge of medications & possible interactions

Physician integration of pain management & sedation into overall treatment plan

Establish pain & agitation management **targets** using validated measures & **reevaluate frequently** to ensure treatment is not under- or overtreating sx (pain or agitation)

Integration of monitoring & management strategy for each is preferred approach. (Barr J, et al. *Crit Care Med*. 2013;41:263–306.)

PAIN/ANALGESIA

Assessing Pain

Pain assessment associated with short duration of MV, ICU LOS, & VAP
(Payen JF, et al. *Anesthesiology*. 2009;111:1308–1316.)
Establish target for pt comfort & use pain scale to determine if pain at target
Assessment tools

Interactive pts

Numerical Rating Scale (0 = "no pain" → 10 = "worst pain ever")

Wong-Baker Visual Scale (smiling face = "no hurt"; crying face = "hurts worst") see Figure 5-1.

Figure 5-1. Visual Pain Scale

Noninteractive pts

Behavioral Pain Scale (BPS): 12-point scale incorporating facial expression, upper limb movements, & compliance with mechanical ventilator. 0 points = no pain; 12 points = severe pain (Payen JF, et al. *Crit Care Med*. 2001;29:2258–2263.)

Behavioral Pain Scale		
Item	**Description**	**Score**
Facial expression	Relaxed	1
	Partially tightened (e.g., brow lowering)	2
	Fully tightened (e.g., eyelid closing)	3
	Grimacing	4
Upper limbs	No movement	1
	Partially bent	2
	Fully bent with finger flexion	3
	Permanently retracted	4
Compliance with ventilation	Tolerating movement	1
	Coughing but tolerating ventilation most of the time	2
	Fighting ventilator	3
	Unable to control ventilation	4

Critical Care Pain Observation Tool (CPOT) assesses 4 domains: facial expression, movements, muscle tension, & ventilator compliance. Each domain scored from 0 to 2. Higher scores indicate greater pain. (Gélinas C, et al. *Am J Crit Care*. 2006;15:420–427.)

Surrogate raters/family members: 79.9% sensitive & 67.7% specific assessing pain. (Desbiens NA, et al. *Crit Care Med*. 2000;28:1347–1352.)

Treating Pain

In many cases, pain can be treated but not completely eliminated → treat to tolerance of pain

Preventing pain is often more effective than treating established pain

Pain may cause agitation → assessing & treating pain reduces need for sedatives (Payen JF, et al. *Anesthesiology*. 2009;111:1308–1316.)

Nonpharmacologic interventions: reposition pt, remove irritating physical stimuli, apply heat/cold, music therapy, & relaxation techniques

Analgosedation: analgesia-based sedation → treat pain 1st, then use sedative, if necessary, to treat persistent agitation

Analgosedation strategy (1st line: morphine prn for pain, 2nd line: short-course [<6 hrs] propofol for persistent agitation) shortens duration of MV, ICU LOS, & hospital LOS (Strøm T, et al. *Lancet*. 2010;375:475–480.)

Procedural pain is common, consider preemptive analgesia

Pharmacologic interventions:

Nonopioid analgesics:

NSAIDs & acetaminophen may be used alone or as adjuncts to opioids. Side effects (GI bleeding, renal toxicity, & hepatotoxicity) may limit use in ICU

Opioid analgesics:

IV administration provides quick onset but shorter duration of effect → more frequent dosing

Control pain with basal pain medication (scheduled or continuous) with prn dosing for "breakthrough" pain

Start with bolus dosing, if needing >3 boluses/hr consider continuous administration

Renal & hepatic failure alter metabolism of opioids and/or prevent elimination → alter dosing to avoid prolonged effects

Older adults may have lower dosing requirements due to changes in body composition, hepatic metabolism, & renal excretion of medications

Avoid morphine in older adults (accumulation of metabolites may cause prolonged effects)

Monitor level of consciousness (see below). Perform daily interruption of continuous infusion and/or hold bolus administration

All pts on opioids should receive bowel regimen (e.g., docusate 100–200 mg PO b.i.d)

See table for commonly used opioids in the ICU

Select Opioid Analgesics

Drug	Equianalgesic Dose	Half-Life	Intermittent Dose	Infusion Dose
Fentanyl	200 mcg	1.5–6 hrs	0.35–1.5 mcg/kg q0.5–1h	0.7–10 mcg/kg/hr
Morphine	10 mg	2–3 hrs	0.01–0.15 mg/kg q1–2h	0.07–0.5 mg/kg/hr
Hydromorphone	1.5 mg	3–7 hrs	10–30 mcg/kg IV q1–2h	7–15 mcg/kg/hr
Remifentanil	—	3–10 min	—	0.6–15 mcg/kg/hr

Agitation/Sedation

Agitation/Sedation Balance

Agitation does not equate to "sedation deficiency" → search for cause of agitation (e.g., pain, hypoxemia, delirium, hypoglycemia, ETT malposition, discomfort from ETT, PTX, GI or bladder distention, ventilator dyssynchrony)

Assessing Level of Consciousness/Agitation

Use sedation scale, Richmond Agitation-Sedation Scale (RASS, see table) or Sedation-Agitation Scale (Riker/SAS, see table) to assess level of consciousness

Richmond Agitation-Sedation Scale (RASS)

Scale	Label	Description
+4	Combative	Combative, violent, immediate danger to staff
+3	Very agitated	Pulls to remove tubes or catheters; aggressive
+2	Agitated	Frequent nonpurposeful movement, fights ventilator
+1	Restless	Anxious, apprehensive, movements not aggressive
0	Alert & calm	Spontaneously pays attention to caregiver
–1	Drowsy	Not fully alert, but has sustained awakening to voice (eye opening & contact >10 s)
–2	Light sedation	Briefly awakens to voice (eyes open & contact <10 s)
–3	Moderate sedation	Movement or eye opening to voice (no eye contact)
–4	Deep sedation	No response to voice, but movement or eye opening to physical stimulation
–5	Unarousable	No response to voice or physical stimulation

(Ely EW, et al. *JAMA*. 2003;289:2983–2991; Sessler CN, et al. *Am J Respir Crit Care Med*. 2002;166:1338–1344.)

Riker Sedation-Agitation Scale (SAS)		
Scale	**Label**	**Description**
7	Dangerous agitation	Pulling at ETT, trying to remove catheters, climbing over bed rail, striking at staff, thrashing side-to-side
6	Very agitated	Does not calm, despite frequent verbal reminding of limits; requires physical restraints, biting ETT
5	Agitated	Anxious or mildly agitated, attempting to sit up, calms down to verbal instructions
4	Calm & cooperative	Calm, awakens easily, follows commands
3	Sedated	Difficult to arouse, awakens to verbal stimuli or gentle shaking but drifts off again, follows simple commands
2	Very sedated	Arouses to physical stimuli but does not communicate or follow commands, may move spontaneously
1	Unarousable	Minimal or no response to noxious stimuli, does not communicate or follow commands

(Riker RR, et al. *Crit Care Med.* 1999;27:1325–1329.)

Establish target level of sedation → most pts can be alert & calm (e.g., RASS 0, SAS 4)

Keep pt at target level of sedation → decrease amount of sedative if over-sedated, increase amount of sedative if under-sedated/agitated. Reassess frequently (every 4–6 hrs)

Deep sedation (i.e., RASS deeper than –3) is associated with longer duration of MV & increased mortality (Shehabi Y, et al., *Am J Respir Crit Care Med.* 2012;15:724–731; Shehabi Y, et al. *Intensive Care Med.* 2013;39:910–918.)

Analgesics may be enough to provide adequate level of sedation, see **Analgosedation**

Principles of Sedation Management

Overall goal should be to use as little sedation as possible to maintain alert/calm state

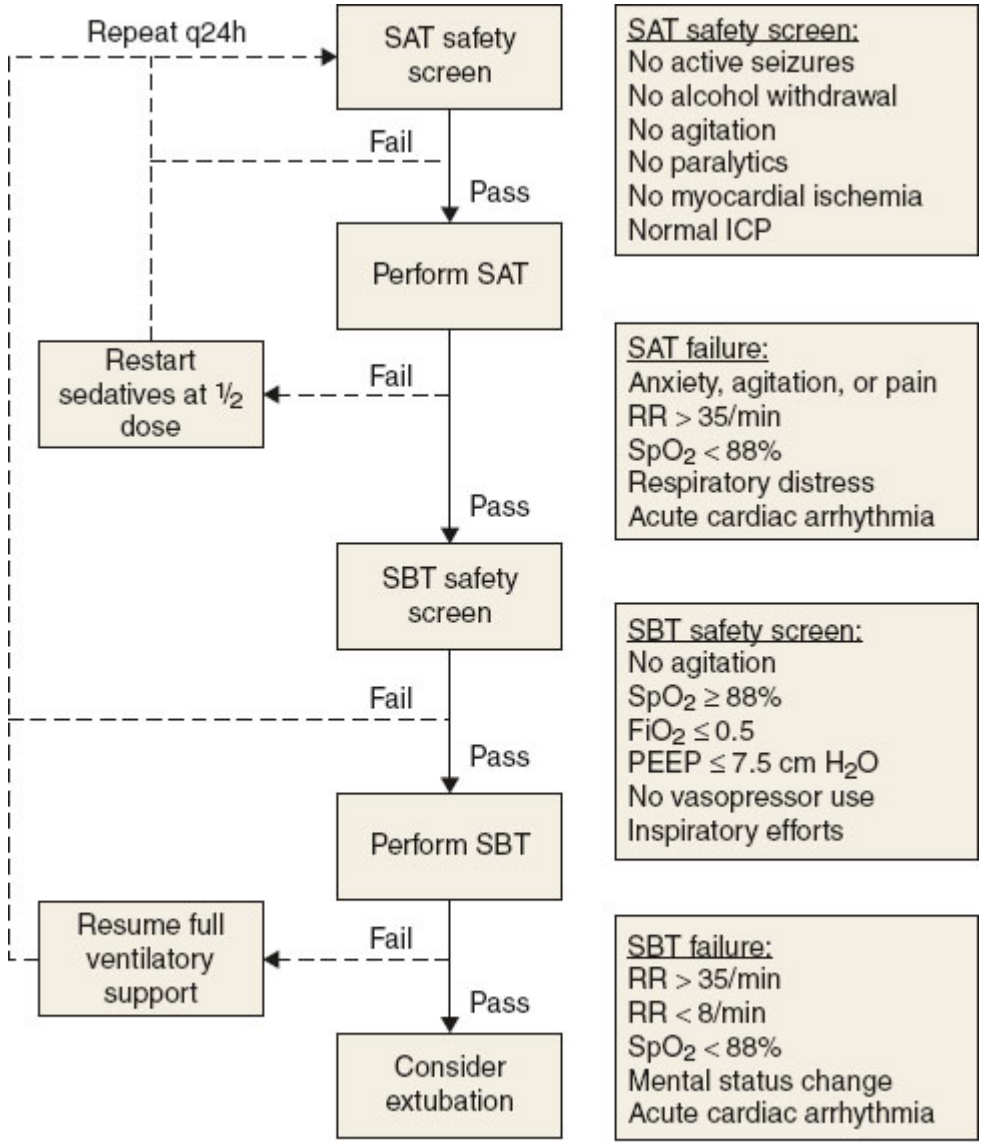
Use intermittent bolus rather than continuous infusion (Kollef MH, et al. *Chest.* 1998;114:541–548.)

If >3 boluses/hr, consider continuous infusion

Use of daily "spontaneous awakening trial" **(SAT)** → shortens duration of MV, ICU & hospital LOS (Kress JP, et al. *N Engl J Med.* 2000;342:1471–1477; Girard TD, et al. *Lancet.* 2008;371:126–134.) (see Fig. 5-2)

Figure 5-2. Wake up & Breathe Flowchart: Integration of Spontaneous Awakening Trials (SAT) & Spontaneous Breathing

Trials (SBT)



Performing the SAT:

Step 1: Screen pt for: sedation given for EtOH withdrawal, increasing agitation, paralytics, myocardial ischemia in last 24 hrs, or elevated ICP. If any are present, do not perform SAT.

Step 2: Hold bolus analgesics/sedatives and/or stop continuous infusions.

Step 3: SAT "pass" = RASS –3 to +1 or Riker 3 to 5. SAT "fail" = RASS +2 to +4 or Riker 6 or 7.

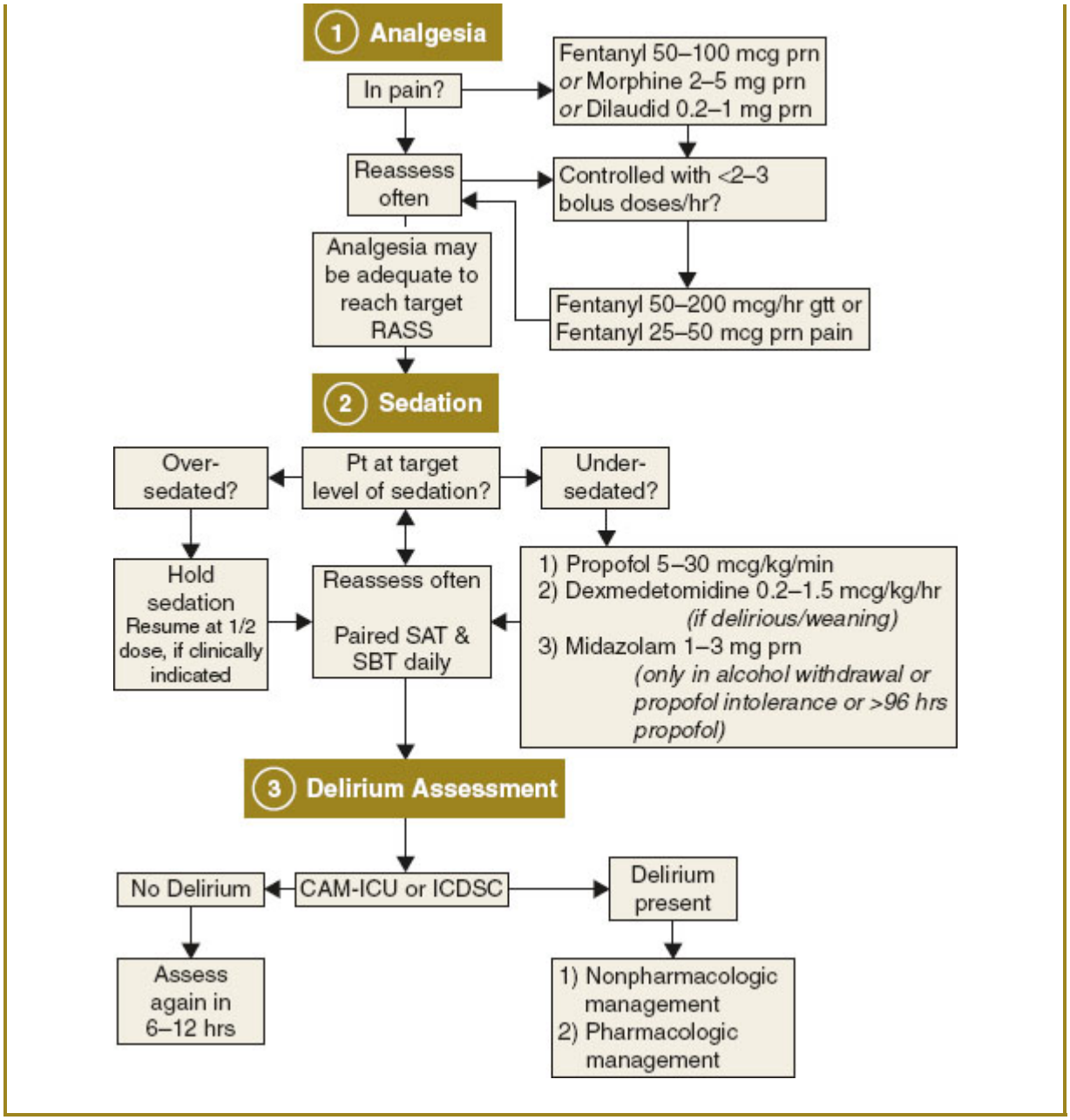
If pt passes SAT: proceed to spontaneous breathing trial (SBT).

If fail SAT: if necessary, resume analgesia/sedation **at ½ previous dosing.**

Paired "awake & breathing" strategy (**daily SAT** + **SBT**) → shorter duration of MV, ICU & hospital LOS & 14% improved mortality at 1 yr (Girard TD, et al. *Lancet.* 2008;371:126–134.)

Use of an analgesia-sedation management protocol → shorter duration of MV, ICU LOS, & hospital LOS (Brook AD, et al. *Crit Care Med.* 1999;27:2609–2615.) (see Fig. 5-3)

Figure 5-3. Pain, Agitation, & Delirium Protocol



Avoid benzodiazepines as 1st- or 2nd-line sedative agents (except in EtOH withdrawal seizure) → benzodiazepines are associated with higher rate of delirium & prolonged MV (Carson SS, et al. *Crit Care Med.* 2006;34:1326–1332; Riker RR, et al. *JAMA.* 2009;301:489; Pandharipande P, et al. *Anesthesiology.* 2006;104:21–26.)

Benzodiazepines are associated with prolonged ICU LOS & greater in-hospital mortality compared with propofol (Lonardo NW, et al. *Am J Respir Crit Care Med.* 2014;189:1383–1394.)

Select Sedative Agents (Also See Appendix)				
Drug	**Mechanism of Action**	**Half-Life**	**Intermittent Dose**	**Infusion Dose**
Propofol	GABA-α agonist	40 min	0.2–0.6 mg/kg	5–80 mcg/kg/min
Dexmedetomidine	CNS-α_2 agonist	6 min	—	0.1–1.4 mcg/kg/hr
Haloperidol	CNS D_1 & D_2 antagonist	18 hrs	2–10 mg (IV)	0.04–0.15 mg/kg/hr
Midazolam	GABA-α agonist	3 hrs	0.02–0.08 mg/kg	0.04–0.2 mg/kg/hr
Lorazepam	GABA-α agonist	8 hrs	0.02–0.06 mg/kg	0.01–0.1 mg/kg/hr

Delirium in the ICU

Acute disturbance of consciousness that develops over a short period of time (hours to days) & fluctuates over time & is usually reversible

Affects 60–80% of mechanically ventilated pts & 40–60% of nonventilated pts

ICU Delirium associated with triple the risk of death 6 months postcritical illness

Delirium associated with prolonged LOS, increased healthcare costs, long-term cognitive impairment & disability outcomes (Pandharipande PP, et al. *N Engl J Med.* 2013;369:1306–1316; Brummel NE, et al. *Crit Care Med.* 2014;42:369–377.)

www.icudelirium.org

Pathophysiology

Neurotransmitter imbalance (ACh deficiency, dopamine excess)

Inflammation (TNF-α, IL-6)

Impaired oxidative metabolism (low cerebral perfusion, hypoxemia)

Changes in large neutral amino acid concentrations (neurotransmitter precursors & toxic metabolites)

Primed microglia → overactivation due to cytokines (e.g., TNF-α) → neuroinflammation

Risk Factors

Average ICU pt has 10+ risk factors for delirium (Ely EW, et al. *Intensive Care Med.* 2001;27:1892–1900.) (see table below)

Risk Factors for ICU Delirium		
Host Factors (Unmodifiable)	**Related to Critical Illness (Potentially Modifiable)**	**Iatrogenic (Modifiable)**
Age (elderly)	Metabolic derangements (acidosis, electrolyte disorders)	Medications (opioids & benzodiazepines)
Alcoholism/drug use	Anemia	Immobility
APO-E4 polymorphism	Infxn/sepsis	Sleep deprivation
Dementia/mild cognitive impairment	Hypotension	>3 infusing medications
Depression	Hypoxemia	Restraints
HTN	Severity of illness	Open ICU room
Smoking	Intracranial processes	Lack of visible daylight
Vision/hearing impairment	Urinary/fecal retention	Lack of visitors
Malnutrition	Fever	

Delirium Diagnosis

3 subtypes (Peterson JF, et al. *J Am Geriatr Soc.* 2006;54:479–484.)

Hyperactive (5%): agitated or combative

Hypoactive (45%): lethargic, drowsy, infrequent spontaneous movement

Mixed (55%): features of both

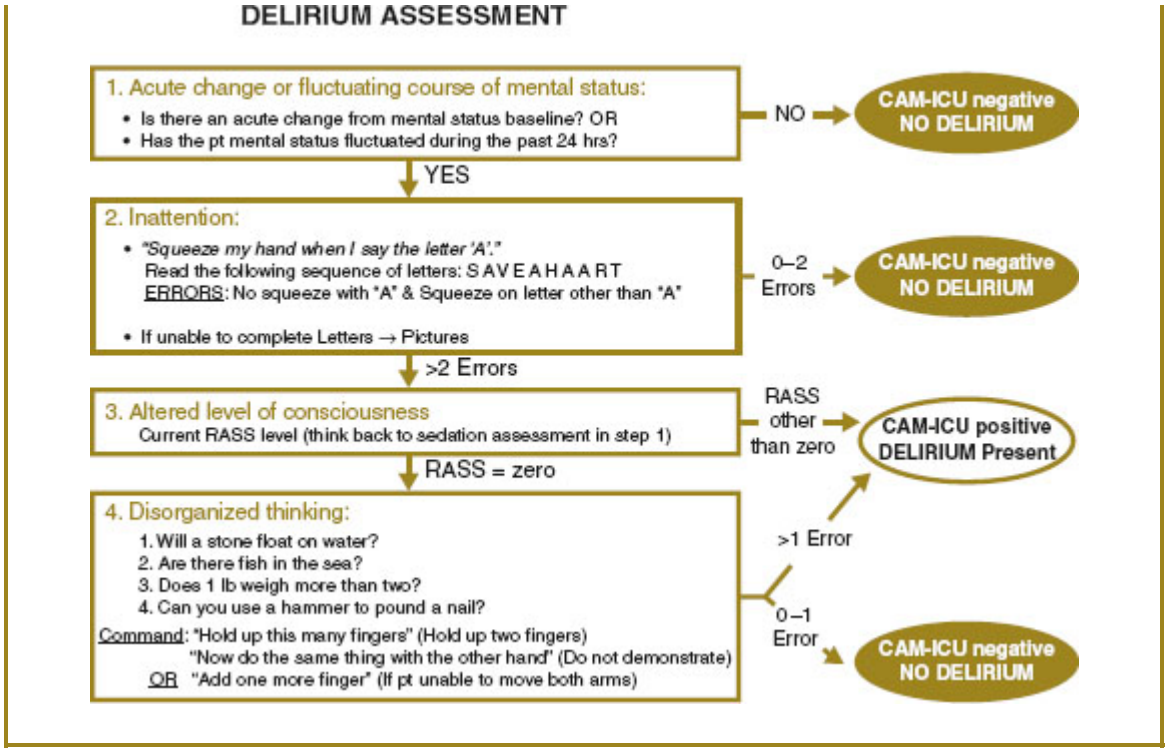
Subsyndromal delirium: some features of delirium, but not the full clinical syndrome (Ouimet S, et al. *Intensive Care Med.* 2007;33:1007–1013.)

Most delirium is mixed/hypoactive → 75% of case missed if not screened for (Spronk PE, et al. *Intensive Care Med.* 2009;35:1276–1280.)

Validated Delirium Screening Tools:

Confusion Assessment Method for the ICU (CAM-ICU) (93% specificity; 89% sensitivity) (Ely EW, et al. *JAMA*. 2001;29:1370.) (see Fig. 5-4)

Figure 5-4. Confusion Assessment Method for the ICU (CAM-ICU)



90% of CAM-ICU assessments take <1 min

2-step process:

Step 1: Assess level of consciousness using RASS table

- If RASS –4 or –5, the pt is too sedated to assess for delirium, if –3 to +4, proceed with step 2

Step 2: Assess for features of delirium:

Feature 1: Acute mental status change/fluctuation in mental status?

- Feature 1 present if mental status changed from baseline or fluctuation in mental status in last 24 hrs

Feature 2: Inattention

- **Cardinal feature of delirium → if attentive,** pt **does NOT have clinical delirium**
- Assess via Attention Screening Exam:

1 Say to the pt "Squeeze my hand when I say the letter 'A'"
Read the following letters, 1 sec apart: S-A-V-E-A-H-A-A-R-T
Error if no squeeze on A or squeeze on letter other than A

2 Feature 2 present if >2 errors

Feature 3: Altered level of consciousness?

- Feature 3 present if pt is any RASS except 0

Feature 4: Disorganized thinking?

- Ask pt these yes/no questions:

1 "Will a stone float on water?"
2 "Are there fish in the sea?"
3 "Does 1 lb weigh >2?"
4 "Can you use a hammer to pound a nail?"

- Feature 4 present if >1 wrong answer

- A pt is delirious (CAM-ICU positive) if features 1 **&** 2 & ***either*** feature 3 **OR** 4 are present

Intensive Care Unit Delirium Screening Checklist (ICDSC) (Bergeron N, et al. *Intensive Care Med.* 2001;27:859–864.)

8-item screening tool based off information from last 8 to 24 hrs

Score of >4, 99% specific; 64% sensitive for delirium

Intensive Care Unit Delirium Screening Check List (ICDSC)	
Checklist Item	**Description**
Altered level of consciousness[a]	
A	No response
B	Response to intense & repeated stimulation
C	Response to mild or moderate stimulation
D	Normal wakefulness
E	Exaggerated response to normal stimulation
Inattentiveness	Difficulty following instructions or easily distracted
Disorientation	To time, place, or person
Hallucination-delusion-psychosis	Clinical manifestation or suggestive behavior
Psychomotor agitation or retardation	Agitation required use of drugs or restraints or slowing
Inappropriate speech or mood	Related to events or situation or incoherent speech
Sleep/wake cycle disturbance	Sleeping <4 hrs/d, waking at night, sleeping all day
Sx fluctuation	Sx of above occurring intermittently
Total score (1 point for obvious presence of features above)	0–8

[a]If level of consciousness A or B no other features are assessed that day.

If delirium diagnosed, **"THINK"** about causes & management (see table below)

"THINK" Mnemonic for Delirium Causes & Management	
T	**T**oxic situations • CHF, shock, dehydration • Deliriogenic medications (e.g., anticholinergics or benzodiazepines) • New organ failures: e.g., liver or kidney **T**ight titration of sedatives & analgesics
H	**H**ypoxemia **H**aloperidol or other antipsychotic for treatment
I	**I**nfxn/sepsis (nosocomial) **I**mmobility
N	**N**onpharmacologic interventions • Hearing aids & glasses • Reorientation • Sleep protocol • Music • Noise control • Ambulation
K	K^+ or other electrolyte abnormalities

(Hipp DM, et al. *Neurotherapeutics*. 2012;9:158–175.)

Delirium Management

Nonpharmacologic:

40% reduction in incidence of delirium in non-ICU pts with multicomponent protocol: reorientation, removal of restraints & catheters as quickly as possible, mobilization, hydration, eyeglasses, & hearing aids (Inouye SK, et al. *N Engl J Med.* 1999;340:669–676.)

Early PT/OT (<72 hrs after ICU admission) → reduced ICU delirium duration by 50% (Schweickert WD, et al. *Lancet.* 2009;373:1874–1882.)

Ear plugs, alone or as part of sleep promotion protocol, associated with 40% reduction in risk of delirium (Litton E, et al. *Crit Care Med.* 2016;44:992–999.)

Pharmacologic:

No FDA-approved drugs for treatment

Benzodiazepines **not** indicated (except for delirium tremens) & **may worsen delirium**

Typical & atypical antipsychotics commonly used despite lack of evidence supporting benefit (Neufeld KJ, et al. *J Am Geriatric Soc.* 2016;64:705–714.)

Typical antipsychotics[1]

Haloperidol: 2–5 mg PO or IV q6h, once calm, use lower doses; in elderly use ½ dose. Doses >20 mg/d increased risk of adverse effects: dystonic reactions, over-sedation, malignant hyperthermia, EPS, & QTc prolongation

Atypical antipsychotics[2] (may reduce serious adverse effects: data mixed regarding efficacy)

Olanzapine: 5 mg PO or SL daily; in elderly use ½ dose

Risperidone: 0.5 mg PO b.i.d; maximum dose 2.5 mg/d

Quetiapine: 25–50 mg PO q12h; titrate to effect q24h

Sedation strategy: Dexmedetomidine (vs. benzodiazepines) reduces duration of ICU delirium (Riker RR, et al. *JAMA*. 2009;301:489–499; Pandharipande PP, et al. *Crit Care Med*. 2010;14:R38.)

[1]Monitor QTc; discontinue drug if baseline ≥450 ms or prolonged from baseline >25%.

[2]Monitor QTc; discontinue drug if baseline ≥450 ms or prolonged from baseline >25%.

Integrating Pain, Agitation, & Delirium: The "ABCDEF" Bundle

(Vasilevskis EE, et al. *Chest.* 2010;138:1224–1233.) (see table below)

"Bundled" evidence-based therapies shown to reduce ventilator time, delirium, & death (Balas MC, et al. *Crit Care Med.* 2014;42:1024–1036; Liu V, et al. *Crit Care Med.* 2016;44:460–467.)

Also see: www.iculiberation.org & www.icudelirium.org

ABCDEF Bundle	
A	**A**ssess & manage pain
B	**B**oth Spontaneous Awakening & Spontaneous Breathing Trials
C	**C**hoice of sedation (i.e., target light sedation & avoid benzodiazepines)
D	**D**elirium monitoring & management
E	**E**arly mobility & physical Rehab
F	**F**amily engagement & empowerment

NUTRITION

MARCUS D. DARRABIE, MD • DANNY O. JACOBS, MD, MPH

Significance

World Health Organization definition: cellular imbalance between the supply of nutrients & energy & the body's demand for them to ensure growth, maintenance, & specific functions

30–50% of hospitalized pts are malnourished (Corkins MR, et al. *J Parenter Enteral Nutr.* 2014;38(2):186–195.)

Severe illness generally leads to a catabolic state, that can be aggravated by inadequate intake of protein & energy

Inflammation, immobilization, sedentarism, as well as age exacerbate loss of lean body mass

Severe stress & malnutrition are associated with negative energy balance

Early recognition of malnutrition is clinically important since ongoing malnutrition can exacerbate organ dysfunction by depleting protein in bodily tissues

Experimental studies in animals have shown early nutrition to reduce septic morbidity, reduce bacterial translocation & reduce infectious complications, whether the same effects occur in humans is controversial (Li J, Kudsk KA, et al. *J Trauma.* 1995;39(1):44–51.)

Optimal nutrition management may facilitate recovery of hospitalized pts

Nutritional Assessment

Hx & physical, lab tests or as percentage of wt change

A subjective global assessment screen may be used to evaluate nutritional status & identify malnourished pts (Detsky AS, et al. *J Parenter Enteral Nutr.* 1987;11(1):8–13.)

Wt change (overall & change in past 2 wks)

Dietary intake (relative to normal wt)

GI sx (none, N/V)

Functional capacity (no dysfunction, or dysfunction & duration)

Physical appearance (subjective assessment of fat loss, muscle wasting, edema, & ascites)

Nutritional status classified as well nourished (SGA A), moderately malnourished (SGA B), or severely malnourished (SGA C)

Anthropometric data (wt, ht, tricep skinfold thickness) correlates well with body composition in large epidemiologic survey studies

In ICU pts these assessments may be inaccurate due to hydration status or difficult to obtain due to sedation. In these circumstances, nutritional risk can be assessed using Nutritional Risk Score (NRS-2002) or NUTRIC (Canadian Nutrition Risk in the Critically Ill) score

Classification of Nutritional Risk

NRS-2002 Score (Kondrup J, Johansen N, Plum LM, et al. Incidence of nutritional risk and causes of inadequate nutritional care in hospitals. *Clin Nutr* 2002;21:461–468.)

Nutritional Status		Severity of Disease	
Absent score 0	Normal nutritional status	Absent score 0	Normal nutritional requirements
Mild score 1	Wt loss >5% in 3 mo OR food intake <50–75% of normal requirement in preceding week	Mild score 1	Hip fx Chronic pts in particular with acute complications: cirrhosis, COPD, chronic hemodialysis, diabetes, oncology
Moderate score 2	Wt loss >5% in 2 mo OR BMI 18.5–20.5+ impaired general condition OR food intake 25–50% of normal requirement in preceding week	Moderate score 2	Major abd surgery, stroke, severe pneumonia, hematologic malignancy
Severe score 3	Wt loss >5% in 1 mo (15% in 3 mo) OR BMI <18.5+ impaired general condition OR food intake <25% of normal requirement in preceding week	Severe score 3	Head injury, bone marrow transplantation, intensive care pts (APACHE II >10)

If age ≥70 yrs, add 1 point for NRS-2002
Total score = (Points for nutritional status) + (Points for dz severity) + (Points for age)
Low nutritional risk = NRS-2002 score ≤3; High nutritional risk = NRS-2002 score ≥5
(Davis CJ, et al. *J Parenter Enteral Nutr.* 2012;36:197–204.)

NUTRIC Score (Heyland DK, et al. *Crit Care* 2011;15:R268.)

	NUTRIC Points			
Factors	**0**	**1**	**2**	**3**
Age (yrs)	<50	50–74	≥75	—
APACHE II Score	<15	15–19	20–27	≥28
Baseline Simplified Organ Failure Assessment Score	<6	6–9	≥10	—
No. of comorbidities	0–1	≥2	—	—
Days in hospital to ICU admit	0	≥1	—	—
Interleukin-6 (μ/ml)	0–399	≥400	—	—

Total score is from 6 separate factors for NUTRIC score
Low nutritional risk = NUTRIC score 0–5; High nutritional risk = NUTRIC score 6–10
(Starke J, et al. *Clin Nutr.* 2011;30:194–201.)

- Ideal body wt (men) = 50 kg + 2.3 kg × (ht [in] – 60)
- Ideal body wt (women) = 45.5 kg + 2.3 kg × (ht [in] – 60)

Major acute changes in wt likely represent changes in fluid status

Though not seen in its pure form in hospitalized pts, chronic deficits in protein, or energy intake lead to protein–energy malnutrition, which can be broadly classified as follows:

Marasmus-type

Acceptable ratio of protein: calorie intake but inadequate total dietary calories

Preserved visceral proteins (short-lived proteins mostly synthesized in the liver such as albumin, pre-albumin, retinol-binding protein)

May manifest as impaired immunity (i.e., decreased total lymphocyte count & positive skin test anergy)

Typical pt may appear with wasting of both muscle & fat (i.e., cachexia, sunken supraclavicular fossae, temporal wasting, muscle pain)

Kwashiorkor type

Adequate calorie but insufficient total protein intake

Reduction in visceral proteins

Typical pt may have evidence of increased extracellular fluid (i.e., anasarca, ascites, decreased skin turgor, liver enlargement, parotid gland hypertrophy)

Clinical Signs of Malnutrition

Location	Signs	Deficiencies
Hair	Alopecia, brittle color change, dryness, easy pluckability	Protein–calorie malnutrition, biotin, zinc, vitamins E & A
Skin	Acneiform lesions, follicular keratosis, xerosis, ecchymosis, intradermal petechiae, erythema, hyperpigmentation, scrotal dermatitis	Vitamin A, vitamin C or K, niacin
Eyes	Angular palpebritis, Bitot spots, conjunctival xerosis	Vitamin B_2, vitamin A
Mouth	Angular stomatitis, atrophic papillae, bleeding gums, cheilosis, glossitis, magenta tongue, loss of taste	Zinc, vitamin B_{12}, niacin, vitamin C, vitamin B_2
Extremities	Genu valgum or varum, loss of deep tendon reflexes of the lower extremities	Vitamin D, vitamins B_1 & B_{12}
Neurologic	Symmetric motor or sensory dysfunction, ataxia, nystagmus, heart failure, mental status changes or confusion	Thiamine
Musculoskeletal	Muscle & fat wasting, weakness, muscle pain, heart failure (cardiomyopathy)	Selenium, protein–calorie malnutrition

Source: Adapted in part from Bernard MA, et al. *Nutrition and Metabolic Support of Hospitalized Patients.* Philadelphia, PA: WB Saunders; 1986.

Nutritional monitoring should include daily fluid balance evaluation, daily wt & nitrogen balance determination

Surrogate markers of nutritional risk include:

Pre-albumin levels (half-life, 2 days)

Transferrin levels (half-life, 8–10 days)

Thyroxine-binding pre-albumin (half-life, 1–2 days)

Retinol binding protein levels (half-life, 10 hrs)

Albumin levels may decrease with chronic malnutrition or may reflect conditions other than malnourishment & may be normal in some pts with protein–calorie malnourishment like kwashiorkor; additionally it is a strong indicator of operative risk but performs poorly as a nutritional marker (half-life, 20 days)

C-reactive protein positive acute phase reactant increases in inflammation, decreases in malnutrition (half-life, 19 hrs)

Electrolyte levels, magnesium, phosphorus, calcium, LFTs, blood urea nitrogen, & creatinine assays

Biochemical markers of nutritional risk such as prealbumin, albumin, & transferrin are negative acute phase proteins & may decrease in the setting of surgery, stress, & infxn due to increased vascular permeability & decreased hepatic protein synthesis

Nutrition Requirements

Energy Expenditure

Determination of energy expenditure is used to decide feeding regimen

Nutritional requirements & energy expenditure can be measured or estimated by predictive formula

Indirect calorimetry is the gold standard & utilizes measurements of CO_2 production & O_2 consumption in a closed ventilator system to indirectly estimate the caloric needs of hospitalized pts

Measured over 15–30 min period then extrapolated over a 24-hr period

Hypermetabolism >100% of predicted energy expenditure

Normometabolism = 90–100% of predicted energy expenditure

Hypometabolism <90% of predicted energy expenditure

Resp quotient (RQ): ratio of CO_2 production & O_2 consumption; provides a rough estimate of substrate utilization during indirect calorimetry

$RQ = VCO_2/VO_2$

Energy Sources and Associated Respiratory Quotients

Substrate	Energy (kcal/g)	O_2 Consumption VO_2 (l/g)	CO_2 Production VCO_2 (l/g)	RQ
Ethyl alcohol oxydation	7.0	1.46	0.98	0.71
Fat oxidation	9.0	1.96	1.39	0.71
Protein oxidation	4.0	0.94	0.75	0.82
Carbohydrate Oxidation	4.0	0.81	0.81	0.9–1.0

Source: Adapted from Bernard MA, et al. Nutrition and Metabolic Support of Hospitalized Patients. Philadelphia, PA: WB Saunders; 1986.

In general RQ >1 indicates excessive calorie load & suggests that a reduction in caloric intake may be indicated

RQ ≥1 indicates a need to decrease carbohydrates or lipids (McClave SA, et al. *J Parenter Enteral Nutr.* 2003;27(1):21–26.)

RQ <0.82 may indicate a need to increase caloric intake

RQ can equal 1.0 after eating; in diabetes RQ = 0.71; in starvation RQ = 0.83

In the absence of indirect calorimetry, calculated or predicted energy expenditure is typically based on body size & a correction factor for metabolic stress

Basal energy expenditure (BEE): amount of energy produced per unit of time under basal conditions (i.e., complete rest, shortly after awakening, after 14-hr fast)

Most recognized calculation of BEE is the Harris–Benedict Equation

BEE (Males): 66 + 13.7 (wt in kg) + 5 (ht in cm) – 6.8 (age in years)

BEE (Females): 655 + 9.6 (wt in kg) + 1.8 (ht in cm) – 4.7 (age in years)

Harris–Benedict equation & many other predictive equations may overestimate or underestimate nutritional needs in critically ill, overweight, & underweight pts

A modification of the HBE that is generally more applicable in the ICU is simply:

$$\textbf{\textit{BEE (kcal/d) = 25 × wt (kg)}}$$

Metabolic stress increases kcal requirements as follows:

Thermal injury (typically the greatest increase in BEE)

0–20% body surface area – BEE × 1.0–1.5

20–40% body surface area – BEE × 1.5–1.85

40–100% body surface area – BEE × 1.85–2.05

Fever: BEE × 1.1 (for each unit of temp in °C greater than normal body temp)

Peritonitis: BEE × 1.2–1.5

Major sepsis: BEE × 1.4–1.8

Major soft tissue trauma: BEE × 1.1–1.4

Multiple long bone fx: BEE × 1.2–1.4

Protein intake requirements can generally be estimated as follows:

Healthy nonstressed metabolism: 0.8–1.0 g/kg/d × wt (kg)

Mild-to-severe malnutrition & catabolic stress: 1.0–1.6 g/kg/d × wt (kg)

Critically ill pts require 1.0–2.0 g/kg/d x wt (kg)

Nitrogen balance measurements allow for a more specific assessment of the need for protein repletion

Nitrogen balance can be estimated as follows: Nitrogen balance: g/d = (protein intake g/d ÷ 6.25 g/d) - (24h urine nitrogen g/d + 2 to 4g) (Dickerson RN, et al. *Nutrition*. 2005;21(3):332–338).

Positive nitrogen balance is indicative of anabolism

Negative nitrogen balance is indicative of catabolism

Nitrogen balance is improved with optimization of the nonprotein calorie to nitrogen ratio

Normal adults during nitrogen equilibrium typically require 1 g nitrogen per 300 kcal

Critically ill pts require 1 g nitrogen per 150 kcal

1 g nitrogen yields 6.25 g protein (i.e., a critically ill pt with a 1,750 kcal energy requirement may require 11.7 g nitrogen or 72.9 g protein)

Nutritional Support Routes

Determination of energy needs or requirements → functional GI tract that can be used safely → determination of optimal route: Oral vs. Enteric feeding tube

OR

Determination of energy needs or requirements → nonfunctional GI tract → consider TPN if expected length of time is at least 5–7 days without feeding → assess for placement of access device

Functional GI Tract—Enteral Nutrition

The gut of postoperative, trauma, or nonsurgical critically ill pts is often functional: enteral nutrition is indicated if pt has high nutritional risk & is unable to eat

Enteral nutrition should be initiated within 24–48 hrs in critically ill pts unable to eat

In the postop pt, enteral feeding can be provided within 24 hrs if feasible

Approx 100 cm of small bowel is required for adequate nutrient absorption

Advantages:

Reduced cost, more physiologic

Animal studies demonstrate reduced mucosal atrophy, reduced bacterial translocation & improved GI immunity (Li J, et al. *J Trauma.* 1995;39(1):44–51.)

Potential contraindication(s) may include:

Ischemic bowel, bowel obstruction, hemodynamic instability, ileus, high output fistula, improper airway protection

Typical enteral formulations (The exact formulas avail. vary by hospital; review of institutional formulations are required):

Enteral Formulas		
Enteral Formulas	**Description**	**Examples**
Standard	Mimics American diet, 50–60% calories from carbs, 10–15% from protein, 25–40% from fat.	Isosource, Osmolite, Boost, Ensure
Concentrated	Similar to standard but density per milliliter is greater. Typically used for pts with fluid restrictions.	Ensure Plus, Impact 1.5, Twocal HN, Nutren Renal, Nutren 2.0
High nitrogen—protein	Contain >15% of calories by nitrogen & protein. Typically used for pts with higher than normal protein needs.	Isosource HN, Osmolite HN, Replete, Boost HP, Peptamen VHP, Ensure HP, Promote
Elemental	For pts with impaired pancreatic & small bowel function. Consists of low residue, partially digested & easily absorbed proteins.	Alitraq, Peptamen, Vivonex PLUS, Vivonex T.E.N.
Fiber containing or blenderized formulas	Contain fiber supplied from added soy or natural food sources. Intended to regulate bowel function by eliminating diarrhea & constipation	Jevity, Compleat, Ensure with Fiber, Promote with Fiber, Nutren 1.0 Fiber

Glutamine is the primary source of energy for enterocytes & helps maintain the integrity of bowel mucosa in animals. Its administration may be associated with decrease risk of infection in surgical pts (Zheng YM, et al. *World J Gastroenterol.* 2006;12(46):7537–7541.)

Enteric Access Routes

Short-term feedings (<4 wks)

Oroenteric—orally placed gastric or enteric tube, maybe favored in pts with nasal or facial injury

Nasogastric—most common, typically large caliber, prepyloric placement

Nasoenteric tube—typically small caliber, postpyloric placement

Long-term feedings (generally recommended for feeding >4–6 wks) require placement of a more permanent gastrointestinal access

Percutaneous enteral device (gastric, gastric jejunal, or direct jejunal)

Surgically placed tube (gastrostomy or jejunostomy)

Endoscopic or radiographically placed in anatomically challenging cases

Enteric Feeding Protocols

Tube position should be confirmed either directly or radiographically

Pts should be placed upright at 30–45° positions

Tubes should be flushed with at least 30 ml of water every 4 hrs to maintain patency; however, this may be adjusted based on free water requirements

Bolus feedings generally are given in 4-hr intervals via nasogastric or gastrostomy tubes with adjustments for gastric residual vol (i.e., tube feedings are typically held if residual is greater than vol of last bolus)

Continuous feedings are typically administered via jejunal feeding tubes & may be administered over the entire day or given intermittently

Small bowel feedings should be initiated at a slow rate (i.e., 15–25 cc/h for continuous feedings) & advanced at a slow & fixed rate until reaching goal feeding rate

No significant difference in aspiration risk between stomach & proximal duodenal feeding but aspiration events are less severe on average with feedings beyond the ligament of Treitz (Marik PE, Zaloga GP. *Crit Care.* 2003;7:R46–51.)

Nonfunctioning GI Tract—Parenteral Nutrition

Total parenteral nutrition (TPN) delivers nutrients via a hyperosmolar solution delivered into a central vein (typically superior vena cava)

Indicated in critically ill, malnourished pts with contraindications to enteral feedings; initiated only if duration of therapy is anticipated to be >5–7 days

Indications per ASPEN guidelines (Brown RO, et al. *J Parenter Enteral Nutr.* 2010;34(4):366–377.) include:

Previously healthy pts with no evidence of protein calorie malnutrition if enteral nutrition is not feasible after 5–7 days of hospitalization

Protein calorie malnutrition upon admission with no enteral feeding options

Severely malnourished pts, prior to major upper GI surgery with no enteral feeding options

Other indications include:

Nonfunctioning gastrointestinal tract

Short gut

Prolonged need for bowel rest (typically >14 days)

TPN formulations consist of dextrose, amino acids, lipids, vitamins, trace minerals, & elements

Commercially avail. dextrose solutions range from 5–70% (i.e., D5W = 50 g dextrose/l, D70W = 700 g/l)

Amino acid preps consist of crystalline protein & synthetic amino acids with standard solutions ranging from 3–10%

Fat solutions are isotonic & can be administered peripherally or centrally without concern for thrombosis. (typical products include: intralipid 10% & 20% composed from soybean, as well as Liposyn II 10% & 20% composed from safflower oil)

Caution should be advised in the following instances of lipid administration:

Fat solutions should be administered at no more than 2.5 g/kg/d & typically constitute 20–30% of total calories

Cautious administration to pts with resp distress syndrome, severe liver dz, or increased metabolic stress

Contraindicated in hypertriglyceridemia (>250 mg/kg), lipid nephrosis, egg allergy, or acute pancreatitis

Other additives such as vitamins may be administered from commercially avail. preps

Trace minerals should be given in accordance with recommended daily allowance

Give vitamin K separately & after evaluation of coagulation status: may jeopardize anticoagulation therapies such as warfarin (Shearer MJ. *Gastroenterology.* 2009;137:S105–118.)

Electrolytes are added to supplement deficits or achieve homeostasis

Typical Initiation Plan

Check all lab tests prior to initiation (glucose, magnesium, phosphorus, calcium, bilirubin, SGOT, SGPT, alkaline phosphatase, BUN, serum creatinine)

Determine fluid needs:

Holliday–Segar method = total daily vol requirement (cc/d) = 100 cc/kg for 1st 10 kg, 50 cc/kg for the 2nd 10 kg, 20 cc/kg for each additional kg

Dextrose solutions provide 15–35% final concentrations (150–350 g/l)

Typical amino acid solution range from 5–10% (50–100 g/l)

Determine caloric & protein needs:

Calorie yield per gram of macronutrient

Fat—9.4 kcal/g; Protein—4.1 kcal/g; Carbohydrate—3.4 kcal/g

Total protein needs = 0.8–1.0 (g/d) × wt (kg)

Total caloric needs = 25 (kcal/kg) × wt (kg)

Determine vol of lipid emulsion

20–30% of caloric intake is supplied by lipids; 2–4% of total caloric needs should consist of essential fatty acids (i.e., linoleic acid & lipoprotein c)

Typical emulsions are provided in 10% & 20% concentrations in unit vol of 50 cc preps & yields 1.1 or 2.0 kcal/cc respectively

Determine standard electrolytes, multivitamins, trace elements & other additives (i.e., H_2 blockers, insulin)

TPN requirements & tolerance should be assessed daily

Goal rate is based on ability to tolerate glucose & fluid load (In general, pts should begin with 1 l on day 1, with advancement of 20–50 ml/h)

Optimal infusion of glucose ranges from 0.5 to 7.5 gm/kg/h, maximum glucose oxidation occurs at an infusion rate of 5 mg/kg/min (Burke JF, et al. *Ann Surg.* 1979;190(3):274–285.)

TPN Electrolyte Amounts

Electrolyte Amounts in TPN

For a 70 kg male:

Fluid requirement: 100 (cc/kg) × 10 + 50 (cc/kg) × 10 + 20 (cc/kg) × 50 = 2,500 cc or 2.5 l

Estimated nonprotein caloric requirement = 25 (kcal/kg) × 70 (kg) = 1,750 kcal

Estimated lipid calories = 1,750 × 20% = 350 kcal

Estimated dextrose calories = 1,750 – 350 kcal = 1,400 kcal

[a]Calculated protein requirement = 1.0 (g/d) × 70 (kg) = 70 g or 70 g/2.5 l = 28.6 g/l

Calculated dextrose: 1,400 kcal/3.4 kcal/g = 411.8 g or 411.8 g/2.5 l = 164.7 g/l

Calculated lipid (20% IV solution) requirement = 350 kcal/2 kcal/ml × 20% = 35 g or 35 g/2.5 l = 17.5 g/l

Final TPN formula = 28.6 g/l protein, 165 g/l of dextrose, 17.5 g/l IV lipids

Vol of 5% amino acid solution: 70 g/5% = 1,400 cc

Vol of 20% IV lipid: 350 kcal/2.0 kcal/cc = 175 cc

Vol of 50% dextrose (D50W) needed: 1,700 kcal per 1 l of 50% dextrose (500 g/l); 1,400 kcal/1,700 kcal/l = 0.82 l = 820 cc; 50–100 cc may be added for electrolytes, additives, or trace vitamins & minerals

[a]Debate exists regarding whether to count protein calorie intake.

Recommended Electrolyte Amounts

Electrolyte	Recommended (Amount/d)	Typical Amount (mmol/l)
Sodium	60–120 mEq	40–150 mmol/l
Potassium	60–120 mEq	30–50 mmol/l
Calcium	0–15 mEq	1.5–2.5 mmol/l
Chloride	60–150 mEq	40–150 mmol/l
Phosphorus	20–40 mmol	10–30 mmol
Magnesium	0–25 mEq	5–10 mmol
12 MVI Formula	10 ml	
Trace Element	5 ml	
Heparin	As needed	
Insulin	As needed	

Source: Ziegler TR. *N Engl J Med.* 2009;361:1088–1097.

Complications of TPN:

Complications related to CV access catheter

Metabolic problems include:

Increased blood glucose levels

Dehydration

Fatty liver

Increased CO_2 production may lead to resp failure

Nutritional complications include over and under feeding

Combined Enteral–Parenteral Feeding:

Enteral nutrition as a sole route may result in underfeeding

Parenteral nutrition may result in overfeeding & associated metabolic & mechanical risks

Enteral feeding should be 1st option

Supplemental parenteral nutrition should be instituted if enteral nutrition is inadequate for caloric needs (unable to meet >60% energy or protein after 7–10 days)

Malnutrition Leading to Pulmonary Failure

Too rapid refeeding may lead to ↓ PO_4 & resp compromise & is accompanied by:

Decreased VC, minute vol, RR, tidal vol, & resp efficiency

Difficult weaning of mechanical ventilation due to impaired pulmonary reserve

Decreased phosphate, magnesium, sodium, & potassium stores

Calorically dense formulations minimize fluid intake

Serum phosphate levels (associated with decrease in hypoxic ventilator response) should be routinely measured

Pts with ARDS or acute lung injury may benefit from enteral feedings supplemented with omega 3 fish oils, & antioxidants (Brown RO, et al. *J Parenter Enteral Nutr*. 2010;34(4):366–377.)

Pts with ARDS, Acute lung injury, or >72 hrs of mechanical ventilation show identical outcomes with trophic feeds (10–20 kcal/h or 500 kcal/d) versus full feeding regimens.

Renal Failure Leading to Malnutrition

Pts may present with impaired electrolyte profiles, glucose intolerance & protein losses from hemodialysis

Protein losses may be extremely high in renal failure requiring hemodialysis or continuous renal replacement therapy; therefore, these pts should not be placed on protein restricted diets

Per ASPEN (McClave SA, et al. *J Parenteral Enteral Nutr.* 2016;40(2):159–211.) guidelines:

Pts receiving hemodialysis or renal replacement therapy may require up to 2.5 g/kg/d of protein to achieve positive nitrogen balance or near nitrogen equilibrium

Acute kidney injury or acute renal failure pts should receive 1.2 g/kg/d of protein

Renal specific nutrient formulations may be considered in pts with significant electrolyte abnormalities

Hepatic Failure Leading to Malnutrition

Estimated 20% child-Pugh class A & 60% of child-Pugh class C have protein energy malnutrition

Nutritional assessment may be difficult in decompensated cirrhotics due to changes in hepatic function & energy metabolism

Simple bedside methods such as Subjective Global Assessment (battery of questions) or anthropometry can identify pts at risk

Per ASPEN (McClave SA, et al. *J Parenteral Enteral Nutr.* 2016;40(2):159–211) guidelines:

Standard enteral nutrition is the preferred route; however, vparenteral nutrition is indicated when oral or enteral nutrition cannot sustain nutritional needs

Obesity and Malnutrition

Obese pts have elevated incidence of malnutrition

Pts with BMI >30 have odds ratio of 1.5 for malnutrition

Altered fuel utilization

Greater risk for insulin resistance

Obese pts should undergo nutritional risk assessment as well as an assessment for metabolic syndrome

Enteral nutrition should be initiated within 24–48 hrs of pts unable to eat or drink

Enteral nutrition goal of 65–70% of energy requirements

Upon initiation of enteral feedings, obese critically ill pts should be monitored for nutritional efficacy (hyperglycemia, hyperlipidemia, hypercapnia, fluid overload, hepatic fat accumulation)

SCORING SYSTEM FOR THE SEVERITY OF ILLNESS IN CRITICAL CARE

EDWARD KELLY, MD

Scoring systems have been devised to describe severity of illness & to predict the morbidity & mortality of critically ill pt populations. Several have been proposed for general use in nonselected ICU populations. APACHE, SAPS, & SOFA are currently in the most widespread use. Each scoring system is based on retrospective analysis of large populations of ICU pts using multivariate linear regression or other statistical tools, to identify physiologic markers of severity of illness that correlate with incidence of complications & mortality. The degree of correlation is then used to weigh the most reliable parameters & construct a numerical score that correlates with complications & mortality better than any individual parameter.

APACHE

(Acute Physiology & Chronic Health Evaluation; Knaus WA, et al. *Crit Care Med.* 1985;13(10): 818–829.)

Began as an index of severity of dz accounting for 12 variables & using weighted multipliers to give a score of 0–71; 71 indicates most severe dz

Renal function, age, Hct, Na, K, oxygenation, temp, HR, RR, WBC, GCS, immune suppression

APACHE II system published in 1985, is in the public domain

There are many online resources to calculate APACHE II score

APACHE II is proprietary, has better accuracy, is based on more robust retrospective dataset & weighs variables differently

Designed to be calculated within the 1st 24 hrs of ICU admission & not repeated

SAPS

(Simplified Acute Physiology Score; Le Gall JR, et al. *JAMA.* 1993;270(24):2957–2963.)

An index of severity of dz accounting for 17 variables & using weighted multipliers to give a score of 0–163; 163 indicates most severe dz

Variables similar to APACHE II, but also include total bilirubin, BUN, type of ICU admission (urgent, emergent or readmission), serum bicarbonate, & systolic BP

Based on large multicenter retrospective dataset, excludes burns, coronary dz, & cardiac surgery pts

Designed to be calculated within the 1st 24 hrs of ICU admission & not repeated

SAPS II system published in 1993, is in the public domain

There are many online calculators

SAPS III was developed in 2005 in an effort to improve prognostic value & to reflect changes in expected complication rate based on new therapies. Prognostication using the SAPS III system requires calibration of the target pt group's data variables with a reference group within the SAPS II cohort

SOFA

(Sequential Organ Failure Assessment; Vincent JL, et al. *Intensive Care Med.* 1996;22:707–710.)

Devised as a daily score, unlike APACHE & SAPS

Grades degree of impairment for 6 vital organ systems: resp, renal, coagulation, hepatic, CV, & central nervous system

Impairment graded as 1–4, 4 being most severe organ failure

Overall score ranges from 6–24, with no zero; a score of 24 indicates greatest burden of organ failure

Descriptive only, no calculations involved for predicted mortality

SOFA system published in 1996 is in the public domain

Many online calculators

No system currently avail. allows predict of mortality for unselected pts, but the 3 systems in common use do facilitate comparison of risk-adjusted morbidity & mortality rates among ICUs.

All of the ICU severity scoring systems both underestimate & overestimate mortality when used to predict outcome for an individual pt. The inaccuracy arises from the model's inability to predict certain adverse events, as well as the inability to account for potentially lethal conditions that do not manifest as organ failure until late in the course.

Several scoring systems are avail. for predicting highly selected individual pts' surgical mortality, based on comorbidities & procedural variables. These systems are highly specific & do not generalize to the rest of the ICU population. Examples include the MELD score, the STS Risk Calculator for cardiac surgery pts, & the Revised Trauma Score.

MELD

(Model for End-stage Liver dz; Malinchoc M, et al. *Hepatology.* 2000;31: 864–871.)

Devised as a scoring system for severity of liver failure & validated to predict mortality following the TIPS procedure (Transjugular intrahepatic portosystemic shunt)

Calculates degree of hepatic impairment using 3 variables: serum bilirubin, serum creatinine, & international normalized ratio (INR) in a weighted index

Later adopted by the United Network for Organ Sharing (UNOS) to predict mortality rate for hepatic transplantation (Wiesner R, et al. *Gastroenterology.* 2003;124: 91–96.)

STS Risk Calculator

Proprietary, based on the Society for Thoracic Surgery National Database (Edwards FH, et al. *Ann Thorac Surg.* 1997;63:903–908.)

Software calculators avail. only from certified vendors

Applied preoperatively to predict surgical outcomes

Includes parameters of renal, neurologic, cardiac, vascular, & pulmonary function, as well as comorbidities, such as diabetes mellitus & HTN

Also includes type of operation, & whether urgent or emergent

Calculates expected mortality, & rates of specific complications including wound infxn, stroke, renal failure, prolonged hospital stay, & need for reoperation

Well validated in prospective studies & used for national & state-wide quality improvement initiatives

Revised Trauma Score

Devised (Champion HR, et al. *Crit Care Med.* 1981;9:672–676) in 1981 as a system to grade severity of traumatic injury based on physiologic response & revised (Champion HR, et al. *J Trauma.* 1989;29:623–629) in 1989 to a simple set of observations easily used in the field

Public domain, in widespread use in the field & in the ICU

Validated in numerous subsequent prospective trials

qSOFA

(also see **Chapter 23** for details & appropriate use)

(RR ≥22; sysBP <90; altered mental status; 1 point each when positive) To be used for pts outside of the ICU. Developed in 2016 in an effort to identify pts with infxn who are at risk for sepsis (Seymour CW, et al. *JAMA.* 2016;315(8):762–774.)

Supported by the Third International Consensus Definitions Task Force

Simple, 3 criteria scoring system, does not require lab values

Predicts in-hospital mortality from sepsis for pts outside of the ICU more accurately than SOFA

Online calculator avail. at www.qsofa.org

ICU scoring systems are frequently utilized for resource allocation & cost effectiveness policy-making (Rothen HU, et al. *Intensive Care Med.* 2007;33:1329–1336.)

Physiologically based scoring systems also enable suitable comparison of outcomes from 1 ICU to another, & facilitate study of new treatments, clinical effectiveness measures, & quality assurance & pt safety initiatives.

PREVENTIVE STRATEGIES AND EVIDENCE-BASED PRACTICE

SHANNON S. MCKENNA, MD

Introduction

Research over the last 10–15 yrs has identified effective ways to prevent many of the common sequelae of critical illness. The challenge for all institutions is to effectively & universally implement evidence-based care improvement practices. This requires commitment & team work across multiple disciplines.

Central Venous Catheter (CVC) Associated Blood Stream Infections (CABSI)

Consequences of CABSI

Increased length of stay
Increased cost of care
Preventable

General Principles for an Effective CABSI Prevention Program

(Marschall J, et al. *Infect Control Hosp Epidemiol.* 2014,35:753–771.)

Institution wide, standardized education (indications for CVC use, proper sterile technique for placement, site maintenance, hub access techniques) for all personnel placing, maintaining or utilizing CVCs
Checklist used during catheter insertion (see below) to assure proper sterility
All essential supplies located in 1 location on a given unit
Infxn rate monitored & data regularly reviewed by ICU & hospital leadership
Must be institutional priority at leadership level

Insertion

Avoid femoral site (limits mobilization while risk of infxn now is lessened by preventive strategies of safe insertion, chlorhexidine biopatch & proper aseptic port access management; some data favor subclavian over IJ)
Use US guidance for IJ & femoral catheter insertion
Use checklist in real time to assure maintenance of compliance with sterility
Observer executing checklist must be empowered to stop procedure for violations

Essential Components of a CVC Insertion Checklist
Operator(s) hand hygiene (alcohol hand rub or antiseptic soap)
Chlorhexidine-based skin prep (allowed to air dry before draping)
Maximum sterile barrier precautions for ALL operators (hat, mask, sterile gloves, sterile gown)
Full body sterile drape employed
Sterility of site/equipment maintained throughout procedure (or procedure stopped & corrective action taken)
Placement of proper transparent occlusive dressing with chlorhexidine biopatch while sterile field is intact

CVC Maintenance

Daily bathing of ICU (>2 mo age) pts with chlorhexidine
Transparent dressing changed q5–7d with chlorhexidine skin prep
Dressing changed immediately if not intact or soiled
Hubs & needleless access ports disinfected with alcohol or chlorhexidine per standard protocol prior to accessing them
Assess pt daily for catheter removal

Practices That Do Not ↓ Infection Rate & Should Not Be Routinely Employed
Antimicrobial ointment at CVC insertion site (except dialysis lines)
Placement of PICCs rather than CVC (infxn rate is the same)
Systemic antimicrobial ppx
Routine catheter replacement
Routine blood cxs drawn through CVC (high false-positive rate)

Adjuncts

For locations or pt populations with CVC infxn rates above target despite adherence to standard prevention measures
For pts at high risk of severe sequela from a CABSI (limited access, implanted intravascular devices)

Adjunctive Approaches with Proven Benefit
Antiseptic-containing hub/connector caps
Use of antimicrobial or antiseptic impregnated catheters
Chlorhexidine sponge dressings
Antimicrobial lock therapy

Ventilator-Associated Events (VAE)

(Klompas M, et al. *Infect Control Hosp Epidemiol.* 2014,35:915–936.)

Definitions

VAE: grouping of all conditions that result in significant & sustained deterioration in oxygenation (≥20% increase in daily min FiO_2, or increase of PEEP ≥3 cm H_2O)

Ventilator-associated condition (VAC): worsened oxygenation (as above) for 2 or more days

Infxn-related ventilator-associated complication (IVAC): VAC plus (temp >38°C or <36°C, **OR** WBC <12K or <4K) & a new antimicrobial is started & continued for at least 4 days

Possible ventilator associated pneumonia (VAP): IVAC plus 1 of the following (respiratory secretions purulent on smear OR respiratory cx positive but excluding oral flora, Candida, coag-neg staph & Enterococcus)

Probable VAP: IVAC plus purulent secretions (on smear) & positive cxs (exclusions as above) OR 1 of the following: positive pleural fluid cx, positive lung histopathology, positive test for Legionella, positive respiratory virus test (influenza, etc)

Pathogenesis of VAP

Inoculation of the formerly sterile lower respiratory tract by:

Aspiration of oral secretions

Colonization of the aerodigestive tract with pathogenic organisms

Use of contaminated respiratory equipment/medications

General Principles for VAE Prevention

Must be institutional priority at leadership level
Institution wide, standardized education
Lung protective ventilation
Early mobilization
Standardized ventilator bundle with compliance monitoring (see below)—ICU specific with regular review of compliance rates
Rigorous adherence to hand hygiene emphasized
Develop institution wide protocols to prevent contamination of respiratory equipment per *Guideline for Disinfection & Sterilization in Healthcare Facilities 2008,* at www.CDC.gov
VAE rate monitored & data regularly reviewed by ICU & hospital leadership

Process Measures to Be Monitored & Reported
Hand hygiene compliance
Daily sedation interruption compliance
Daily assessment of readiness to extubate
Oral care compliance
Head of bed elevation compliance (greater than 30°)

Specific Interventions Shown to Lower VAP Rates (Yokoe DS, et al. Am J Infect Control. 2014,42:820–828.)

Interventions to Minimize Duration of Mechanical Ventilation

Utilization of noninvasive ventilation when possible
Use of weaning protocols
Daily sedation interruption
Daily assessment of readiness to extubate (formalized protocol)
Early mobilization

Interventions to Minimize Microaspiration & Lower Respiratory Tract Contamination

Elevate head of bed >30° at all times
Maintain ETT cuff pressure of at least 20 cm H_2O
ETTs with supraglottic suction ports (if intubated >48 hrs)

Other Interventions That May Lower VAP Rates

Regular oral care with chlorhexidine
Mechanical tooth brushing
Prophylactic probiotics
Automated control of ET cuff pressure
Ultrathin polyurethane ETT cuffs
Selective digestive tract decontamination

Venous Thromboembolism (VTE)

(Kahn SR, et al. *Chest.* 2012;141:e195s–226s.)

Epidemiology

DVT rates without ppx range from 10% (medical pts) to 60% (major orthopedic surgery)

Major cause of morbidity & mortality

Most common cause of preventable in hospital death

Effective ppx avail. & most hospitalized pts should receive ppx

Low rate of clinical bleeding with pharmacologic ppx

Risk Factors for VTE	
Surgery	Acute medical illness
Trauma	Erythropoiesis-stimulating agents
Cancer	Inflammatory bowel dz
Venous compression	Nephrotic syndrome
Immobility	Myeloproliferative disorders
H/o prior VTE	Obesity
Pregnancy & postpartum period	CVC
Estrogen-containing therapies	Thrombophilia
Spinal cord injury (SCI)	Hypercoagulable states

General Principles for an Effective VTE Prevention Program

Each hospital should develop a formal written VTE ppx policy; pt group specific approach recommended

Education alone has been ineffective at assuring high compliance rates with VTE policies

Computer decision support, preprinted orders, & standard order sets should be used whenever possible

Periodic audit of compliance & feedback is necessary

Specific Prevention

Prophylactic Options	
Agent	**Considerations**
Mechanical[a]	Sole agent only in those pts at high risk of bleeding
Aspirin	Not recommended as sole agent
Low-dose unfractionated heparin (LDUH)	Administer b.i.d. to t.i.d.
Low–molecular-wt heparin (LMWH)	See product literature for specific dosing
Fondaparinux	Dosage adjustment for renal insufficiency required
Warfarin	Target INR: 2–3
Oral direct thrombin inhibitor (dabigatran)	Requires dose adjustment for renal & hepatic insufficiency
Oral Xa inhibitor (rivaroxaban, apixaban, edoxaban)	See product literature for specific dosing

[a]Mechanical devices may be effective when used as adjuncts to pharmacologic measures.

Prophylaxis by Indication	
Minor surgery/mobile medical pts	Aggressive ambulation
Medical pts (bed rest or sick)	LDUH, LMWH, fondaparinux
Most surgical pts undergoing major operations (gen surg, GYN surg, urology)	LDUH, LMWH, fondaparinux
Surgical oncology pts undergoing pelvic or abd surgery	LMWH for 4 wks
Major orthopedic surgery (hip/knee arthroplasty; hip fx)	LMWH, fondaparinux, oral vitamin K antagonist, oral direct thrombin inhibitor, oral Xa inhibitor (LMWH favored; all for min duration of 1–14 days)
Major trauma (including SCI)	LMWH, fondaparinux, oral vitamin K antagonist (unless contraindicated due to risk of bleeding)
High risk of bleeding	Mechanical ppx (until bleeding risk ↓)

Special Considerations

Renal impairment

LMWH, fondaparinux & dabigatran are cleared by kidneys

Renal function should guide agent choice & dosing regime

Increased monitoring may be needed for LMWH (antifactor Xa)

Neuraxial anesthesia

Increased risk of spinal or epidural hematoma must be considered

Institution wide guidelines to address common scenarios recommended

Heparin-induced thrombocytopenia (HIT)

LMWH has lower rate of HIT than LDUH

LMWH cannot be used in a pt with HIT

Platelet count monitoring recommended for pts treated with LDUH & LMWH

Do not send routine screening HIT test (ELISA) in the absence of clinical suspicion of HIT

Bariatric surgery

Pts may benefit from wt based doses of LDUF or LMWH (optimum dosing not well defined)

Pregnant pts

If VTE ppx indicated, LMWH preferred (Bates SM, et al. *Chest*. 2012;141:e691s–e736s.)

Neurosurgery pts

Are at increased risk of VTE

Intermittent pneumatic compression devices appear effective for VTE prevention in this group

LDUH may be used; LMWH may be used but may increase bleeding rate

Cancer pts

6-fold higher risk of VTE

Independent predictor of VTE ppx failure

t.i.d. LDUH more effective than b.i.d. LDUH

LWMH also effective; limited cancer specific data for fondaparinux

Stress Ulcers

Definition

Mucosal ulceration of esophagus, stomach, or duodenum
Forms within hours of start of major illness or trauma
Often multiple superficial lesions; bleeding from capillaries
Causative factors: impaired mucosal protection from splanchnic hypoperfusion; increased acid secretion in some pts

Epidemiology (Martindale RG. *Am Health-Syst Pharm.* 2005;62:S11–17.)

Evident on EDG in 75% ICU pts at 72 hrs if ppx is not administered
Clinically important bleeding (hypotension, orthostasis, Hb drop ≥2 g/dl) in 3–6% ICU pts
Overt bleeding in 15% ICU pts without ppx
Mortality associated with clinically important bleeding is 50%
Mechanical ventilation >48 hrs & coagulopathy most important risk factors

Risk Factors for Stress Ulcers in ICU Patients	
Mechanical ventilation >48 hrs	Head trauma
Coagulopathy	Multitrauma
Shock	Burns >35% BSA
Sepsis	H/o GI bleed
Renal failure	Organ transplantation
Hepatic failure	

Prophylaxis

Which pts:

Mechanical ventilation >48 hrs

Coagulopathy (platelet <50K; INR >1.5; PTT >2 × normal)

GI bleeding or ulceration in the last year

2 or more other risk factors

General Principles:

Maintain adequate perfusion

Pharmacologic ppx for high-risk pts

Enteral nutrition when possible (decreases GI bleeding in many studies; not adequate as sole measure)

H_2RAs & PPIs may increase the rate of nosocomial pneumonia (stomach overgrowth with enteric bacteria) & *Clostridium difficile*

Pharmacologic Agents for Stress Ulcer Prophylaxis	
Class	**Properties**
H_2 receptor antagonists (H_2RAs)	PO/IV; ↑ gastric pH; ↓ GI bleeding by >50% vs. placebo
Proton pump inhibitors (PPIs)	PO/IV; ↑ gastric pH; meta-analysis (Lin PC, Chang CH, Hsu PI, et al. The efficacy and safety of proton pump inhibitors vs histamine-2 receptor antagonists for stress ulcer bleeding prophylaxis among critical care patients: a meta-analysis. *Crit Care Med.* 2010;38:1197–1205.) shows minimal, if any, ↓ in GI bleeding over H_2RA, & no pneumonia difference
Sucralfate	PO only; must get to stomach; improves mucosal barrier function; does not change pH so potentially fewer pneumonias; less effective than H_2RAs & PPIs
Antacids	PO; administered q2h; do not work as well as H_2RAs or PPIs; electrolyte alterations are common side effects; no longer routinely recommended

Economic Considerations:

H_2RAs & PPIs major budget item for most institutions, many pts receive unnecessarily

Treat only those at risk

Stop treatment when no longer at risk

Use enteral rather than IV formulations whenever possible

H_2RAs over PPIs for most pts (more cost effective with little outcome difference)

Pressure Ulcers

Epidemiology

Incidence (acute care setting) 0.4–38%

Can cause delayed functional recovery, pain, & infxns

Prolongs hospital stay & associated significant cost of treatment

Now targeted by CMS & other payment agencies

Overall paucity of good clinical trials data in field complicates prevention & management strategies for institutions (Reddy M, et al. *JAMA.* 2006;296:974–984.)

Pathogenesis

Prolonged pressure between a bony prominence & an external surface leads to impaired capillary blood flow & subsequent tissue injury (Lyder CH. *JAMA.* 2003;289:223–226.)

Can develop in 2–6 hrs

Risk Factors for Pressure Ulcer Development	
External Factors	**Patient Specific Factors**
Pressure	Immobility
Shear forces (gravitational)	Incontinence
Friction (skin across external surface)	Malnutrition
Moisture	↓ Skin perfusion (hypotension, hypovolemia, vasopressor use, CHF)
	Microcirculatory impairment (diabetes, peripheral vascular dz, sepsis, etc.)
	Sensory deficit limiting pts ability to detect & respond to tissue injury

Risk Assessment & Mitigation

Skin assessment & documentation for every pt on admission; daily reassessment

Pressure Ulcer Staging	
Stage I	Intact skin with non-blanchable erythema[a]
Stage II	Partial thickness skin loss (ulcer, abrasion, shallow crater)
Stage III	Full thickness skin loss (subcutaneous fat may be visible; undermining & tunneling may occur)
Stage IV	Full thickness skin loss with involvement of muscle, fascia, bone, tendon or joint
Unstageable	Base covered with slough or eschar (depth cannot be determined)

[a]Deep purple or maroon color may indicate deep tissue injury. (Prevention & Treatment of Pressure Ulcers: Quick Ref Guide, 2014, www.NPUAP.org)

Risk assessment on admission with standardized scoring system (Braden or Norton Scale); daily reassessment

Institution of standardized measures for all at risk pts starting at time of hospital admission

Specific Interventions

Minimize immobility: limit sedation, aggressive early physical therapy, programs to mobilize ventilated pts

Pt positioning: repositioning at least every 2 hrs (expert opinion) with attention to bony surfaces; must avoid friction & shear forces during repositioning

Prophylactic dressing (polyurethane foam) to bony prominences

Specialized support surfaces

Classification of Pressure Reducing Support Surfaces[a]		
Type	**Properties**	**Best Use**
Static (nonpowered)	Mattress or overlay: gel, high-specification foam, air, water	Low-risk pts (least expensive)
Dynamic (powered) group 1	Alternating pressure mattresses; low–air-loss mattresses	Moderate- & high-risk pts
Dynamic (powered) group 2	Air-fluidized mattresses (silicone-coated beads that liquefy with air circulation)	Pts with nonhealing stage III & IV ulcers

[a]Minimal data avail. to compare different products; most trials with significant methodologic problems.

Optimum nutrition—full caloric intake with optimum protein balance; no convincing data to support any particular supplement in the absence of known deficiency

Moisture & incontinence management: goal is to keep skin clean & dry; wicking under-pads, fecal containment systems, barrier creams may be appropriate

Skin care: dry skin is a risk factor & moisturizers may help; vigorous rubbing & massage can injure skin & should not be used

Catheter-Associated Urinary Tract Infections (CAUTI)

Epidemiology

UTIs are the most common hospital-acquired infxn

80% attributable to catheter use

Environmental contamination from bacteriuria may lead to epidemic outbreaks of resistant gram negative infxn

Risk Factors for CAUTI
Duration of catheter use
Female gender
Older age
Failure to maintain a closed drainage system

General Principles for an Effective CAUTI Prevention Program

(Lo E, et al. *Infect Control Hosp Epidemiol.* 2014;35:464–479.)

Develop processes to decrease catheter insertion rates (define indications, utilize bladder scanners & straight catheter techniques for retention)

Promote timely removal (daily review on rounds; electronic prompts; protocols for nursing directed catheter removal)

Train personnel for sterile insertion (hand hygiene, sterile gloves & drape, antiseptic cleaning of urethral meatus)

Train personnel for appropriate maintenance (secure catheter to prevent urethral mucosal injury; hand hygiene prior to system manipulation; maintain sterile closed drainage system; access system aseptically when needed)

Conduct routine surveillance of CAUTI rates; feedback to local & hospital leadership

Practices Not Helpful in Preventing CAUTI; Should Not Be Routinely Employed
Routine use of silver or antimicrobial impregnated catheters
Routine urine cx of asymptomatic pts
Routine treatment of asymptomatic bacteriuria
Routine systemic abx for ppx
Routine change of catheter on a set schedule
Continuous bladder irrigation with an antimicrobial (as a preventive measure)

Nosocomial Transmission of Methicillin-Resistant *Staphylococcus Aureus* (MRSA)

(Calfee DP, et al. *Infect Control Hosp Epidemiol.* 2014,35:772–796.)

Epidemiology

45–60% of hospital associated *S. aureus* infxns are methicillin-resistant
MRSA infxn associated with higher mortality, longer length of stay & higher cost of care compared to MSSA infxn
Asymptomatic MRSA colonization common
Colonized pts: 29% risk of developing active MRSA infxn within 18 mo

Hand Hygiene

Colonized or infected pts contaminate their environment
MRSA can spread from person to person via healthcare workers' hands
Universal compliance with hand hygiene fundamental to prevention of spread of MRSA & other nosocomial pathogens
Hand hygiene compliance should be monitored & reported

Identification of MRSA Colonized or Infected Patients

Hospitals need automated systems to promptly identify affected pts
Contact precautions instituted for these pts: private room (cohort if not avail.), gown & gloves to enter room with gown & gloves removed to exit room; strict enforcement of hand hygiene
Work processes & environment must be modified to promote compliance
Active surveillance (nasal swabs) for units or pt populations with high endemic MRSA rates & for control of active outbreaks
Some data support decolonization therapy in certain pt populations

Environmental Control

Pts with MRSA contaminate their environment & care equipment; leads to transmission of MRSA to other pts

Institutional protocols for daily/terminal cleaning can reduce transmission

Attention to high-touch areas important (bed rails, carts, commodes, doorknobs)

Dedicate pt equipment when possible (stethoscopes, etc.)

Routine chlorhexidine bathing of ICU pts associated with decreased MRSA infxns & decreased MRSA transmission (reduction in environmental contamination)

Daily Assessment: FAST HUGGS

(Vincent JL. *Crit Care Med.* 2005;33:1225–1229.)

Feeding: can the pt be fed? (oral, enteral, parenteral)

Analgesia: titrated to VAS or behavioral pain scale

Sedation: aim for "calm, comfortable, collaborative," use sedation score, treat pain 1st, try to avoid benzodiazepines

Thromboembolic prevention: appropriate therapy ordered?

Head of the bed elevated: 30–45° unless contraindicated

Ulcer ppx: usually H_2 antagonists; sometimes proton pump inhibitors (consider the risk of increased of *C. difficile* infxn) (Linsky A, et al. *Arch Intern Med.* 2010;170:772–778.)

Glucose control: maintain a blood glucose target of 180 mg/dl or less & avoid hypoglycemic episodes (NICE-SUGAR Study Investigators, Finfer S, et al. *N Engl J Med.* 2009;360:1283–1297.)

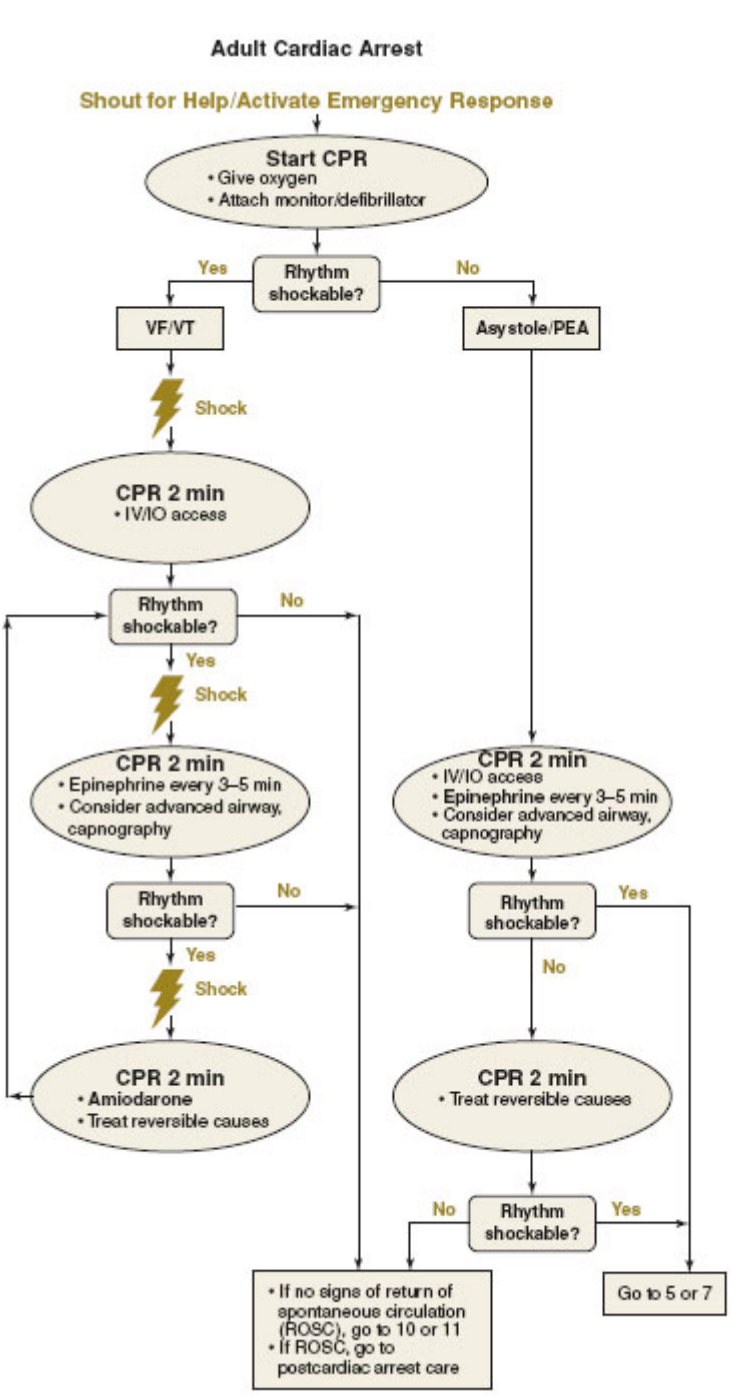
Geriatric: delirium evaluation, ADL evaluation, sensory aids in place (glasses, hearing aids), early mobilization, early occupational & physical therapy, review of medications, removal of restraints & devices

Social: involvement of social worker, identification of surrogate decision maker or proxy, clarification of DNR/DNI orders

ADVANCED CARDIAC LIFE SUPPORT (ACLS)

SAMUEL M. GALVAGNO, JR., DO, PhD, FCCM • JESSE J. KIEFER, MD

Updated 2015 Guidelines (Link MS, et al. *Circulation.* 2015;132:S444–464.)



CPR Quality
- Push hard (>2 in [5 cm]) & fast (>100/min) & allow complete chest recoil
- Minimize interruptions in compressions
- Avoid excessive ventilation
- Rotate compressor every 2 min
- If no advanced airway, 30:2 compression–ventilation ratio
- Quantitative waveform capnography
  - If $PETCO_2$ <10 mm Hg, attempt to improve CPR quality
- Intra-arterial pressure
  - If relaxation phase (diastolic) pressure <20 mm Hg, attempt to improve CPR quality

Return of Spontaneous Circulation (ROSC)
- Pulse & BP pressure
- Abrupt sustained increase in $PETCO_2$ (typically >40 mm Hg)
- Spontaneous arterial pressure waves with intra-arterial monitoring

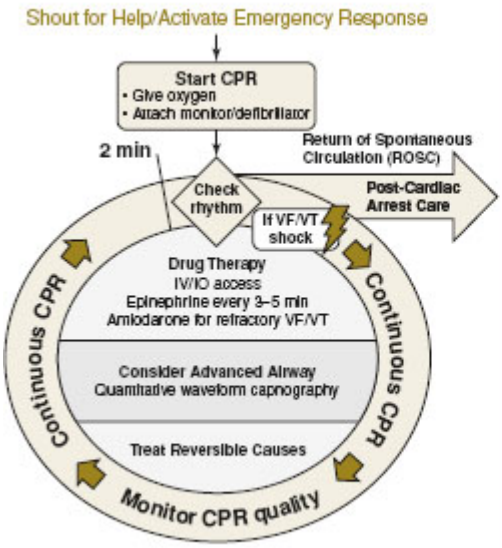
Shock Energy
- **Diphasic:** Manufacturer recommendation (e.g., initial dose of 120–200 J); if unknown, use maximum avail. Second & subsequent doses should be equivalent, & higher doses may be considered.
- **Diphasic:** 360 J

Drug Therapy
- **Epinephrine IV/IO dose:** 1 mg every 3–5 min
- **Vasopressin IV/IO dose:** 40 units can replace first or second dose of epinephrine
- **Amiodarone IV/IO dose:** First dose: 300 mg bolus Second dose: 150 mg

Advanced Airway
- Supraglottic advanced airway or ET intubation
- Waveform capnography to confirm & monitor ET tube placement
- 8–10 breaths/min with continuous chest compressions

Reversible Causes
- Hypovolemia
- Hypoxia
- Hydrogen ion (acidosis)
- Hypo-/hyperkalemia
- Hypothermia
- Tension pneumothorax
- Tamponade, cardiac
- Toxins
- Thrombosis, pulmonary
- Thrombosis, coronary

Adult Cardiac Arrest



CRP Quality
- Push hard (>2 in [5 cm]) & fast (>100/min) & allow complete chest recoil
- Minimize interruptions in compressions
- Avoid excessive ventilation
- Rotate compressor every 2 min
- If no advanced airway, 30:2 compression–ventilation ratio
- Quantitative waveform capnography
  - $PETCO_2$ <10 mm Hg, attempt to improve CRP quality
- Intra-arterial pressure
  - If relaxation phase (diastolic) pressure <20 mm Hg, attempt to improve CRP quality

Return of Spontaneous Circulation (ROSC)
- Pulse & BP
- Abrupt sustained increase in $PETCO_2$ (typically >40 mm Hg)
- Spontaneous arterial pressure waves with intra-arterial monitoring

Shock Energy
- Biphasic manufacturer recommendation (e.g., initial dose of 120–200 J); if unknown, use maximum avail. Second & subsequent doses should be equivalent, & higher doses may be considered
- Monophasic: 360 J

Drug Therapy
- Epinephrine IV/IO dose: 1 mg every 3–5 min
- Vasopressin IV/IO dose: 40 units can replace first or second dose of epinephrine
- Amiodarone IV/IO dose: First dose: 300 mg bolus. Second dose: 150 mg

Advanced Airway
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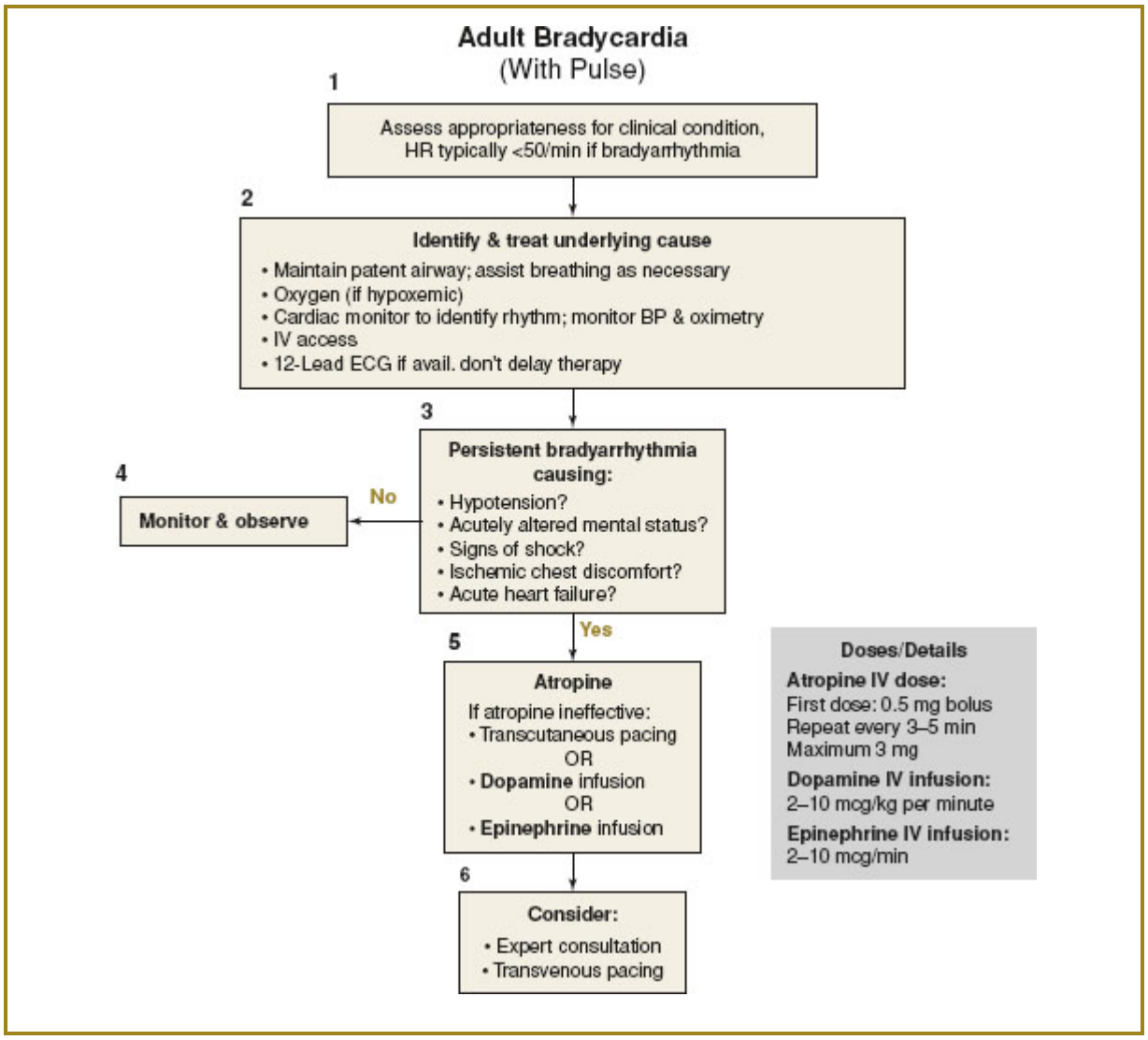
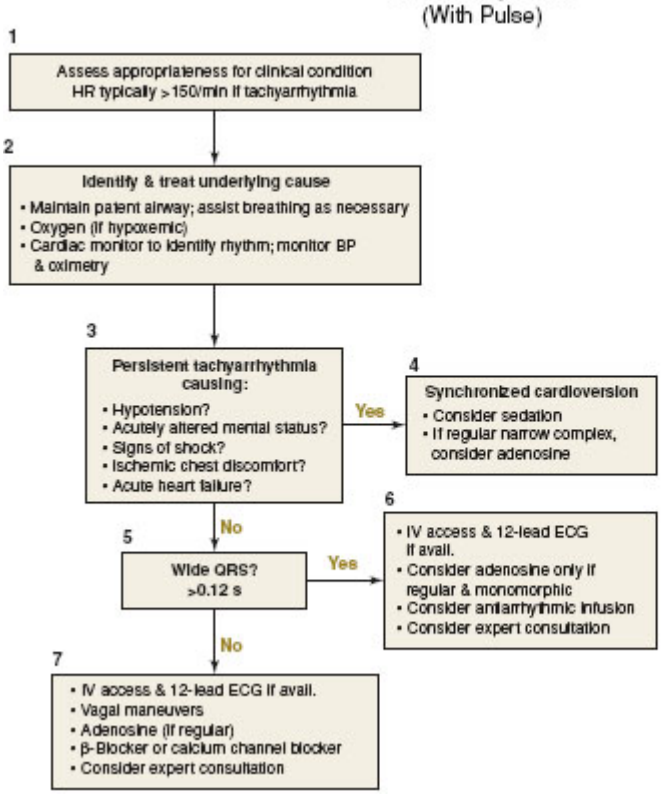
- Thrombosis, pulmonary
- Thrombosis, coronary


Adult Bradycardia
(With Pulse)
1
Assess appropriateness for clinical condition,
HR typically <50/min if bradyarrhythmia
2
Identify & treat underlying cause
• Maintain patent airway; assist breathing as necessary
• Oxygen (if hypoxemic)
• Cardiac monitor to identify rhythm; monitor BP & oximetry
• IV access
• 12-Lead ECG if avail. don't delay therapy
3
Persistent bradyarrhythmia causing:
• Hypotension?
• Acutely altered mental status?
• Signs of shock?
• Ischemic chest discomfort?
• Acute heart failure?
No
4
Monitor & observe
Yes
5
Atropine
If atropine ineffective:
• Transcutaneous pacing
OR
• Dopamine infusion
OR
• Epinephrine infusion
6
Consider:
• Expert consultation
• Transvenous pacing
Doses/Details
Atropine IV dose:
First dose: 0.5 mg bolus
Repeat every 3–5 min
Maximum 3 mg
Dopamine IV infusion:
2–10 mcg/kg per minute
Epinephrine IV infusion:
2–10 mcg/min

Adult Tachycardia
(With Pulse)



Doses/Details

Synchronized Cardioversion
Initial recommended doses:
- Narrow irregular: 50–100 J
- Narrow irregular: 120–200 J biphasic or 200 J monophasic
- Wide regular: 100 J
- Wide irregular: defibrillation dose (NOT synchronized)

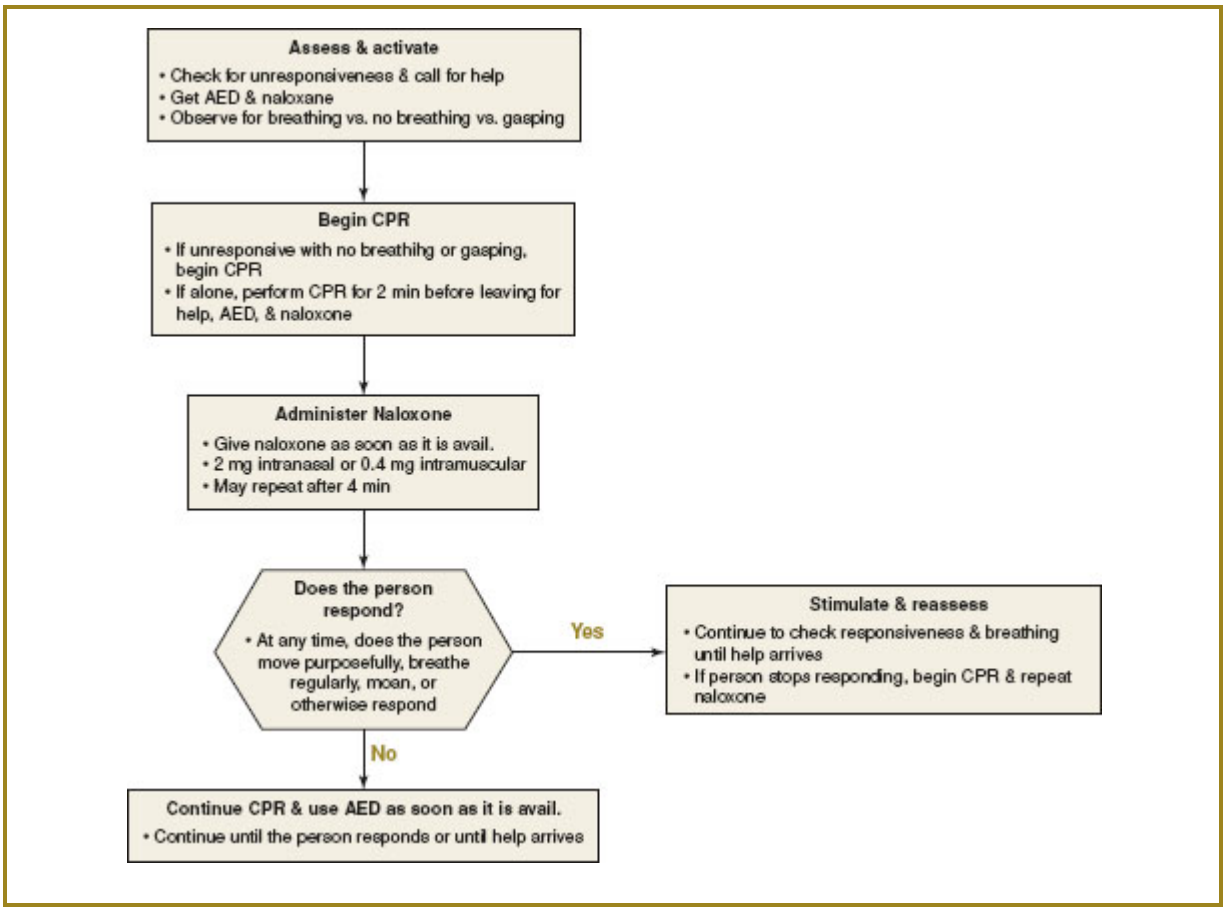
Adenosine IV dose:
First dose: 6 mg rapid IV push; follow with us flush.
Second dose: 12 mg if required.

Antiarrhythmic Infusions for Stable Wide-QRS Tachycardia

Procainamide IV dose:
20–50 mg/min until arrhythmia suppressed, hypotension ensues, QRS duration increases >50%, or maximum dose 17 mg/kg given.
Maintenance infusion; 1–4 mg/min.
Avoid if prolonged QT or CHF.

Amiodarone IV dose:
First dose: 150 mg over 10 min.
Repeat as needed if VT recurs.
Follow by maintenance infusion of 1 mg/min for first 6 hrs.

Sotalol IV dose:
100 mg (1.5 mg/kg) over 5 min.
Avoid if prolonged QT.


Assess & activate
• Check for unresponsiveness & call for help
• Get AED & naloxane
• Observe for breathing vs. no breathing vs. gasping
Begin CPR
• If unresponsive with no breathihg or gasping, begin CPR
• If alone, perform CPR for 2 min before leaving for help, AED, & naloxone
Administer Naloxone
• Give naloxone as soon as it is avail.
• 2 mg intranasal or 0.4 mg intramuscular
• May repeat after 4 min
Does the person respond?
• At any time, does the person move purposefully, breathe regularly, moan, or otherwise respond
Yes
Stimulate & reassess
• Continue to check responsiveness & breathing until help arrives
• If person stops responding, begin CPR & repeat naloxone
No
Continue CPR & use AED as soon as it is avail.
• Continue until the person responds or until help arrives

EMERGENCY DEPARTMENT TO ICU COMMUNICATION STRATEGIES

PETER C. HOU, MD

Key Elements of Integrated Pre- and Intrahospital Care

Protocolized care per current standards

Multidisciplinary care, often by specialized care teams (trauma, cardiac arrest, STEMI, stroke, sepsis, etc.)

Communication

Consider instituting a close-loop mechanism to prevent errors of omission

Institute appropriate, standardized hand-off processes

SBAR (Situation–Background–Assessment–Recommendation) technique
(Haig KM, et al. *Jt Comm J Qual Patient Saf.* 2006;32:167–175.)

Describe pt situation & reason for admission

State pertinent hx

Summarize facts & give your best current assessment

What tests are pending requiring f/u, who has been consulted & what recommendations require f/u, which therapies need to be continued & f/u

Care and Communication Strategies for Specific Disease Conditions

Trauma (Kortbeek JB, et al. *J Trauma.* 2008;64(6): 1638–1650; see Chapter 41)

Trauma team activation from EMS or ED—emergency physician; traumatologist; neurosurgeon; orthopedic surgeon; emergency radiologist; interventional radiologist; intensivist; anesthesiologist; respiratory therapist; ED, interventional radiology (IR), OR, & all ICU personnel

Hospitals designated as Level I Trauma Center (Level I TC)

Blood bank

Massive transfusion protocols

Protocols for administering reversal or adjunctive agents for hemorrhage (i.e., protamine, prothrombin complex concentrate, tranexamic acid, humanized monoclonal antibody)

Hospitals not designated as Level I TC

Pts with multitrauma, life threatening, or limb threatening injuries

Immediate transfer to a Level I TC (Newgard CD, et al. *J Trauma.* 2007;63:965–971.)

Initial stabilize airway & breathing

No CT should be performed

Plain films may be obtained without delaying pt transfer

Facilitate transfer from ED → TC, ED → ICU, ED → OR → ICU, or ED → IR → ICU

Cardiac Arrest (Nolan JP, et al. *Circulation.* 2003;108:118–121; Neumar RW, et al. *Circulation.* 2008;118:2452–2483, & https://eccguidelines.heart.org/index.php/circulation/cpr-ecc-guidelines-2/part-8-post-cardiac-arrest-care/; also see Chapter 20)

Activation of cardiac arrest team from EMS or ED—emergency physician, intensivist, neurologist, ED & ICU personnel

Continuous chest compressions (use automated chest compression devices if avail.)

Consider activating cardiac catheterization lab (CCL) if ECG shows ST-elevation or if high clinical suspicion for acute coronary syndrome

Consider therapeutic hypothermia (TH) after return of spontaneous circulation (ROSC)

For ventricular fibrillation (level I evidence), pulseless ventricular tachycardia, & other nonperfusion rhythms

Review institutional inclusion of indications & contraindications

Avoid hyperoxia after ROSC (Kilgannon JH, et al. *JAMA*. 2010;303:2165–2171.)

Transfer to institutions with TH protocol

Facilitate coordinated transfer from ED → ICU or ED → CCL → ICU

ST-Elevation Myocardial Infarction (STEMI) (Kushner FG, et al. *Circulation.* 2009;120:2271–2306.)

STEMI team activation from the prehospital setting or ED—emergency physician; interventional cardiologist; anesthesiologist; respiratory therapist; intensivist; ED, CCL, & ICU personnel

ECG performed <10 min from presentation (prehospital ECG if avail.)

Prehospital transfer to institution with percutaneous coronary intervention (PCI)

Goal door to balloon time: <90 min

Prehospital transfer to institution without PCI

Consider transfer to PCI institution if there is no expected delay

Otherwise, consider thrombolysis (door to needle time: <30 min)

Consider transfer of pt after thrombolysis from ED to PCI institution

Initiate other appropriate medical therapies

Facilitate coordinated transfer from ED → CCL → ICU

Acute Stroke

Stroke team activation—emergency physician; neurologist; emergency radiologist; interventional neuroradiologist; neurosurgeon; ED, IR, & ICU personnel

Prehospital & ED stroke assessment—National Institute of Health Stroke Scale

Thrombolysis for sx onset <3 hrs (Level I evidence)

Review contraindications to thrombolysis

May consider thrombolysis for sx onset up to 4.5 hrs

Hospitals not designated as stroke centers (SC)

Facilitate transfer of pts to SC with or without thrombolysis

Consider intra-arterial thrombolysis in selected pts

Initiate other appropriate medical therapies

Nothing PO until swallow evaluation to prevent aspiration

Facilitate coordinated transfer from ED → SC, ED → ICU or ED → IR → ICU

Sepsis and Septic Shock (Dellinger RP, et al. *Crit Care Med.* 2013;41:580–637; Singer M, et al. JAMA. 2016;315(8):801–810; also see Chapter 23)

Sepsis team activation—emergency physician; intensivist; radiologist; interventional radiologist; surgeon; ED, IR, OR, & ICU personnel

Prehospital sepsis screening with point of care lactate if avail.

Consider instituting ED sepsis screening protocol for early identification

Consider international guidelines for management of sepsis & septic shock (Singer M, et al. *JAMA*. 2016;315(8):801–810)

Early & appropriate antimicrobial therapy (administer abx within the 1st hour)

Consider IV fluid resuscitation, serial lactate measurements, & frequent dynamic reassessments of volume status

Sepsis redefined as life-threatening organ dysfunction caused by a dysregulated host response to infxn, & organ dysfunction can be identified as an acute change in total SOFA score ≥2 points consequent to the infxn. (Singer M, et al. *JAMA*. 2016;315(8):801–810.)

Facilitate coordinated transfer from ED → ICU, ED → IR → ICU, or ED → OR → ICU

Acute Respiratory Distress Syndrome (ARDS; also see Chapter 18)

Airway team activation—emergency physician; anesthesiologist; respiratory therapist; intensivist; ED & ICU personnel (rapid response team if avail.)

Prevent aspiration during ET intubation (consider rapid sequence intubation)

Consider low tidal volume (TV) ventilation (6 cc/kg) for pts with ARDS (ARDSNet, et al. *N Engl J Med.* 2000;342:1301–1308.)

Use predicted body wt for tidal volume calculation

Maintain plateau pressure (Pplat) ≤30 cm H_2O

Apply appropriate fractional inspired oxygen & peak end-expiratory pressure

Avoid high TV & Pplat to prevent ventilator-associated lung injury

Avoid hyperoxia

Facilitate coordinated transfer from ED → ICU

Summary

Care of the critically ill (Chalfin DB, et al. *Crit Care Med.* 2007;35:1477–1483.)

Starts from prehospital setting & ED by way of CCL, IR, OR, into the ICU

Must focus on:

Timely delivery of the standards of care for the specific dz condition

Improving the continuity of care between ED to the ICU

Facilitating pt transfer from EMS & ED (to sites of required resources & intervention) to the ICU

Requires a coordinated multidisciplinary team approach

Requires commitment from EMS, hospital, local, & regional resources

INFORMED CONSENT, PROCEDURAL STANDARDIZATION, AND SAFETY

JENNIFER HOFER, MD • MICHAEL F. O'CONNOR, MD

Informed Consent

(Jonsen AR, et al. *Clinical Ethics: A Practical Approach to Ethical Decisions in Clinical Medicine.* 7th ed. 2010:51; Beauchamp TL, et al. *Principles of Biomedical Ethics*, 6th ed. 2009:99.)

Definition

"The willing acceptance of a medical intervention by a pt after adequate disclosure by the physicians of the nature of the intervention, its risks & benefits, & also its alternatives with their risks & benefits"

Purpose

Legal authorization to proceed with a procedure: may be documented on a form, or a note in the chart

Promotes shared decision making between physician & pt

Preserves pt autonomy to actively authorize a procedure through voluntary consent rather than passive agreement

Difficulties with Informed Consent in the ICU

Physician

Use of technical language

Uncertain risks & benefits of interventions

Limited time

Unclear how the pt or proxy is receiving the information, & how to deliver the information to not frighten the pt

Deciding if the pt is competent to consent or who serves as surrogate decision maker for the pt

Time-sensitive procedures which require immediate consent

Pt or proxy agent (surrogate decision maker)

Limited understanding

Selective hearing & comprehension

Fear & denial which affect decision making ability

Undisclosed conflicts of interest

Five Elements of Informed Consent

Competence, disclosure, understanding, voluntariness, & consent

Competence

Medical context definition: the ability to "understand a therapeutic or research procedure, deliberate regarding its major risks & benefits, & make a decision in light of this deliberation"

Changes in competence

Chronic (dementia)

Waxing & waning (delirium) affected by severity of illness, sedatives

If the pt exhibits delirium but has periods of clarity with consistent decision making, then these decisions should be corroborated with supporting evidence (predefined wishes & goals of care, living will) before being implemented.

Delirium screening (Fan E, et al. *Crit Care Med.* 2008;36:94–99.)

2-step approach to obtaining consent: (1) Richmond Agitation–Sedation scale (RASS) & Confusion Assessment Method for the ICU (CAM-ICU), (2) Assessment of competency followed by request for informed consent

Identifying the surrogate decision maker if the pt is unable to consent

Surrogate or powers of attorney previously appointed by the pt which supersede family members

If no surrogate or powers of attorney, then the proxy is state specific, but usually 1st spouse, parents, children, siblings, then court appointed guardian. Some states have statutes that designate nearest, competent relatives as POA.

Types of proxy decision making

Substituted judgment: when the surrogate or proxy uses knowledge of pt preferences to make medical decisions on behalf of the pt

Best interest standard: when the surrogate acts in the best interest of the pt when the pt's preferences are unknown

Disclosure

Requirements

Stating the pt's current dx, medical status, & prognosis or if no treatment is provided

Explaining risks & benefits of a proposed procedure

Offering a professional opinion of alternatives avail. to the pt

Physician recommendation based on clinical judgment

Ethically should include the level of experience of the provider

Understanding

Pt

Repeat the proposed procedure

Describe the procedure

Demonstrate understanding of the risks & benefits

Recognize the right to refuse the intervention

Physician

Encourage pt questions & offer answers

Consent

2 parts

Written: documentation of the procedure, risks & benefits, often signed by the pt or their surrogate decision maker

Verbal: consent discussion that leads to the signing of the consent form; discussion contents should be documented by the physician in medical record

Emergency Situations

Medical necessity consent: in life-threatening situations when the pt is unable to consent & a surrogate is unavailable

Implied consent

Assumes the pt would consent if they could in a severe situation as the alternative is death or severe morbidity (e.g., similar to the administration of CPR to a stranger)

Protects the physician legally against battery charges

Procedural Standardization

Procedural standardization is key to improving safety, reducing adverse events, like in the case of CVC where it saved costs & lives. Such standardization efforts are now gradually extending to all common ICU procedures (see Chapters 8, 45 & 47).

Reducing infxn & CVC–related complications (see Chapter 8)

OCCUPATIONAL AND PHYSICAL THERAPY

BHAKTI K. PATEL, MD • JOHN P. KRESS, MD

ICU-Acquired Weakness (ICU-AW)

Definitions

Generalized symmetrical weakness ranging from paresis to true quadriplegia sparing the facial muscles (Schweickert WD, et al. *Chest.* 2007;131:1541–1549.)

Electrophysiologic testing & histology defines additional categories of ICU-AW

Critical illness polyneuropathy (CIP)—diffuse & symmetric axonal neuropathy manifested typically by distal motor & sensory deficits with normal distal tendon reflexes (Hough CL. *Clin Chest Med.* 2006;27(4):691–703.)

Critical illness myopathy (CIM)—acquired primary myopathy clinically recognized by proximal muscle weakness without sensory deficits & decreased or absent reflexes (Hough CL, et al. *Curr Opin Crit Care.* 2007;13(5):489–496.)

Causes

CIP

CIM

Immobilization leading to disuse atrophy & deconditioning

Epidemiology

Neuromuscular weakness is prevalent in 46% of adult ICU pts with sepsis, multiorgan failure, or prolonged mechanical ventilation (Stevens RD, et al. *Intensive Care Med.* 2007;33:1876–1891.)

Risk factors for ICU-acquired weakness

Female sex, number of days with multiorgan dysfunction, prolonged mechanical ventilation prior to awakening, corticosteroid administration (De Jonghe B, et al. *JAMA.* 2002;288(22):2859–2867.)

Inflammatory states (e.g., sepsis), neuromuscular blockade, hyperglycemia

Clinical Features

Diaphragmatic weakness/atrophy occurs within hours of mechanical ventilation (Jaber S, et al. *Am J Respir Crit Care Med.* 2011;183:364–371; Levine S, et al. *N Engl J Med.* 2008;358:1327–1>335.)

Mechanically ventilated pts lose 12.5% & 17.7% of skeletal muscle mass at day 7 & 10 of critical illness, respectively.

Presence of multiorgan failure exaggerates muscle loss as compared to single organ failure (Puthucheary ZA, et al. *JAMA.* 2013;310:1591–1600.)

Functional deficits persist in ARDS survivors up to 5 years later despite return to near normal lung function (Herridge MS, et al. *N Engl J Med.* 2011;364:1293–1304.)

Diagnosis

ICU-acquired weakness is recognized in 2 clinical scenarios

Difficulty in liberating a pt from mechanical ventilation

Profound persistent weakness despite return of sensorium

Electrophysiologic evaluation

A reduced amplitude of the compound muscle action potential (CMAP) & sensory nerve action potential (SNAP)—measure conduction velocity & amplitude of the sural SNAP & peroneal CMAP in 1 leg, using surface stimulation & recording electrodes

If SNAP or CMAP decreased by more than 25% on 2 consecutive days, a complete electrophysiologic test should be performed (Latronico N, et al. *Crit Care.* 2007;11:R11.)

Medical Research Council (MRC) Score

Strength testing of 3 muscle groups in each limb on a scale of 1–5

Assess function when sedation is interrupted:

Upper extremity: wrist flexion, forearm flexion, shoulder abduction

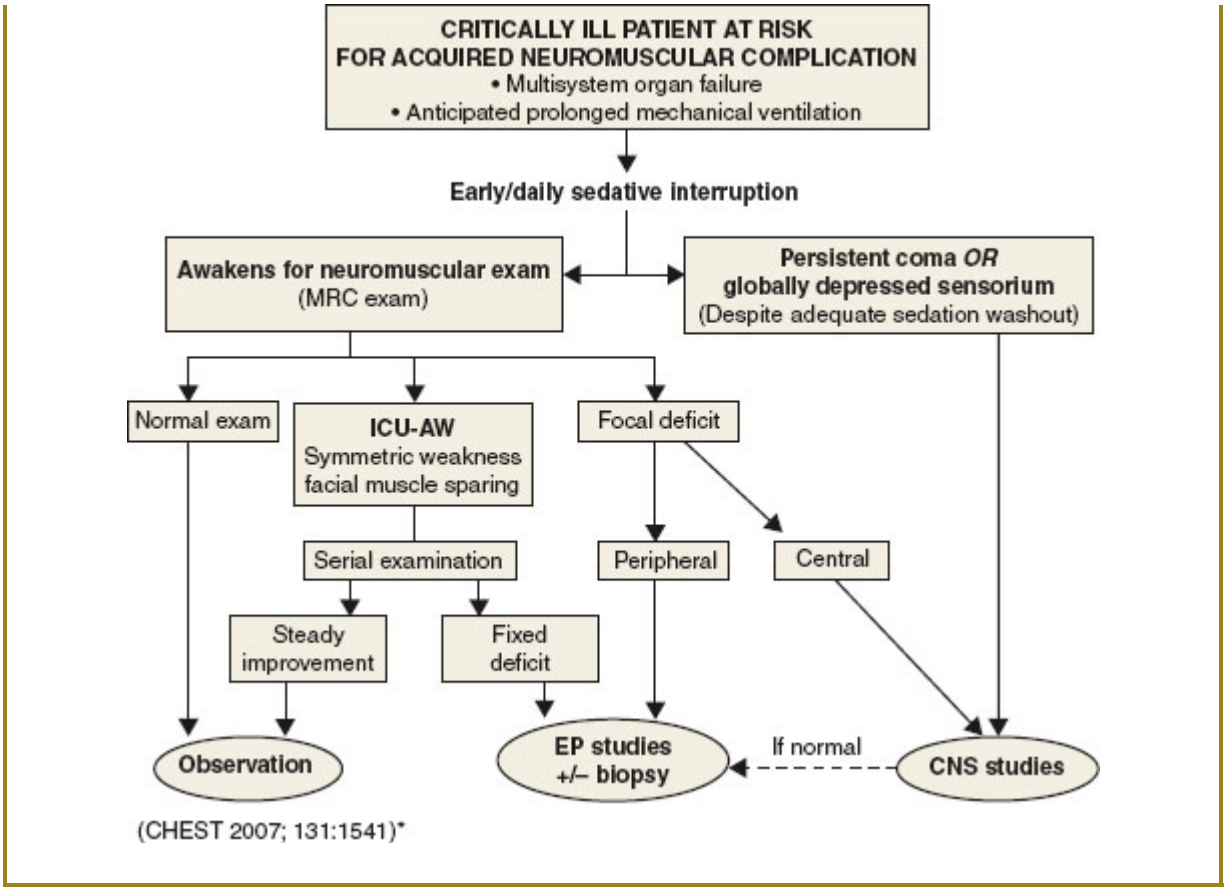
Lower extremity: ankle dorsiflexion, knee extension, hip flexion

ICU-AW defined as an MRC score <48 (De Jonghe B, et al. *JAMA.* 2002;288:2859–2867.)

MRC: Muscle Examination Score for Each Movement
0—No visible contraction
1—Visible muscle contraction, but no limb movement
2—Active movement, but not against gravity
3—Active movement against gravity
4—Active movement against gravity & resistance
5—Active movement against full resistance
Maximum score: 60 (15 pts per limb) & Minimum score: 0 (quadriplegia)

Diagnostic algorithm for ICU-AW Figure 12-1

Figure 12-1. Proposed Algorithm for Assessing Neuromuscular Complications in the Critically Ill



Schweickert WD, et al. *Chest.* 2007;131:1541-1549.
EP, electrophysiology; +/-, with/without.

Consequences

Prolonged mechanical ventilation
Increased ICU length of stay
Increased in-hospital mortality

Prevention and Treatment

Electrical muscle stimulation

Daily EMS is performed simultaneously on the quadriceps & peroneus longus muscles of both lower extremities

After leg shaving & skin cleaning, place rectangular electrodes on the quadriceps & peroneus longus muscles of both legs

Stimulator is set to deliver biphasic, symmetric impulses of 45 Hz, 400 s pulse duration (12 s on & 6 s off), at intensities able to cause visible contractions

Duration of the session is approx. 1 hr

Clinical outcomes of electrical muscle stimulation (Gerovasili V, et al. *Crit Care.* 2009;13:R161; Routsi C, et al. *Crit Care.* 2010;14:R74.)

Preservation of muscle mass in stimulated muscles compared to control

Reduced incidence of ICU-AW by MRC score (12.5% vs. 39.3%, $p = 0.04$)

Improved overall MRC scores (58 vs. 52, $p = 0.04$)

Glycemic control

Intensive insulin therapy (van den Berghe G, et al. *N Engl J Med.* 2006;354:449–461; van den Berghe G, et al. *N Engl J Med.* 2001;345:1359–1367.) While this is no longer recommended practice, due to the high incidence of hypoglycemic episodes, good glucose control (keeping blood glucose below 160–180 mg/dl) is essential for good outcomes.

Tight glycemic control was associated with decreased incidence of critical illness neuromyopathy in medical (38.9% vs. 50.5%, $p = 0.02$) & surgical (28.7% vs. 51.9%, $p = 0.001$) pts in the ICU for ≥7 days

Intensive insulin therapy was protective against critical illness neuromyopathy (Van den Berghe G, et al. *Neurology.* 2005;64:1348–1353; Hermans G, et al. *Am J Respir Crit Care Med.* 2007;175:480–489.)

Early mobilization has been shown to reduce exogenous insulin requirements by two-thirds suggesting a euglycemic effect of early activity in mechanically ventilated pts (Patel BK, et al. *CHEST.* 2014;146:583–589.)

Early Mobilization

Definition

Initiation of physical activity at the time of initial physiologic stabilization & continuing throughout ICU stay (Bailey P, et al. *Crit Care Med.* 2007;35:139–145.)

May occur as early as 1.5 days after ET intubation/ICU admission (Schweickert WD, et al. *Lancet.* 2009;373:1874–1882; Pohlman MC, et al. *Crit Care Med.* 2010;38:2089–2094.)

Perceived Barriers to Early Mobilization

Severity of illness

Early mobilization has been shown to be feasible & safe in critically ill mechanically ventilated pts

In 1 trial of early mobilization 89% of the therapy sessions were completed despite a perceived contraindication to mobility including ALI (58%), shock (17%), delirium (53%). Obesity (41%), & continuous renal replacement therapy (9%) (Schweickert WD, et al. *Lancet.* 2009;373:1874–1882.)

Device removal occurred in <1% of all sessions

Physiologic changes such as desaturation, tachycardia, tachypnea, agitation occurred in <5% of sessions & was transient (Schweickert WD, et al. *Lancet.* 2009;373:1874–1882; Leditschke IA, et al. *Cardiopulm Phys Ther J.* 2012;23:26–29; Zanni JM, et al. *J Crit Care.* 2010;25:254–262.)

Postsurgical condition

Bicycle ergonometer was successfully performed in mechanically ventilated surgical pts with improvement in 6-min walk distance, quadriceps strength, & trend toward discharge to home (Burtin C, et al. *Crit Care Med.* 2009;37:2499–2505.)

Femoral catheterization

In a prospective observational study of 210 separate mobility sessions with a femoral catheter, there were no catheter related thrombotic or mechanical complications (Perme C, et al. *Cardiopulm Phys Ther J.* 2013;24:12–17.)

Cost/resources

Direct inpatient costs of pts who were mobilized vs. usual care were not different (Morris PE, et al. *Crit Care Med.* 2008;36:2238–2243.)

Given the reduction in ICU/hospital length of stay & likelihood of discharge to home, financial modeling suggests a net cost savings of $817,836 in an ICU with 900 annual admissions (Lord RK, et al. *Crit Care Med.* 2013;41:717–724.)

Physical therapists are 3 times more likely to mobilize surgical ICU pts to standing & ambulation than nurses despite similar severity of illness (Garzon-Serrano J, et al. *PM R.* 2011;3:307–313.)

Timeliness of early mobilization

Late implementation of mobility does not improve short or long-term outcomes despite intensive therapy sessions on the ward (Denehy L, et al. *Crit Care.* 2013;17:R156; Moss M, et al. *Am J Resp Crit Care Med.* 2016;193(10):1101–1110.

Initiation of Early Mobilization (Pohlman MC, et al. *Crit Care Med.* 2010;38:2089–2094.) Figure 12-2

Perform daily interruption of sedation unless neuromuscular blocking agents are being given or severe agitation is present (also see Chapter 5)

Assess for contraindications for initiating PT/OT, these are:

MAP <65

HR <40, >130 bpm

RR <5, >40 breaths/min

Pulse oximetry <88%

Evidence of elevated ICP

Active GI blood loss

Active myocardial ischemia

Actively undergoing a procedure

Pt agitation requiring increased sedative administration in the last 30 min

Insecure airway (device)

If no contraindication to early mobilization pt, "wakefulness" is assessed during daily interruption of sedation (DIS)

"Wakefulness" demonstrated when the pt is able to follow at least 3 of 4 commands: opening eyes, using eyes to track, squeezing hand, & protruding tongue on request

If pt is unresponsive after DIS, passive range of motion (PROM) exercises are performed on all 4 limbs

If unresponsiveness persists for >6 hrs then a 2nd session of PROM should be performed

If "wakefulness" present, therapy should be delivered by a team consisting of a physical & occupational therapist. ICU nursing & physician staff should coordinate efforts for screening & safety for therapy sessions

Preparing for therapy session

All devices (vascular access catheters, enteral tubes, ETTs) must be assessed & secured

Any unnecessary noninvasive devices should be removed (pneumatic compression stockings, etc) & enteral feedings should be stopped

All equipment should be moved to the side of the bed where the mechanical ventilator is located. Similarly, the pt should be mobilized to that side of the bed

If ambulation is anticipated, a transport ventilator should be present

Graduated Stepwise Physicotherapy Approach	
Active or Active-Assisted Range of Motion in Semirecumbent Position	
Active ROM of all limbs for exercise & assessment of strength & ability to follow complex commands	
↓	
Bed Mobility Excercises	
Lateral rolling & transferring from semire - cumbent position to upright	Progress to sitting at edge of bed if pt can follow commands
↓	
Sitting Balance Activities	
Targets postural muscle groups & is performed at edge of bed	Balance activities: reaching in & out of base of support, postural retraining, righting reactions
↓	
Activities of Daily Living	
Bathing, dressing, grooming, toileting, eating performed in sitting & standing positions	
↓	
Transfer Training	
Transfers include sit-stand, bed-to-chair, & bed-to-commode	Progress to standing based on sitting balance, lower extremity strength, & absence of unsafe behavior
↓	
Promote Standing Balance	
Pt improves standing balance & tolerance by reaching, marching in place, & wt shifting	
↓	
Ambulation	

Contraindications to continuing of PT/OT:

Mean arterial pressure <65

HR <40, >130 bpm

RR <5, >40 breaths/min

Pulse oximetry <88%

Marked ventilator dyssynchrony

Pt distress (nonverbal cues or physically combative)

New arrhythmia

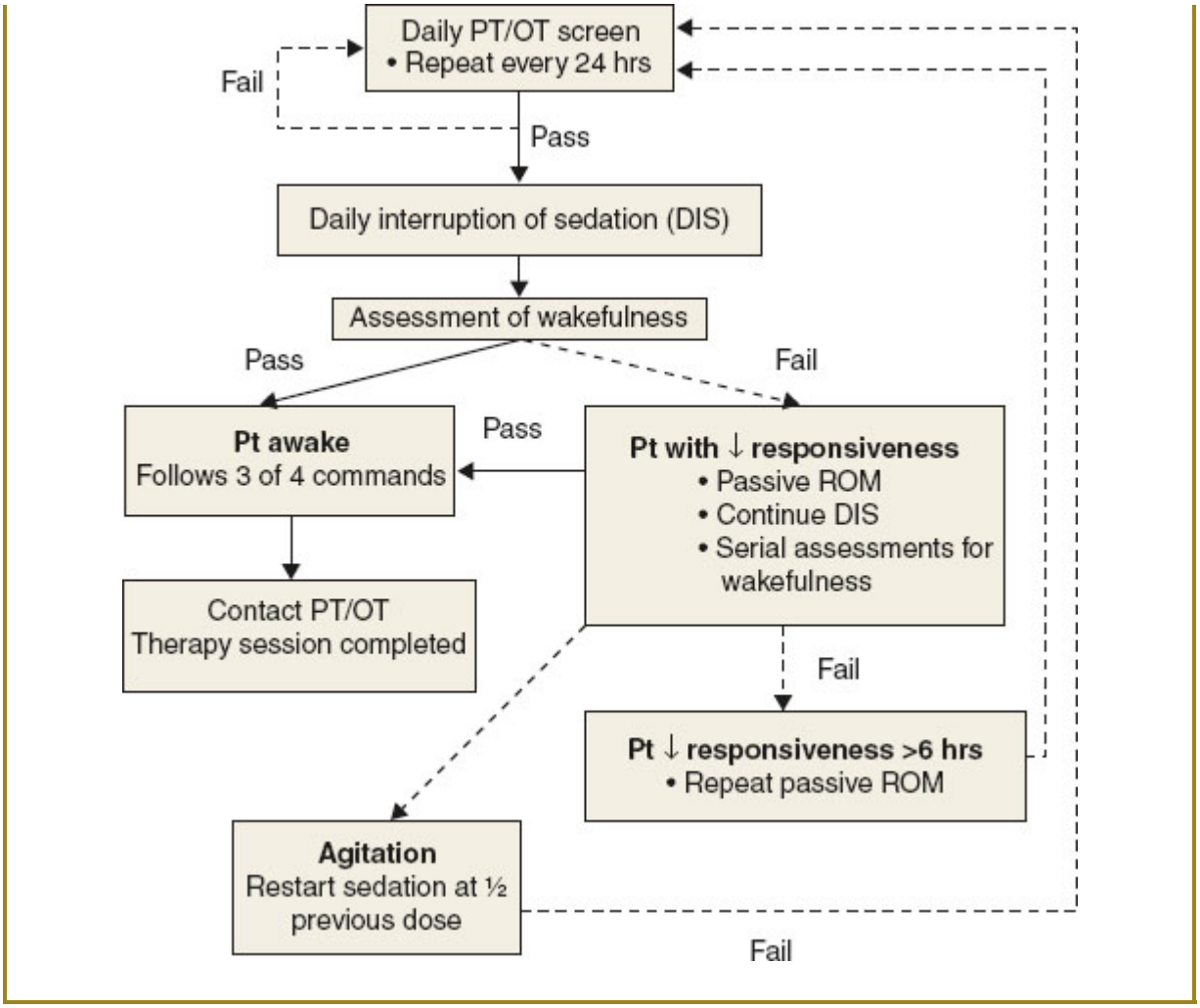
Concern for myocardial ischemia

Concern for airway device integrity

Fall to knees

Concerns for inadvertent ETT removal

Figure 12-2. Summary of Early Mobilization Protocol



(Pohlman MC, et al. *Crit Care Med*. 2010;38:2089–2094.)

Clinical Outcomes of Early Mobilization (Schweickert WD, et al. *Lancet.* 2009;373:1874–1882; Morris PE, et al. *Crit Care Med.* 2008;36:2238–2243; Burtin C, et al. *Crit Care Med.* 2009;37:2499–2505.)

Increased return to independent functional status at hospital discharge (59 vs. 35%, $p = 0.02$)
Shorter duration of delirium (2.0 days vs. 4.0 days, $p = 0.02$)
Increased ventilator free days (23.5 days vs. 21.1 days, $p = 0.05$)
Improved ICU length of stay 5.5 days vs. 6.9 days ($p = .025$)
Improved hospital length of stay 11.2 days vs. 14.5 days ($p = 0.006$)
Improved 6-min walking distance (196 m vs. 143 m; $p < 0.05$)
Improved subjective feeling of functional well-being (as measured with "physical functioning" item of the Short Form 36 Health Survey questionnaire) (21 pts vs. 15 pts; $p < 0.05$)
Improved isometric quadriceps force

PATIENT- AND FAMILY-CENTERED CARE

MARY PENNINGTON, RN, MSN, CCRN • PATRICE K. NICHOLAS, DNSc, DHL (Hon.), MPH, RN, ANP-C, FAAN

Introduction

The national pt safety movement, regulatory agency directives, pt advocacy groups, & a growing complexity in technology & therapeutics have created the impetus for a paradigm shift towards pt- & family-centered care esp. in the ICUs.

Definitions

Pt- & family-centered care: a partnership among physicians, nurses, other providers. Clinical decisions made are congruent with the pt's wants, needs & preferences. pt & families are encouraged to participate in their own care & decision making (Institute of Medicine (IOM). *Crossing the Quality Chasm: A New Health System for the 21st Century*. 2001.).

Family-centered care: takes pt-centered care & widens the circle of concern to include the family. This is a holistic model of care based on the concept that pt are part of a larger "whole" that defines them & must be integrated into the healthcare team.

From the Institute for Pt- & Family-Centered Care website (http://www.ipfcc.org):

"Pt- & family-centered care is an approach to the planning, delivery, & evaluation of health care that is grounded in mutually beneficial partnerships among healthcare providers, pt, & families.

Pt- & family-centered practitioners recognize the vital role that families play in ensuring the health & well-being of infants, children, adolescents, & family members of all ages. They acknowledge that emotional, social, & developmental support are integral components of health care. They promote the health & well-being of individuals & families and restore dignity & control to them.

Pt- & family-centered care is an approach to health care that shapes policies, programs, facility design, & staff day-to-day interactions. It leads to better health outcomes & wiser allocation of resources, & greater pt & family satisfaction."

Objective

Doctors & nurses respect & understand pt' & families' values, preferences, & cultural beliefs.

Pt & families are included in the plan of care & are informed & actively involved in medical decision making.

Pt care is coordinated & communicated among all healthcare providers participating in the pt's care.

The physical comfort & emotional support of pt & family members is a priority for all members of the healthcare team.

Rationale

Directives from professional organizations, regulatory bodies, & consumer advocacy groups:

The Joint Commission (TJC), Institute of Medicine (now the National Academy of Medicine, Society for Critical Care Medicine, & the American Association of Critical Care Nurses (AACN) have declared that quality health care must be safe, pt-centered, culturally focused, & equitable.

The American Nurses Association's (American Nurses Association (ANA). *American Nurses Association Code of Ethics for Nurses with Interpretive Statements*. 2015) Provision 1 & Provision 2 of the *Code of Ethics for Nurses with Interpretive Statements* central ethical tenet guiding the nursing profession is respect for persons & supporting their value systems across the health-illness continuum. This extends & encompasses the nurse's commitment to the pt, whether an individual, family, group, or community. The *American Nurses Association Social Policy Statement* focuses on nursing as inclusive of advocacy in the care of individuals & families as well as communities & populations (American Nurses Association (ANA). *Nursing's Social Policy Statement*. 2010).

Recommendations from professional organizations:

The Society of Critical Care Medicine (SCCM) has developed models to improve pt- & family-centered care in critical & ICUs (website: www.sccm.org).

Institute for Healthcare Improvement (IHI) has developed a pt- & family-centered approach that includes the development of an action plan to advance meaningful partnerships with pt & families in hospitals—including in critical/intensive care settings. The IHI has developed a Pt- & Family-Centered Care Organizational Self-Assessment Tool (website: www.ihi.org).

Key Concepts

Most of the pt/family dissatisfaction relates to poor communication & restricted access to pt.

Increased & flexible visitation for pt & families are associated with improved outcomes & satisfaction.

Visitation policies must be highly individualized to meet the needs of the pt & family as well as the unit.

Families of critically ill pt experience challenges that are unique to each family & may produce disruption in family functioning that are linked to crisis-like behaviors that include confusion, shock, & intense fear. Anxiety, anger, sadness, & resignation may occur in the family. However, enhanced pt- & family-visitation may limit the negative effects of a critical/intensive care stay for the pt.

Family members often do not pay attention to their own needs & health care. Providers underestimate the complex needs of family members.

> Families have essential needs in the critical/intensive care settings including information, reassurance, proximity to the pt.

Patient- and Family-Centered Care Interventions

Communication

Providing ongoing information to families is an important priority.

Keep explanations brief & clear.

Early, accurate, & use language that families can understand (try to use wording at the 9th grade level of comprehension).

The need for hope is universal.

Family members place great importance on being called at home if the condition of the pt changes.

Avoid misunderstandings by reinforcing & reiterating facts.

Structured communication in the form of regular & shift-by-shift contact is essential.

Family members have a need to speak to a physician at least every day regarding the condition of & the prognosis for the pt.

Involving the family in pt rounds can be very helpful.

Daily & postmorning round telephone calls to update the family or inviting family members to bedside rounds may be very helpful.

Regular meetings with the identified family contact person as often as needed.

Pt & family education of what to expect after hospitalization.

Alternatives to treatment (Davidson JE, et al. *Crit Care Med.* 2012;40:618–624.)

Pt- & family-centered care requires that a nurse explain to them about the care, the unit, the equipment & what the families can do for the pt when visiting. Families often feel helpless & appreciate participating in care.

Opportunities must be established for pt/family to state their goals.

ICU Family Information booklets must be readily avail. for families:

Provide concrete information about the ICU, work flow, technology.

Write names ICU physician, nurse, social worker in the booklet for the family.

Daily reviews with family members are essential in establishing the routine & plan with the family: always ask if they have questions/concerns.

Encourage family to bring in familiar objects, picture, & mementos that have meaning to the pt & family.

Shared decision making:

Family assumes the voice of the pt in helping to make decisions for incapacitated individuals.

Families may feel burdened when asked to be solely responsible for making decisions.

Highly emotional and/or crisis states.

Complexity of medical dx.

Prognosis uncertainty.

ICU team shares accountability with families in a true partnership for decisions made.

Decreases family anxiety.

Allows pt preferences to be identified.

Flexible Visitation Policy

Allows the family to visit any time, as often as they desire & for as long as they wish (unless the pt requests no visitors):

Improves family & pt perceptions of the quality of care.

Reduction of anxiety of the pt:

Less likely to worry about family members when they can see them often.

Pt feel loved & more secure when they have more frequent visitors.

Family members are more satisfied with a liberal visitation policy:

Allows them to visit at times that are more convenient for them.

Other responsibilities may limit when they can visit.

May live long distances from the hospital & can see the pt when they arrive.

Family members report less exhaustion with an open visiting policy.

Restriction to visiting is at the discretion of the nurse:

If there is an emergency on the unit.

If their presence is detrimental to the pt.

Visitation in Critical Care

65% indicated that more open visitation was desirable
90% felt that visitors were very important to them
85% stated the desire that family perform personal care for them
75% denied feeling fatigued after visiting.

(Roland P, et al. *J Nurs Care Qual*. 2001;15:18–26.)

Family's Level of Involvement

Families come with specific & unique strengths, limitations, characteristics, challenges, & skills.

Assess individually to determine capacity & desire regarding participating in care & develop & individualized plan of care for each pt & family.

Important to be aware of the psychosocial issues present that may influence how family members react or involve themselves in the pt's care.

Family Presence during Codes

Evidence suggests that the majority of families (60–80%) would be at their loved one's bedside during CPR if given the option. (AACN News. *Practice Alert: Family Presence During CPR & Invasive Procedures*. 2004;21(11).)

Family Member Presence during CPR

Removes doubt, know everything done.
Reduces anxiety & fear.
Supports & helps pt: active role.
Sustains pt–family connectedness & bonding.
Facilitates closure.
Facilitates grief process.
No adverse psychological effects among families at f/u.

Patients

Almost universally, children want parents present.
Reports from adult pt:
Felt comforted, less scared, less alone, safer, able to better cope with event.
Poor communication & restricted access during CPR were identified as among the most stressful aspects of care & recovery for family members.

Cultural Issues

Culturally competent care: physicians, nurses, other healthcare team members mirror the multicultural backgrounds of the pt population.

Clashes between pt/families & healthcare providers can occur when cultural differences & values are not understood. Consult from ethics service, pt & family relations, social work, and/or chaplaincy.

To understand & support pt & their families during the crisis of critical care admission, knowledge of differences in cx is essential.

When the needs of the pt's families are met, families are better able to cope with the ICU environment, clinical trajectory & contribute to the pt's care during & after discharge.

TRANSITIONING FROM ACUTE CARE TO REHABILITATION

SHANNON S. MCKENNA, MD

The Need

An increasing number of patients (pt) survive acute critical illness with significant disability & ongoing organ system dysfunction. Factors contributing to this trend: (Kahn JM, et al. *Crit Care Med.* 2015;43:282–287)

Increasing age
Increasing complexity of treatment
Decreased mortality from sepsis, ARDS, & cancer

If these pt are cared for at the acute care facility for the entire duration of their illness, ICU beds are occupied by long stay chronically critically ill pt. The result:

Pt are "boarded" in the PACU or ED when ICU beds are in short supply
ED may have to go on diversion
Newly critically ill pt experience delays in receiving definitive critical care, which may worsen outcomes

Reimbursement patterns & limited acute care beds have driven the development of post acute care facilities

Types of Post Acute Care Facilities

Broadly classified as long-term acute care (LTAC), inpatient rehab, & skilled nursing facilities (SNF)

LTAC: average length of stay >25 days; complex medical management including ventilator weaning & dialysis; daily physician assessment & the availability of specialty consultation; IV medication administration; wound care; intensive rehab therapy (PT, OT, speech therapy) is avail. for pt able to participate

Inpatient rehab: intense rehab is a primary need; ongoing medical management is a secondary concern

SNF: low complexity medical needs not requiring daily physician visits; less intense rehab needs or not able to participate in intense rehab program

Most pt being discharged directly from the ICU will require LTAC level care

Outcomes

Paucity of data avail.

Study of Medicare pt >64 y/o transferred from ICU to an LTAC between 2004 & 2006 found: 27% discharged home, 35% discharged to SNF, 14% transferred back to acute care facility, & 23% died. 1-yr postadmission mortality was 52% (Kahn JM, et al. *JAMA.* 2010;303:2253–2259)

Overall 1-yr survival of pt requiring prolonged mechanical ventilation about 50% (multiple studies)

Evaluating Patients for Suitability of Transfer to an LTAC

Each pt should be evaluated for the suitability of transfer. Those who are unlikely to do well at an LTAC should not be transferred even if bed availability issues are critical

Triage Criteria for Patient Transfer	
Appropriate for Transfer	**Not Appropriate for Transfer**
Hemodynamically stable	Hemodynamically unstable
On stable medication regiment	Likely to need urgent physician assessment
Tracheostomy in place if ventilated; not requiring continuous IV sedation	Likely to need complex diagnostic work-up (MRI, CT, etc.)
Dressing changes (if needed) b.i.d. or less	Likely to need urgent therapeutic interventions (bronchoscopy, etc.)
Permanent feeding tube & IV access in place (if needed)	Requires suction more than q2h (may vary by facility)
Hemodialysis on 3 times a week schedule	Agitated delirium requiring 1:1 sitter (unless facility can provide)
Organ system failures persistent but stable	Worsening organ system failure
	Terminal illness with little chance of recovery (LTAC is not a hospice)
	Low complexity medical needs—inpatient rehab or SNF more appropriate

Steps to Ensuring a Successful Transfer

Know the Facility

What is the staffing pattern, what services are avail. on site, how are urgent situations handled, how much rehab can be provided?

Create a means for regular follow-up. Discuss which pt did well at the facility & which did not. What can be learned for the future from past experiences?

Partnering with a single facility, or a small number of facilities, is likely to increase the success of transfer.

Prepare the Patient and Family

Staffing is different at LTACS—routine care may be provided by assistants (bathing, vitals), RNs are not continually in sight, physician contact time may be less Pt & families should expect to be somewhat anxious for the 1st few days in a new environment. Discuss this up front. Emphasize that "different" doesn't mean "bad"

Some pt will transfer back & forth between the LTAC & acute care several times. Pt & families should be prepared for this & not see it as a failure of the LTAC

Make sure appropriate airway, enteral, & IV access are in place

Adjust medication routes/schedules: enteral when possible, batch administration times together, avoid middle of the night doses

Establish stable bowel regime

Remove any tubes, catheters, drains, staples, or sutures that can be removed before transfer

Communication

Focused but complete sign out to the care team at LTAC prevents the need to “reinvent the wheel”. Verbal sign outs between physicians, nurses, respiratory therapists, & physical therapist rapidly identify the unique features & needs of a given pt

Detailed written summaries should accompany the pt to add to & reinforce the information given verbally

Provide a person/number to call 24 hrs a day if the facility has questions about the pt. Timely contact may allow appropriate treatment of known problems to be initiated at the LTAC without transfer back to acute care

ETHICS, PALLIATIVE AND END-OF-LIFE CARE

MICHAEL F. O'CONNOR, MD • ALLISON K. DALTON, MD

Palliative Care is the prevention or treatment of suffering in dying pt

Represents a change in focus from treating the dz to alleviating its sx

Emphasizes the importance of comfort for the pt & access for family & friends during the dying process

The critical care team provides emotional support for the family & pt

Palliative care is initiated when the pt or family has decided to discontinue curative treatment of the terminal illness

Ethical issues in the ICU (Gavrin JR. *Crit Care Med*. 2007;35:S85–94

Pt autonomy is of primary importance when establishing goals of care

Capacity: The understanding that pt have the ability to make decisions for themselves based on an understanding of their condition, prognosis, treatment options, & they are able to participate in the process of informed consent

Pt Self-determination Act (1990) includes the right to participate & direct their own healthcare decisions, right to refuse or accept medical interventions, right to prepare advance directive, & right to obtain specifics about provider's policies governing the rights of an advance directive

The "Surrogate" or "Proxy" makes decisions that should represent the pt's values & wishes once the pt has lost capacity

Proxy agent should act under the principle of **substituted judgment** to make decisions given the pt's values & wishes

Paternalism gives physicians a moral basis for the ability to compromise a pt's autonomy to promote the pt's welfare

Advance Directives help establish the pt's wishes when they are incapacitated

Instructional documents, such as a living will, establish the treatments that the pt would accept or refuse if they become incapacitated

Some states do not recognize these documents as legally binding

A healthcare proxy document or durable power of attorney (POA) is a legally binding document that designates a surrogate by the pt to make treatment decisions based on the pt's wishes if they become incapacitated

Power of attorney is valid any time the pt is incapacitated

Pt without a designated surrogate should have either a court appointed guardian or an ethics committee review to determine the goals of care

Statute in some states (e.g., Illinois) can designate POA, typically nearest competent living relatives

Beneficence is the moral obligation to promote goodness or benefit to the pt & family, provide care that maintains or improves health, reduces disability, & alleviates physical, & existential, pain & suffering

Physicians are ethically bound to not injure pt (nonmaleficence)

Establishing Goals of Care (Truog RD, et al. *Crit Care Med*. 2008;36:953–963; Blinderman CD, et al. *N Engl J Med*. 2015;373:2549–256.)

Ideally, goals of care would be discussed at onset of illness or hospitalization prior to medical crisis

Physicians should clarify goals of care with the pt & family: restoring health, extending life, discussion of acceptable/unacceptable states, & alleviating pain & suffering

Communicating to the family realistic expectations about whether the goals of care can be achieved with the current treatments is essential to resolving conflict

Physicians are not obligated to provide treatment to pt that they believe cannot achieve the goals of care as defined by the family & physicians

Physicians are not obligated to provide care they deem futile

Mediation by a hospital ethicist/ethics committee may be beneficial in resolving conflicts between families & physicians or between discordant medical providers

There is no legal distinction between extraordinary vs. ordinary treatments such as mechanical ventilation vs. nutrition & hydration

Medical interventions should be evaluated by weighing the benefits & burdens they confer to the pt

Therapy should always be focused on whether they will accomplish the goals of care

Treatment that merely prolongs the dying process should be eschewed

Changing Goals of Care

3 ethical principles guide the withdrawal of life-sustaining care in the United States

Philosophical & legal analyses do not differentiate between withholding or withdrawing care

The withdrawal of life-sustaining care is not legally considered murder

The actions of the physician during withdrawal of care are considered to allow the pt to die from the underlying illness

The “doctrine of double effect” allows a physician to treat a pt’s pain even though it may hasten the dying process

Pain medication given with the intention to make the pt comfortable is acceptable even if it hastens death

Practical aspects of changing goals of care to **intensive comfort measures**

The goals for the pt are to:

Provide adequate pain & sx management

Avoid undesired prolongation of dying

Allow the pt to sustain a sense of control

Continuous monitors should be masked or discontinued to ensure the family focuses on the pt & not alarms or numbers

Discontinue labs/tests not benefiting the pt goals, which prioritize comfort

Once the decision to change goals of care to "intensive comfort measures" (previously "withdrawal of care") has been made care should continue to be provided in the current room as long as it does not hinder care of other pt

Allow family members to stay with the pt during dying process

A multidisciplinary team (physicians, nurses, therapists, social workers, chaplain) may be beneficial for pt & families

Sedatives & Analgesics (Blinderman CD, et al. *N Engl J Med*. 2015;373:2549–2561.)

Alleviate pain, dyspnea, & other distressing sx

Opioids for treatment of pain & dyspnea; titrated to pt comfort

Pt may not be able to report their pain

Physiologic variable & behavioral observations may be best gauge of pain (tachycardia, tachypnea, fearful facial expression)

Benzodiazepines are mainstay for anxiolysis, amnesia, & sedation. They do not have any analgesic properties

Opioid Analgesic Agents

Opioids	Equivalent Dose, IV[a]	Onset to Peak Effect (mins)	Duration of Effect (hrs)	Typical Adult Dose, IV	Typical Pediatric Dose, IV	Typical Infusion Rate
Morphine	10 mg	20–30	3–4	2–10 mg	0.1 mg/kg	0.05–0.5 mg/kg/hr
Fentanyl	100 mcg	2–5	0.5–2	0.5–2 mcg/kg	1–5 mcg/kg	0.5–10 mcg/kg/hr
Hydromorphone	1.5–2 mg	20–30	3–4	0.5–2 mg	—	—

IV, intravenous.

[a]Equivalent doses are approximations & are of limited value due to differences in onset & duration of effect.

Source: Truog RD, et al. *Crit Care Med*. 2008;36:953–963.

Sedative Agents						
	Onset to Peak Effect (mins)	Duration of Effect (hrs)	Typical Initial IV Dose		Typical Initial Infusion Dose	
			Adult	Pediatric	Adult	Pediatric
Sedatives						
Lorazepam	20–25	2–4	1–3 mg	0.05 mg/kg	0.5–4 mg/hr	0.05–0.1 mg/kg/hr
Midazolam	5–10	1.5–2	0.02–0.1 mg/kg	0.1 mg/kg	1–5 mg/hr	0.05–0.1 mg/kg/hr
Propofol	1–2	0.1–0.4	1 mg/kg	1 mg/kg	10–50 mcg/kg/min	10–50 mcg/kg/hr
Neuroleptics						
Haloperidol	25–30	2–4	0.5–20 mg	—	3–5 mg/hr	—

IV, intravenous.
Source: Truog RD, et al. *Crit Care Med.* 2008;36:953–963.

- Once the pt has died communication should use simple & unambiguous language stating the pt has died
- Reassure family that appropriate care & decisions were made

NURSING STANDARDS IN CRITICAL CARE

MARY PENNINGTON, RN, MSN, CCRN • VINCENT M. VACCA, RN, MSN, CCRN, SCRN

Introduction

Connect with, & know your patient (pt) as an individual, humanize a highly technologic & busy environment & ensure a safe passage for pt & families.

Critical Care Nursing Work Flow

Shift Report

Prepare for end-of-shift report

Transitions in care are pivotal moments for pt safety.

Utilization of a systematic handoff system can promote pt safety from high-stress transitions such as admission to the ICU following a surgical procedure performed in a procedural area or OR, a rapid response or a code.

Review pt code status, isolation/precaution status, medical record, flow sheet, medication administration record, labs, & licensed independent provider (LIP) orders.

Evidence suggests shift report is optimized when done at the bedside in the presence of the pt.

In addition to review of pt chart and/or telephone or taped communication; person to person verbal contact entails cues, such as facial expression, posture, & eye contact, & may provide additional information regarding the level of concern about the pt's medical problems while ultimately enhancing the receiver's ability to interpret the information being relayed.

The pt whose care is transferred from nurse to nurse or from LIP to nurse may be incapacitated & unable to participate, making them vulnerable to error & preventable harm.

Enhances safety by promoting nurse–pt & nurse–nurse communication.

Increases the pt's & family's trust and sense of security.

Handoffs should be conducted with limited interruptions in order to enhance communication.

Optimal handoff among healthcare professionals for hospitalized pt should involve a combination of both verbal & electronic communication to maximize pt safety & care continuity.

Receiving end-of-shift report

Given the large amount of information necessary to hand off pt care from nurse to nurse or LIP to nurse, it would be beneficial to use a structured handoff communication tool developed using a participatory approach. Standardization of information communicated during handoffs can minimize variations across settings (see sample report sheet)

Review the nursing and medical assessments

Goals of care

Ventilator settings/plans for weaning

Medication infusions/titrations

Activity/mobilization limitations/barriers/goals

Identify/discuss psychosocial and emotional needs

Family needs (religious/cultural/language/interpreter)

Preliminary assessment is done as part of the hand-off

Allergies, vital signs, physiologic parameters/goals, wt, level of consciousness (LOC); airway, breathing, circulation (ABCs), vascular access, tubes, lines and drains; wound dressings; medications including dosage and rates of IV infusions; fluid balance/goals, amount of fluid left in the IV infusion bags; invasive line calibration/leveling; & safety issues

Document vital signs, ventilator settings, medication infusion rates, pain/agitation using validated scales.

Print an ECG rhythm strip, include intervals and rhythm identification, and a copy (if an electronic copy is not automatically saved) of all transduced waveforms & pressure from the physiologic monitors.

Strategize Shift Activities and Goals

Organize the sequence of activities based on pt condition

Stabilize pt *if not already done*

Prioritize and when possible cluster activities to provide periods of rest for the pt

Prepare for traveling to a procedure/test

Dressing changes/bed bath/oral care/skin care/repositioning

IV catheter (commonly called “line”) labeling, verify IV pump settings for infusions, changes/tubing changes

Assessment

The nurse continuously assesses & monitors physiologic data, interpreting it based on the pt's physical, emotional, and psychological state and response. The work-flow changes min to min & is driven by these assessments.

Airway

Secure airway

If intubated: check for secure and stable ETT and record position, size, and stabilization device

Ability to maintain patent protected airway can be compromised due to decreased LOC, effect of medications, & muscular skeletal ability

Prepare for interventions including airway adjuncts and suctioning as indicated

Prepare for intubation

Breathing

Rate: <25/min (expected as upper limit of normal)

Quality, depth, pattern

Equal and symmetrical chest excursion, bilateral breath sounds? Presence of adventitious breath sounds?

Able to complete a sentence?

If artificial airway present and on mechanical ventilation, assess patient for:

a. comfort
b. synchrony with set RR
c. ventilator settings are adequate to meet metabolic demand
d. readiness to wean

Assess circulation:

LOC

HR

Rhythm

Hx of or current cardiac dysrhythmias?

Evaluate a rhythm strip: rate, presence/configuration of P waves, PR interval, QRS complex, presence and configuration of T waves, QT interval, presence of extra waves (U waves) and presence of dysrhythmias

If paced—identify type of pacemaker (internal/permanent, external/temporary)

Central and peripheral pulses

Skin color and temp

Continuous infusions

Tubes, lines, and drains

Chest tube(s) patent and secured: drainage, suction, air leak, dressing occlusive/intact.

Trace IV tubing from pt back to the pumps

Assure that they are patent, secure, and labeled

Confirm all IV drips: check if they are the correct medications as ordered, correct concentration, rate, and dose: ALWAYS DOUBLE CHECK

Adequate IV volume left or replacement immediately avail. to avoid interruptions in continuous delivery.

Know the code status of your pt

DOCUMENT assessment on the ICU flow sheet (whether paper or electronic format depending on the institution you work at) in real time

Environmental assessment/checks

Check arrhythmia alarms—are they on and appropriately set to pt specific condition & set to appropriate level of alarm

Suction/ bag-valve-mask set-up

Identify and label IV access catheter port or lumen as the “emergency IV push line”

Know where the emergency equipment is located and verify that it is pt-ready at all times.

Identify hemodynamic, respiratory, sedation and pain parameters being targeted

Check label to make sure that what is infusing correlates to what is programmed in IV pump & what was ordered

Check all IV connections making sure that tubing is luer locked and infusing correctly

Verify volume remaining in each infusion—and if volume in bag or syringe is low, make sure that another bag or syringe is immediately avail.

Planning Care

This time perform a complete assessment (see Appendix II). Compare and contrast your findings to previous 24 hrs & pt baseline.

Address present & potential problems:

Pain & sedation, altered hemodynamic states, impaired physical mobility, impaired skin integrity, deficient or excess fluid volume, nutrition, sleep deprivation, pt/family coping

Evaluate fluid status of pt & impact on other body systems. Assess electrolytes & identify cause of electrolyte imbalance, clinical manifestations, & treatment

Evaluate pt progress & possible need for revisions in plan of care

Prepare for interdisciplinary rounds

Seek consultation from knowledgeable colleagues: nurse, physician, nurse practitioner, physician assistant, respiratory therapist, pharmacist, social worker, nutritionist, spiritual care

Access resources to assist with clinical dilemmas & problem solving

Prioritize & sequence activities for the pt by clustering some, & providing periods of rest. Activities: dressings, turns, line changes, traveling for a test, getting the pt out of bed to a chair or ambulating. Consider when the family is coming & create opportunities for a quality visit for all.

Be flexible! Your plan for the day is highly subject to change based on the pt's condition.

Complete your note before you give report which will help identify salient issues

Give hand-off report

Ensure the Accuracy of Technology and Physiologic Data

Priming of the pressure tubing:

Use only sterile NS 0.9% NS 500 ml as flush solution or follow institutional policy.

Air bubbles in the tubing system are a frequent & important cause of error in hemodynamic monitoring creating a dampened waveform (even tiny air bubbles)

Air-free priming

Remove all air from the flush solution

Entire tubing system should be flushed

Stopcocks, luer-lock interconnections, & transducer common locations of air entrapment

Leveling of the transducer

Level transducer to the phlebostatic axis or ordered anatomic reference of the pt

Phlebostatic axis: intersection of the 4th ICS & ½ the anterior–posterior diameter of the chest (midaxillary in line with right atrium/tricuspid valve)

Follow institutional protocol for transducer placement (pole or pt)

Rationale:

Eliminates effects of hydrostatic forces on hemodynamic pressure

Ensure the transducer is leveled before zeroing and/or obtaining pressure readings

Note: relevel the transducer with any change in the pt's position to assure accurate readings

Zero referencing:

Rationale: ensure that pressure being measured reflect the pt's hemodynamics & not the effects of atmosphere or fluid in the system

Procedure:

Turn the stopcock port nearest the transducer off to the pt

Remove the dead end cap, keeping interior sterile, open stopcock to air

Activate the zero function key on monitoring device

Confirm that the monitor displays ZERO

Replace cap, turn stopcock open from pt to transducer, & confirm waveform/pressure on monitor

Dynamic response testing/square wave test:

Helps evaluate whether your monitoring system's dynamic response is accurate

Perform at the beginning of your shift & anytime you suspect values are not accurate or after opening the closed system.

Done by activating the fast flush device on the transducer for 1–2 s. Evaluate the "bounce back"

You should see the waveform should square off oscillate (bounce) once & come back to *rest*

Nursing Preparation for Intrahospital Transport of Critically Ill Patients (also see Chapter 17)

The transport of critically ill pts to procedures or tests outside the ICU is potentially hazardous, & occurs only when urgently required for the provision of care. *It is strongly recommended that a minimum of 2 people accompany a critically ill pt when travelling out of the ICU.*

Pretransport coordination & plan

Clarify urgency & rationale for test & procedure

How long will you be travelling?

How unstable is your pt?

What resources are avail. at the destination?

Ensure destination is ready on arrival. Secure an elevator in advance.

All critically ill pts need secure IV access and a secure airway before transport. A pt should not be transported before airway stabilization if it is judged likely that airway intervention will be needed.

What pt care orders do you need? (Example: analgesia or sedation orders)

Medications administered (If on "drips" or infusions, ensure adequate supply is avail. at all times.)

Premedications ordered & administered

If pt is now NPO & has an insulin drip, check blood sugar for hypoglycemia

NPO appropriate amount of time

Identify IV push line

Are you going to need peripheral access?

If going to MRI, ensure MRI checklist is complete. (ECG electrodes are changed once at MRI)

Ensure all relevant consents are completed

Preprocedure prep completed?

Transport equipment

A BP monitor (or standard BP cuff), pulse oximeter, & cardiac monitor/defibrillator accompany every pt

Resuscitation medications & equipment that may be necessary (not for every pt):

Portable mechanical ventilator

Defibrillator

Resuscitation drugs: epinephrine & antiarrhythmic agents

Supplemental medications such as sedatives & narcotic analgesics based on pt needs

IV fluids & continuous drip medication

All battery-operated equipment is fully charged & capable of functioning for the duration of the transport

Suction for chest tubes (CT's) if required

Oxygen tank/bag-valve-mask & face mask

IV pumps

Elevator key to facilitate travel

Accompanying personnel

Respiratory therapist if the pt is mechanically ventilated

Nursing assistant/transport aide to assist with transportation

If pt is hemodynamically unstable, an LIP with expertise in airway management, advanced cardiac life support & critical care training should accompany the pt

If the pt is stable & an LIP will not be accompanying the pt, orders or protocols are needed to permit the administration of medications & fluids by RN if needed

Nurse to provide continuity of care, monitoring of physiologic data, & ensure pt safety

Port

Prior to transport, ETT position should be noted & secured & adequacy of oxygenation & ventilation is confirmed.

Monitoring & documentation required:

Assure the same level of basic physiologic monitoring during transport as in the ICU.

If the procedure will be prolonged & the receiving unit is staffed by appropriately trained nurses, pt care may be transferred to those nurses. If

care is not transferred, the ICU nurse remains with the pt until returned to the ICU.

Sleep Deprivation in the ICU Patient

Sleep duration & quality (alteration in sleep/wake cycles) is recognized as critical in the prevention & treatment of (CV), lung & blood dz (*National Heart, Lung and Blood Institute.* 2007). Critically ill adult pt have markedly fragmented sleep compared to healthy adults, with approx. 50% of sleep occurring during daytime hrs. Kamdar BB, et al. *J Intensive Care Med.* 2012;27(2):97–111. In order to promote nighttime sleep, the secretion of melatonin is maximal at night, when there is no light.

Pt who are eventually discharged from the ICU (ICU survivors) report that inability to sleep was among the major sources of stress or bad memories during their ICU stay. In 1 study, 60 pts were interviewed at 6–12 months after their discharge from the ICU, & 50% reported sleep disturbances during their ICU stay, such disturbances persisting after discharge in approx. 30%. A significant number of medications that are commonly used in the ICU can cause changes in the amount & quality of sleep. Poor/inadequate sleep can lead to: cardiovascular, respiratory, metabolic, immune system dysfunction as well as contribute to delirium (Beltrami FG, et al. *J Bras Pneumol.* 2015;41(6):539–546).

Characteristics of sleep in the ICU
Fragmented
Short naps distributed over 24 hrs
Average uninterrupted sleep in ICU is 50 min to 2 hrs
Increased arousals & awakening
BP measurements, temp, suctioning, mouth care, back care, turning, baths
Factors associated with sleep disturbances in ICU pt
Environment—lights, noise, alarms
Clinical care
Mechanical ventilation
Sleep vs. sedation
Staff conversations are disruptive noises
Pain
Noise reduction strategies
Closing doors
Earplugs
Plan uninterrupted blocks of time with dimmed lights & decreased sound
Relaxation music
Increase staff awareness of noise, conversations in close proximity to pt
Maximize environmental opportunities to decrease noise
Adjust lighting if possible
Natural sleep vs. sedation: assessment
Sedation does not equate with quality sleep
Natural sleep
Spontaneous
Reversible with external stimuli
Circadian
Interventions for sleep

Back massage can improve quality & length of sleep

Clustering/timing clinical care activities to provide blocks of uninterrupted sleep

Collaboration with all providers to cluster care (x-rays, medications, procedures)

Mechanical ventilator sleep promotion strategies

Promote ventilator synchrony—rest from weaning

Comfort—pain/anxiety relief & thirst relief

Promote feeling of safety

Wound Care and Pressure Ulcers (Figure 16-1)

ICU pt are often immobilized & on bedrest due to hemodynamic instability, putting them at great risk for skin breakdown & delayed wound healing

Causes of pressure ulcers:

Pressure: perpendicular force results in compression of tissues between a bony prominence & an outside surface

Capillary pressure >32 mm will cause occlusion

Sustained disruption of blood flow → ischemia, hypoxia, tissue acidosis, edema, & eventually necrosis

Moisture: excess moisture directly affects the friction coefficient of skin: causing maceration

Immobility: oxygen deprivation to the affected area

Poor nutrition: wasting & excessive loss of lean body mass, dehydration

Vulnerable pressure points in the bedbound body:

Most common pressure points—sacrum and heels

Any bony prominence that experiences pressure: occiput, ears, scapula, elbows, spine, coccyx, iliac crest, lateral & medial knees, anywhere the leg touches the bed

"PUs commonly occur at bony prominences such as the sacrum or heels, but recent research shows PUs also occur in mucous membranes & skin lying over soft tissue. Because of external pressure on the tissue on which they are positioned, medical devices such as nasal cannulas, ETTs, & continuous positive airway pressure (CPAP) masks cause tissue damage, resulting in medical device–related pressure ulcers (MDR PUs). (Hanonu S, Karadag A. *Ostomy Wound Management*. 2016;62(2):12–22.)

PREVENTION IS BEST PRACTICE. Prevention strategies:

Assess skin on admission & daily using the Braden (or facility approved skin assessment/pressure ulcer risk) scale. Check skin over all bony prominences.

Daily skin care:

Mild cleansing agent for bathing; avoid hot water & *rubbing. Don't rub the red.* Apply barrier lotion after bathing

Bowel & bladder program

Uncontrolled incontinence: cleanse, topical barrier

Use nonalcohol based moisturizers for dry skin

Manage incontinence:

Use absorbent cloth incontinence pads

Urine collection device

Fecal diversion device

Scheduled toileting: offer bedpan/urinal before each turn

Avoid diapers

Manage nutrition

Nutrition screen on admission

Consult dietitian

Offer supplements, fluids

Assist pt with food choices

Consider calorie count

Admission & daily wts/BMI

Manage friction & shear

Repositioning:

Ceiling lift (ensure there are no folds in the sling if it is left under the pt)

Trapeze

Protect elbows/heels, areas exposed to friction with: transparent film dressings (Tegaderm®), skin protective barrier film, or protective dressings such as hydrocolloids (extra-thin Duoderm®)

Offload at-risk heels with pressure off-loading device (pressure-relieving heel protectors), vertically placed pillow with heels off mattress

Mobilize pt; consider PT consult

Reposition all tubes, lines & drains to eliminate pressure on the skin. Every 2 hrs or more frequently if possible.

Make sure devices are not positioned underneath immobile pt.

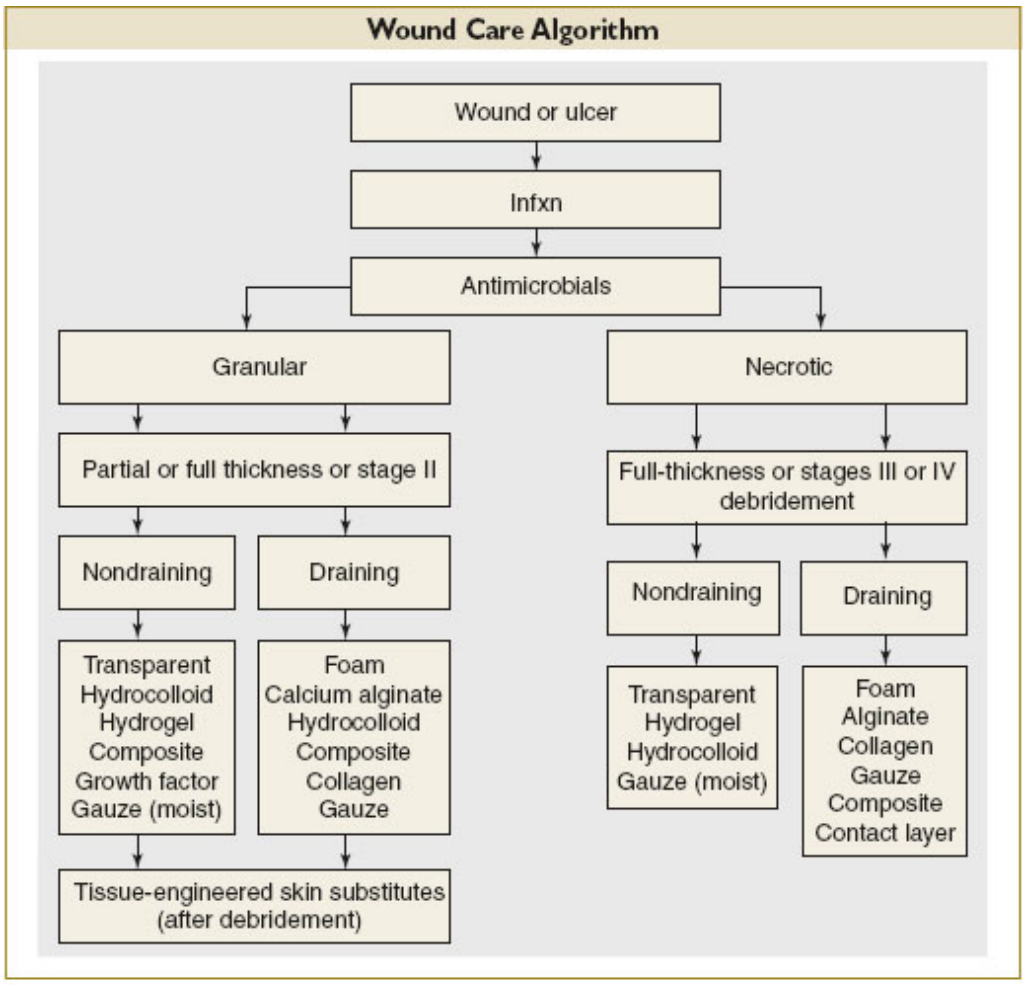
Cushion & protect skin under device when possible.

Figure 16-1. The Braden Scale for Predicting Pressure Sore Risk

BRADEN SCALE FOR PREDICTING PRESSURE SORE RISK

Patient's Name _____ Evaluator's Name _____ Date of Assessment

SENSORY PERCEPTION ability to respond meaningfully to pressure-related discomfort	**1. Completely Limited** Unresponsive (does not moan, flinch, or grasp) to painful stimuli, due to diminished level of consciousness or sedation. OR limited ability to feel pain over most of body	**2. Very Limited** Responds only to painful stimuli, cannot communicate discomfort except by moaning or restlessness OR has a sensory impairment which limits the ability to feel pain or discomfort over 1/2 of body.	**3. Slightly Limited** Responds to verbal commands, but cannot always communicate discomfort or the need to be turned. OR has some sensory impairment which limits ability to feel pain or discomfort in 1 or 2 extremities.	**4. No Impairment** Responds to verbal commands. Has no sensory deficit which would limit ability to feel or voice pain or discomfort.				
MOISTURE degree to which skin is exposed to moisture	**1. Constantly Moist** Skin is kept moist almost constantly by perspiration, urine, etc. Dampness is detected every time pt is moved or turned.	**2. Very Moist** Skin is often, but not always moist. Linen must be changed at least once a shift.	**3. Occasionally Moist:** Skin is occasionally moist, requiring an extra linen change approx. once a day	**4. Rarely Moist** Skin is usually dry, linen only requires changing at routine intervals.				
ACTIVITY degree of physical activity	**1. Bedfast** Confined to bed.	**2. Chairfast** Ability to walk severely limited or nonexistent. Cannot bear own wt and/or must be assisted into chair or wheelchair.	**3. Walks Occasionally** Walks occasionally during day, but for very short distances, with or without assistance. Spends majority of each shift in bed or chair	**4. Walks Frequently** Walks outside room at least twice a day & inside room at least once every two hours during waking hours				
MOBILITY ability to change & control body position	**1. Completely Immobile** Does not make even slight changes in body or extremity position without assistance	**2. Very Limited** Makes occasional slight changes in body or extremity position but unable to make frequent of significant changes independently.	**3. Slightly Limited** Makes frequent though slight changes in body or extremity position independently	**4. No Limitation** Makes major & frequent changes in position without assistance.				
NUTRITION usual food intake pattern	**1. Very Poor** Never eats complete meal. Rarely eats more than 1/2 or any food offered. Eats 2 servings or less of protein (meat or dairy products) per day. Takes fluids poorly. Does not take a liquid dietary supplement OR in NPO and/or maintained on clear liquids or IV's for more than 5 days.	**2. Probably Inadequate** Rarely eats a complete meal & generally eats only about 1/2 of any food offered. Protein intake includes only 3 servings of meat or dairy products per day. Occasionally will take a dietary supplement. OR receives less than optimum amount of liquid diet or tube feeding	**3. Adequate** Eats over half of most meals. Eats a total of 4 servings of protein (meat, dairy products per day. Occasionally will refuse a meal, but will usually take a supplement when offered OR is on a tube feeding or TPN regimen which probably meets most of nutritional needs	**4. Excellent** Eats most of every meal. Never refuses a meal. Usually eats a total of 4 or more servings of meat & dairy products. Occasionally eats between meals. Does not require supplementation.				
FRICTION & SHEAR	**1. Problem** Requires moderate to maximum assistance in moving. Complete lifting without sliding against sheets is impossible. Frequently slides down in bed or chair, requiring frequent repositioning with maximum assistance. Spasticity, contractures or agitation leads to almost constant friction	**2. Potential Problem** Moves feebly or requires minimum assistance. During a move skin probably slides to some extent against sheets, chair, restraints or other devices. Maintains relatively good position in chair or bed most of the time but occasionally slides down.	**3. No Apparent Problem** Moves in bed & in chair independently & has sufficient muscle strength to lift up completely during move. Maintains good position in bed or chair.					
				Total Score				



(www.nursing2008.com)

Moist wound therapy dressings
Nutrition
Control of infxn

Transitioning to Intermediate Care and the Transfer Process (Figure 16-2)

Evaluate pt stability:

Clarify that all IV continuous infusions are either:

a. not needed & discontinued or

b. infusing within a rate/dose range appropriate for intermediate (step-down) phase of care.

Remove all invasive monitoring catheters that are not clinically indicated; ex. Pulmonary Artery Catheter, Arterial Line or Venous Sheath). Document site assessment.

Pt bathed, dressings changed, drainage bags emptied prior to transfer

Ensure that all labs are done, results recorded & abnormal results treated & communicated to receiving nurse

Transfer note either on clinical pathway or nursing progress/transfer note completed

Update all documentation (electronic and/or paper), all appropriate orders are taken off prior to transfer.

Call report, gather pt belongings & all appropriate equipment (respiratory equipment, pneumatic boots, IV pumps, medication…) to send with pt

If pt requires telemetry to travel it is strongly recommended that the nurse accompany pt to intermediate floor

Figure 16-2. Sample Patient Report (Hand-off) Sheet

Appendix I: Example Patient Report (Hand-Off) Sheet

Room#:	Age:	PatientName:
DOA:	DOB:	Precautions: Code:

DX

NEURO:
Neuro Checks q__hr Muscle Strength:
GCS: Posturing:
Pupils: ICP:
LOC: Responsiveness?

PMH/PSH:

ALLERGIES:

CARDIAC?
Rhythm:
Rate:
BP:
CVP:
PP/CSM:

TESTS/PROCEDURES:

Time:	Test/Procedure

PULMONARY:
O_2 Sat:
RR:
Labored?
Airway:
ET tube:
Wean??

VENTILATOR:
Mode:
Rate:
FiO_2:
V_T: V_M:
PS:
Peep:

Pain:
PCA/E:
Settings:

GI:
Ostomy:
Stoma:
LBM:

Diet:
TPN/Tube Feeds:
Ambulation:

MEDICATIONS:

Name	Dosage

GU:
Color/Amt:

LAB VALUES:

Magnesium:
Ionized Ca:
Calcium:
Lactate:
Albumin:
Bilirubin:
Phosphorus:

Cardiac Markers Set#___
CK:
CKMB:
Troponin:

Blood Gases

pH:	pH:
pCO_2:	pCO_2:
pO_2:	pO_2:

Coagulation
INR:
PT:
PTT:

SKIN:
Color:
Temp:
Edema:

IV Access:
IVF:
A-line:
PA-line:

JP Drain(s)	Chest Tube(s)	Drain(s)
Output:	Output:	Type:
Location:	Air leak:	Output:

Courtesy of Erica Lopes Cabral RN, BSN

Guide for Head-to-Toe Nursing Assessment

Head

LOC, orientation, memory, language, emotional state, general appearance
Pupils—size, shape, reaction, eye movements
Hearing
Vision
Extremity strength & sensation
ROM
Gait (if applicable)
LEVEL OF SEDATION
Pain/character/location/intensity
Oral assessment—dentures? thrush?

Heart

Point of maximal intensity (PMI)—(L. midclavicular line at the 5th ICS)
Rate/rhythm—document strip/intervals, check alarm limits
12-lead ECG if needed, check all intervals
Heart sounds
Edema
Capillary refill/clubbing
Peripheral pulses
Extremity temp
BP (on admission both arms if indicated)
CVP, PA pressure, PCWP, CO/CI (if applicable)

Lungs

Evaluate airway patency

Evidence of inadequate airway—stridor, noisy respirations, supraventricular & intercostals retractions, flaring of nares, labored breathing with use of accessory muscles

RR/depth/pattern

Auscultate breath sounds

Absent breath sounds, diminished breath sounds, crackles (rales), rhonchi, wheezes, pleural friction rub

Cough, character of sputum

SpO_2

Assess arterial blood gases (ABG's)

Oxygen delivery

Nasal prongs, face mask, tracheostomy tube, ETT

Consider end-tidal carbon dioxide ($ETCO_2$) measurement

Assess ETT

Security of tube

Size

Position of tube (centimeter mark at lip line or nares)

No audible cuff leak

Tracheostomy—size & confirm that there is a spare 1 of same size & manufacturer in room

Suction set up

Chest tubes—suction or water seal, mark drainage, check for air leak, have 2 chest tube clamps avail. for each chest tube

Palpate the neck & anterior chest for subcutaneous emphysema

CXR results

Ventilator Assessment

Equipment check: manual resuscitation bag-valve-mask bag, oxygen reservoir, tubing, & flow meter are at bedside (PEEP valve if >5 cm PEEP in use)

Assess the ventilator tubing as follows:

Trace the tubing from the ETT to the ventilator, making sure all connections are secure

(No longer done)

Make sure the inspired/humidified air temp is 31°–37°C

Identify the mode of ventilation

Check & confirm the ventilator settings

Check the set PEEP level

Note the peak inspiratory pressure (commonly referred to as PIPs)

Note the minute ventilation

Note expired tidal volume (VTe)

Check essential ventilator alarms to ensure limits are set appropriately (collaborate with respiratory therapist)

Abdomen

Pain/tenderness/distension

N/V

Nasogastric tube (NGT) check placement

Inject 10 ml of air with a 60-ml syringe into the NGT while listening over the left upper quadrant for air entering the GI tract

Check placement of NGT every 4 hrs by checking for residual using a 60 ml-syringe aspirate stomach contents (replace)

NOTE: insufflation of air alone is not sufficient to verify tube position. Aspirated stomach contents indicate that the NGT is in the stomach. The traditional bedside techniques of gastric aspiration & insufflation test often give false reassurance that the NGT is properly positioned. Capnometry method has the highest specificity & sensitivity (not widely used as yet). Nevertheless, the other techniques still aimed at early detection of anticipated adverse events rather than prevention. Al Saif N, et al. *Case Rep Crit Care*. 2015;2015:690–742.

NGT drainage—quantity/character/color/guaiac/pH

Jejunostomy tube (JT)—patent

Feeding tolerance/nutritional status

Bowel sounds 4 quadrants

Bowel movements—character of stool, guaiac

Rectal bag

GU

Foley catheter:

Indwelling urinary catheters (IUC) are the primary cause of CAUTIs!!

Sterile technique on insertion

Strict hand washing & gloves when manipulating IUC

IUC-secure device in place

IUC tubing free of kinks & tension on balloon.

Collection bag below bladder & off the floor

Empty collection bag when half full

Urine quality, color

BUN/Creatinine

Hourly output/I & O/wt daily

Skin

Color, texture, turgor, temp
Rashes, abrasions, wounds, burns, bruises, inflammations
Status of bony prominences
Incisions
Decubitus
Wounds/drains/dressings
Cyanosis/mottling
Evaluate need for specialty mattress & splints

IV Access

Assess IV sites
Identify your infusions & trace tubing from pt back to IV pump
Identify medication/dosage/rate
IV bags & syringes (on syringe pumps) have correct medication labels, check to see how much is left to infuse (you may need to mix another bag)
Compatibility of drugs infusing in same line
IDENTIFY YOUR IV PUSH LINE

INTER- AND INTRAHOSPITAL TRANSPORT OF CRITICALLY ILL PATIENTS

MICHAEL G. FITZSIMONS, MD • AGNIESZKA LESICKA, MD

Definitions

Interhospital transport (secondary transport) involves the transport of a pt between 2 separate hospitals.

Intrahospital transport involves the movement of a pt throughout the same hospital for diagnostic care & interventional procedures that cannot be performed at the bedside.

The reasons for inter- & intrahospital transport vary between hospitals, healthcare systems, & countries (Table 17-1).

Table 17-1. Reasons for Patient Transport

Interhospital	Intrahospital
Diagnostic technology not avail. Procedural & interventional procedure not avail. Higher expertise Pt/family request Regionalization of procedures Advanced pt precautions (Ebola)	Imaging Surgery Interventional procedures Higher level care (intensive care)

Risks

The risks associated with pt transport should always be weighed against the potential benefit to that pt. There are no absolute contraindications to pt transport other than refusal by a competent pt or proxy. Conditions such as hemodynamic instability & respiratory failure may make transport undesirable but if movement to a new destination offers the potential for improvement, benefit exists.

Assessment and Management

Assessment & management of pt during transport focuses primarily on the "ABCDEs."

Airway with Cervical Spine Control

Pt transport is associated with an increased risk of displacement of an artificial airway. The current status of the airway should be assessed. Physical examination includes location & security of any airway. CXR can confirm ETT position. Placement of an ETT during transport can be successful by transport personnel. However, it may be prudent to secure the airway prior to transport in pt that may present significant challenges for airway management, such as those with worsening hypoxemia, cervical spine injury, laryngotracheal trauma, facial injury, burns, & neurologic compromise. Airway management is safer in a controlled environment with back-up help & airway devices (video laryngoscope, bronchoscopy) than in areas with limited equipment & constrained spaces.

Breathing with Effective Oxygenation and Ventilation

Respiratory compromise associated with transport may include hypoxemia, hypercarbia with respiratory acidosis, & hyperventilation with alkalosis. Hypoxemia during transport is more likely when pt require a higher FiO_2 or PEEP prior to transport. Assessment includes RR, level of FiO_2, & recent CXR. The trend in respiratory status may be more important than the current status.

Circulation and Hemodynamic Stability

No definitive study has demonstrated which pt will demonstrate hemodynamic instability during transport but it is logic that pre-transport instability portends instability during movement. HTN or hypotension occurs in at least half of all transport (Evans A, et al. *Am J Crit Care.* 1995;4:106–111). Arrhythmias are commonly seen during transport following MI. Assessment includes current status, trends, pharmacologic intervention, & appropriateness of current level of physiologic monitoring. Invasive monitoring may be less susceptible to interference during ground or air transport between hospitals.

Debility (Neurologic Status)

Factors considered within debility include neurologic status along with sedation & pain control. Hypercarbia, hypocarbia, & hypoxemia may worsen neurologic outcome associated with intracranial bleed, traumatic brain injury, & increased ICP. Excessive spiral movement may exacerbate cervical spine injury. Excessive sedation may impair ability to provide ongoing pt assessment while lack of sedation can result in release of stress hormones.

Exposure, Environment, and Equipment

The changes in pt environment during transport are associated with certain risks. Removal from warm rooms, cool fluids, & administration of sedatives may result in hypothermia, shivering, increased myocardial oxygen consumption, pt discomfort, & agitation. Relative hyperthermia may worsen head injury. Those at highest risk for temp alteration include the elderly, children, as well as victims of burn & spinal injury.

Displacement of monitoring & therapeutic devices is a real risk with pt movement. Tubes, lines, & drains may be pulled during movement between stretchers & beds, may be caught on equipment left in narrowed hallways, or displaced by confused/agitated pt.

Lifting of pt by healthcare providers is associated with back injury & a high percentage of nurses leave the profession due to such problems (Stubbs DA, et al. *Int J Nurs Stud.* 1986;23:325–336).

No national standards exist regarding the appropriate equipment or level of monitoring that is required for pt transport, but guidelines do exist. Critically ill pt, at a minimum, should be monitored with continuous electrocardiography (ECG), invasive or noninvasive BP, & pulse oximetry. Monitors utilized for transport should have screens that are easy to read, rugged enough to withstand sudden movement & collisions, audible & visible alarms, & long battery life. Infusion devices should have “smart pump” technology including preprogrammed drug libraries, free-flow prevention, & occlusion alerts. Personnel must be familiar with the technology. Ideally devices are compatible between locations & across systems.

Communication, Safety, and Quality

Communication of complete & accurate information is critical to safe pt transfer. Written consent from the pt or proxy is important & should always

be obtained if possible. Physician-to-physician as well as nurse-to-nurse verbal transfer of critical information is imperative. A contingency plan for management of potential complications en route is necessary. Copies of all medical records, studies, & consultations should accompany a pt during transport when pt are moved between hospitals, as electronic medical records are not readily accessible.

The use of well-designed checklists to assure that complete assessment has occurred, information has been communicated, equipment is avail., functioning, & durable, & contingency plans are established reduces unexpected events during transport (Choi HK, et al. *Am J Emerg Med.* 2012;30:1433–1440; Nakayama DK, et al. *J Pediatr Surg.* 2012;47:112–118). Structured hand-off such as the "I-PASS" model results in a reduction in transport related complications (Bérubé M, et al. *Intensive Crit Care Nurs.* 2013;29:9–19).

Pt transfer ideally falls under systematized processes that are subject to continual process improvement & critical analysis. The largest & best study of transport is the Australian Incident Monitoring Study in Intensive Care (Beckmann U, et al. *Intensive Care Med.* 2004;30:1579–1585). Almost one-third of transport was associated with serious events, equally divided between human & system issues. Recommendations for improved transport care included dedicated teams, checklists, improved event documentation, & compliance with standards.

MECHANICAL VENTILATION AND PULMONARY ISSUES

REBECCA M. BARON, MD

Gas Exchange

Oxygenation:

1. *Is there an A-a (Alveolar-arterial O_2) gradient?*

- Alveolar gas equation (most accurately determined on room air or 100% FiO_2 on ventilator; PAO_2 is alveolar partial pressure of O_2; PaO_2 is arterial partial pressure of O_2; P_{ATM} is atmospheric pressure; PH_2O is saturated vapor pressure of water; $PaCO_2$ is partial pressure of CO_2; FiO_2 is fraction of inspired gas that is O_2):

$$PAO_2 = (FiO_2 \times (P_{ATM} - PH_2O)) - \frac{PaCO_2}{RQ}$$

- Where P_{ATM} = 760 mm Hg, PH_2O = 47 mm Hg, RQ (respiratory quotient) = 0.8, then:

$$PAO_2 = (FiO_2 \times 713) - \frac{PaCO_2}{0.8}$$

- **On room air (FiO_2 = 0.21):**

$$\mathbf{PAO_2 = 150 - \frac{PaCO_2}{0.8}}$$

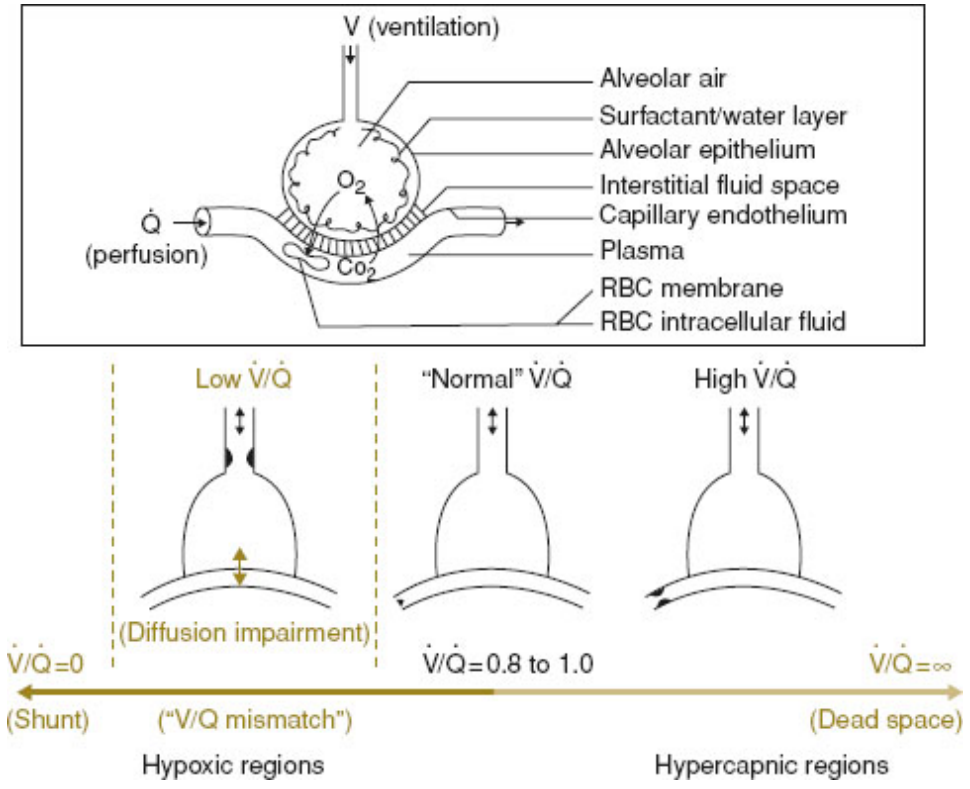
A-a gradient: $PAO_2 - PaO_2$

- Normal gradient: $4 + \frac{age}{4}$ (*e.g.,* about 9 for a 20-yr old)
- If an A-a gradient is NOT present, then *alveolar hypoventilation* must be considered as a mechanism of hypoxemia.

2. *If there is an A-a gradient, is the hypoxemia responsive to 100% FiO_2?*

- If there is an A-a gradient, then *V/Q mismatch, shunt, or diffusion impairment* must be considered (though diffusion impairment is rare unless very severe lung dz is present); if the hypoxemia is NOT responsive to 100% FiO_2, then is consistent with shunt; if is responsive to 100% FiO_2, then likely is V/Q mismatch—see Figure 18-1.
- V/Q mismatch: regions of low V/Q, usually caused by alveolar filling (blood, pus, or water), & hypoxemia usually O_2-responsive
- Shunt: regions where V/Q = 0, can be intrapulmonary, e.g., from atelectasis, or extrapulmonary; not O_2-responsive in that PaO_2 doesn't significantly increase or at least rise above 100 mm Hg with 100% FiO_2 administration
- Diffusion impairment: rare cause of hypoxemia but possible with severe barrier to gas exchange from interstitial lung dz or pulmonary HTN

Figure 18-1. Overview of Ventilation–Perfusion Relationship



Ventilation:

Determinants of $PaCO_2$

$$PaCO_2 = \frac{k\dot{V}CO_2}{V_A} = \frac{k\dot{V}CO_2}{V_E \times (1 - V_D/V_T)}$$

CO_2 Production

Minute Ventilation (V_E) = RR × TV (requires drive to breathe and the ability to generate adequate V_E)

Dead Space Fraction = V_D/V_T

k, constant; V_A, alveolar ventilation; V_E, minute ventilation; RR, respiratory rate; TV & V_T, tidal volume; V_D, dead space.

Thus, $PaCO_2$ determined by balance of CO_2 production (e.g., increased work of breathing [see below], increased metabolism, fever, *etc.*) & elimination of CO_2 (ability to generate adequate minute ventilation). Efficiency of CO_2 elimination determined in part by physiologic dead space (e.g., proportion of alveoli ventilated but not perfused) & can be measured using end-tidal CO_2 device hooked up to exhalation port of ventilator that measures P_ECO_2 (exhaled CO_2), where V_D/V_T is dead space fraction & $PaCO_2$ is arterial CO_2:

$$V_D/V_T = \frac{PaCO_2 - P_ECO_2}{PaCO_2}$$

Fatigue: Imbalance of supplies (O_2, nutrition, energy extraction) & demand (work of breathing, muscular strength, & efficiency)

Work of breathing: proportional to mean pressure per breath required of inspiratory muscles (P_i) & minute ventilation; increased with elastic (e.g., edema) or resistive load (e.g., asthma)

Efficiency: ratio of external work performed to energy consumed; e.g., poor efficiency in emphysema perhaps due to flattened diaphragm & disadvantageous force/length relationship

General:

Indications for intubation (and parameters to consider when weaning)

Refractory hypoxemia

Ventilation impairment (and failed or noncandidate for noninvasive ventilation)

Mental status/airway protection

Secretion management (often in conjunction with issues above)

"Other": e.g., metabolic acidosis, airway protection for procedure, etc.

Initial settings:

Choose a "standard" mode you're comfortable with

All modes require understanding and monitoring of same principles

Generally, AC mode safest with full support, though pt will usually need sedation & "acclimation" to be in synchrony

Unless specific reason, try to set tidal volumes 6–8 cc/kg (see Chapter 19 on ARDS management) with RR generally 10–12 & guided by pH/min ventilation

Initial FiO_2 settings usually 100%, but try to wean down as quickly as possible, as long as maintaining adequate oxygenation

Often will choose "physiologic" PEEP (positive end expiratory pressure) of 5 cm H_2O, unless other factors (see Chapter 19 on ARDS)

Flow rates on standard volume-cycle modes usually set at 60 l/min (1 l/sec) but can adjust (see COPD below); correlative setting on PCV is setting inspiratory time (I-time); in aggregate, flow & I-time settings determine inspiratory:expiratory (I:E) ratios.

Modes of Mechanical Ventilation			
Ventilator Mode ***(of note, names of modes based upon Puritan-Bennett ventilator—other ventilators have similar modes with different names)***	**Parameter(s) set ("Controlled" Parameters)**	**Parameter(s) Monitored ("Variable" Parameters)**	**Comments**
"Standard Modes"			
Assist-control (AC)	Tidal volume (TV), Respiratory rate (RR), flow	Peak & plateau pressure	Every breath taken by patient (pt) (including spontaneous) are delivered at set TV
Synchronized intermittent mandatory ventilation (SIMV)	TV, RR, flow	Peak & plateau pressure	Spontaneous breaths aren't supported
Pressure control ventilation (PCV)	Driving pressure, inspiratory time, RR	TV (flow can be variable within set parameters)	PCV can be set in "AC" mode (each breath supported by set driving pressure) or "SIMV" mode
Pressure support ventilation (PSV)	Driving pressure (also set % rise which determines how fast the preset pressure is delivered & E_{sens}, often at 25% of peak flow, which determines onset of exhalation)	TV, RR, flow	No backup rate (except apnea mode from ventilator), so pt must be able to maintain adequate minute ventilation
"Newer Modes" Use with experienced personnel avail. to assist & guide			
Volume control plus (VC+) (termed pressure regulated volume control [PRVC], on servo ventilator)	Targeted TV, inspiratory time, RR	TV, RR, pressure delivered & flows variable; monitor peak pressure; estimated driving pressure needed to deliver targeted TV: PIP – PEEP	Volume-targeted pressure ventilation in PCV mode: Set targeted TV, & machine makes determination from 3 delivered breaths as to required pressure to deliver volume; thus, parameters of ventilation can change
Volume support plus (VS+)	Targeted TV, %rise, E_{sens}	TV, RR, peak pressure (as above for VC+)	As above, for VC+, except delivered breaths using PSV mode
Bilevel ventilation	High & low pressure levels ($PEEP_{high}$ & $PEEP_{low}$); cycling synchronized with pt breathing with time set at higher PEEP (T_{high}); PSV set for spontaneous breaths; Airway pressure release ventilation (APRV) represents Bilevel with very short periods of time "released" from $PEEP_{high}$ (or long T_{high} settings)	Minute ventilation, peak pressure; driving pressure on spontaneous breaths is determined by PSV set pressure minus difference between $PEEP_{high}$ & $PEEP_{low}$ (e.g., if PSV is set at 20 cm H_2O & $PEEP_{high}$ is 20 cm H_2O, $PEEP_{low}$ is 5 cm H_2O, then driving pressure is PSV – [$PEEP_{high}$ – $PEEP_{low}$] or 5 cm H_2O)	May have higher risk of barotrauma; not clearly beneficial above other modes; similar to PCV mode if pt not breathing spontaneously; oxygenation adjusted with $PEEP_{low}$ & ventilation via $PEEP_{high-low}$ gradient or via increased PSV on spontaneous breaths

RR, respiratory rate; PEEP, positive end expiratory pressure; P, pressure; T, time.

Monitoring pt on the ventilator (measure on volume-cycled ventilation with square wave & constant flow [ideally 60 l/min or 1 l/sec to facilitate calculations]; measurements may be more accurate with pt sedated):

Measurement of peak inspiratory pressure, plateau pressure (end inspiratory hold to derive estimate of alveolar pressure); in pt heavily sedated or paralyzed, can perform an end expiratory hold to measure intrinsic PEEP (auto-PEEP), which can indicate gas trapping

Calculation of resistance & compliance can assist in monitoring & managing ongoing issues on the ventilator (see Fig. 18-2):

"High PIPs" or peak inspiratory pressure can arise from problems with elevated *resistance* (increased peak pressure relative to plateau pressure) and/or reduced *compliance* (increased plateau pressure for given TV)

Examples of conditions causing increased resistance (airflow obstruction):

Bronchoconstriction

Mucus plugging

Ventilator tubing or ET tube obstruction

Examples of conditions causing reduced compliance (lung stiffness):

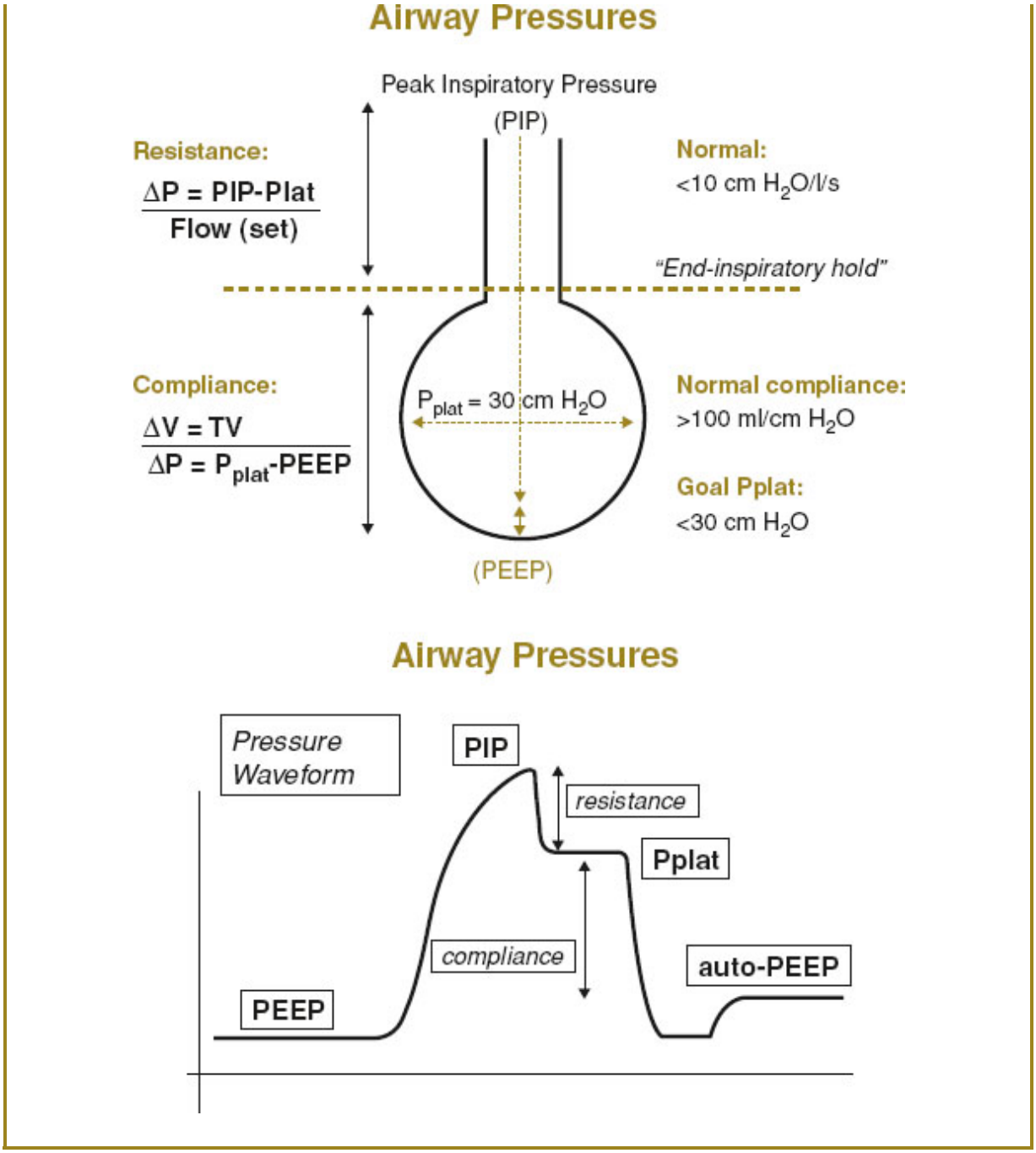
Tension pneumothorax

CHF

Pulmonary hemorrhage

Pneumonia/ARDS

Figure 18-2. Description and Measurement of Airway Pressures in Patients on Mechanical Ventilators



P, pressure; PIP, peak inspiratory pressure; P_{plat}, plateau pressure (in this example, P_{plat} is 30 cm H_2O); V, volume; TV, tidal volume; PEEP, positive end expiratory pressure.

Acute Failure to Liberate from Ventilator Support

Causes

Incomplete resolution of illness precipitating mechanical ventilation
Development of new condition limiting independent ventilation
Neurologic—prolonged sedation, critical illness polyneuropathy, inadequate pain control
Muscular—atrophy, critical illness myopathy, diaphragmatic paralysis
CV—decreased oxygen delivery, LV failure, RV dysfunction or failure
Pulmonary—flail chest, noncompliant chest wall, pleural effusions, airway obstruction, intrinsic PEEP
Abdomen—tight surgical dressings, tense ascites, intra-abdominal HTN
Nutrition—protein calorie malnutrition
Electrolytes—hypophosphatemia, hypomagnesemia, hypokalemia, hypoCa+
Infectious dz—VAP (ventilator-associated pneumonia), underlying sepsis, resistant microorganisms

Investigations after careful physical examination might include:
Labs—electrolytes, prealbumin, CRP, ABG, blood/sputum/stool/urine cx
Radiographic imaging, echocardiogram
Respiratory mechanics, check bladder pressure

Respiratory Failure and Ventilator Management (Roussos C, et al. *Eur Respir J Suppl*. 2003;47:3s–14s)

Respiratory failure can be "Lung"/gas exchange/hypoxemic vs. "Pump"/ventilatory/hypercapneic failure

Hypoxemic failure (most commonly V/Q mismatch ± shunt regions):

Alveolar filling processes (e.g., blood, pus, or water)

e.g., pneumonia, CHF, alveolar hemorrhage

Restrictive lung dz (can also cause hypercapnia)

Parenchymal: e.g., pulmonary fibrosis, drug-induced pneumonitis
Chest wall: e.g., postthermal injury eschar, morbid obesity, abd compartment syndrome

Hypercapneic failure

“Won’t Breathe”: CNS derangement, sedation

“Can’t Breathe”: COPD, status asthmaticus, neuromuscular weakness

Excessive physiologic *Dead Space;* significant concern for inability to wean with 60% or higher dead space fraction

Ventilator Management

Specific scenarios (while treating the underlying cause of respiratory failure):

Ventilator Management for Hypoxemic Respiratory Failure

Alveolar filling processes: see Chapter 19 on ARDS

Avoid overdistention & aim tidal volumes 6 cc/kg & try to keep plateau pressure <30 cm H_2O

PEEP can redistribute fluid from alveolar to interstitial spaces & can, therefore, be beneficial in CHF, alveolar hemorrhage

Restrictive lung dz:

Relieve restriction if possible (e.g., escharotomy, abd surgery, etc.)

Avoid overdistention esp. in interstitial lung dz; higher PEEP application in stiff lungs can worsen physiologic dead-space via compressing adjacent alveolar capillaries & creating areas of "high" V & "low" Q (see V/Q figure above)

Ventilator Management for Hypercapneic Respiratory Failure

"Won't Breathe"

Careful not to over-ventilate

Tube often in place for airway protection until underlying cause can be reversed

"Can't Breathe" (e.g., airflow obstruction or neuromuscular weakness)

COPD: May have higher baseline $PaCO_2$ & should aim not to ventilate below this if possible to facilitate future weaning

If treating a nonintubated pt, DO NOT deprive pt of adequate oxygenation because of fear of hypercapnia. Can limit O_2 supplementation to achieve saturation of 90–92%. If hypercapnia develops, may need to assist ventilation by noninvasive ventilation (NIV) or intubation

In intubated pt: concern for exacerbation of hyperinflation & auto-PEEP

Watch for incomplete exhalation & development of auto-PEEP: can consider decreasing RR, TV, and/or increasing flow rates to increase exhalation time

Watch BPs closely, as some pt with COPD may have developed pulmonary HTN and/or cor pulmonale & therefore be more likely to be hypotensive with intubation, positive pressure in general from the ventilator, & application of PEEP

Consider abx for COPD flares in sick pt

Consider earlier extubation to NIV

Asthma: might need to tolerate high peak pressure in order to deliver sufficiently high flows in light of airway resistance & need for adequate exhalation time to avoid air trapping

Medications to consider: steroids, β-agonists

Also can consider Heliox (Helium–oxygen mixture; lower-density gas converts turbulent to laminar flow predominantly in larger airways but might also have benefit in smaller airways in asthma and/or through improving albuterol deposition in smaller airways, though debated)

Neuromuscular weakness—look for reversible causes; provide adequate nutrition; consider early tracheostomy if underlying process isn't quickly reversible

Sedation, Analgesia, and Neuromuscular Blockade for Mechanically Ventilated Patients (see Chapter 5)

Community Acquired Pneumonia and Atypical Pneumonias (Mandell LA, et al. *Clin Infect Dis*. 2007;44:S27–72; Musher DM, et al. *N Engl J Med*. 2014; 371:169–1628)

Site of care: A number of possible scoring systems have been evaluated to determine which pt require ICU admission, & more recent data has suggested that the Pneumonia Severity Index (Fine MJ, et al. *N Engl J Med*. 1997;336:243–250) may be the most sensitive index (Abers MS, et al. *QJM*. 2014;107:595–596).

Diagnostic testing & treatment: dx is established with suggestive clinical features (e.g., cough, fever, sputum, pleuritic chest pain) & supported by chest radiography demonstrating an infiltrate (although some pt, such as the elderly, may not display traditional signs/symptoms of pneumonia).

For pt requiring ICU admission, the following testing is recommended, **although testing should not delay early broad-spectrum abx administration, as each hour of delay in appropriate abx has been associated with increased mortality:**

Blood cx

Gram stain & cx of sputum (if intubated, ETT aspirate & consider bronchoscopy depending upon clinical situation)

Legionella urinary antigen test

Pneumococcal urinary antigen test (highly sensitive)

Can consider PCR assays for *Mycoplasma pneumoniae, Chlamydia pneumonia,* respiratory viruses

If pleural effusion present, consider thoracentesis & pleural fluid cx

During outbreaks, isolation & rapid testing is recommended in particular for influenza

For other subpopulations of pt, additional diagnostic & therapeutic approaches should be considered (see table)

Types of Pneumonia and Pathogens			
Host	**Likely Pathogens**	**Additional Testing**	**Empiric Treatment**
"Normal" ICU host within 48 hrs of hospital/ICU admission	"Typical bacterial pathogens": *Streptococcus pneumoniae, Hemophilus influenzae, Moraxella catarrhalis;* "Atypical bacterial pathogens": *C. pneumoniae, M. pneumoniae, Legionella pneumophilia;* Numerous viral pathogens, including influenza	See above; "atypical pathogens" may be difficult to detect & therefore empiric treatment must be considered esp. in absence of detecting another pathogen; of note, no cause for CAP is found for about half of hospitalized pt	β-lactam plus macrolide or fluoroquinolone alone; low threshold for oseltamivir during influenza season—if influenza suspected, low threshold for coverage for MRSA pneumonia superinfection
Hospital/ICU-acquired (>48 hrs of hospitalization); ventilator-associated pneumonia (fever, new infiltrate, increased secretions)	Above pathogens for "Normal host," plus gram-negative bacilli & Methicillin-Resistant *Staphylococcus aureus* (MRSA)	Consideration of bronchoscopy if no pathogen isolated from sputum & not improving	Addition of 3rd generation cephalosporin with antipseudomonal activity & Vancomycin (for MRSA coverage)
Severe COPD, chronic steroid use, chronic or frequent antibiotic use, alcoholism	High risk for pseudomonas & other gram-negative pathogens; pt on chronic steroids at risk for atypical infxns including PCP, Nocardia, semi-invasive aspergillosis	Consider CT chest for additional evaluation for structural lung dz, abscess; sputum for PCP (and serum β-D-glucan & LDH); modified AFB stain, Nocardia cx, fungal stain/cx, serum galactomannan (to look for invasive aspergillus)	Coverage as above for hospital/ICU acquired infxn, plus consideration of other pathogens listed based upon clinical presentation; consideration of anaerobic coverage if aspiration event suspected
Neutropenic host	In addition to hospital-acquired organisms, increased risk for fungal infxns; for viral pathogens (e.g., RSV, adenovirus, parainfluenza)	Rapid viral panel from nasal swab; Sputum for fungal stain & fungal cx; Blood β-D-glucan & galactomannan (for fungus & aspergillus)	For neutropenic fevers, antipseudomonal 3rd generation cephalosporin; consider broader coverage (MRSA coverage & antifungal if persistent fevers)

PCP, *Pneumocystis carinii* pneumonia (also known as *Pneumocystis jirovecii*); LDH, lactate dehydrogenase; AFB, acid-fast bacilli; RSV, respiratory syncytial virus; MRSA, Methicillin-resistant *Staphylococcus aureus*.

Duration of antibiotic treatment:

Abx should be narrowed to cover identified pathogens after ~48 hrs of cx growth

Definitive data is lacking, but in ICU pt with severe pneumonia, an 8-day course is reasonable if clinical response is observed, unless infxn is documented with nonfermenting gram-negative rods (e.g., *Pseudomonas aeruginosa*), for which a 15-day course may be more effective (Chastre J, et al. *JAMA.* 2003;290:2588–2598). Some clinicians will also treat *S. aureus* pneumonia with a more prolonged course.

Nonresponding pneumonia:

As many as 15% of pt with CAP (Community-Acquired Pneumonia) & perhaps larger percentage of pt with impaired immune systems may not respond to initial treatment, & as many as 40% of pt admitted to an ICU with pneumonia may worsen after initial stabilization (e.g., within 72 hrs)

Causes of failure to improve, or worsen:

Wrong abx (e.g., missed pathogen or resistant organism)

Reculture, recheck existing cx data/sensitivities

Consider bronchoscopy/bronchoalveolar lavage

Extension of infxn and/or complicated infxn

Local (e.g., parapneumonic effusion, empyema, lung abscess, development of ARDS; postobstructive)

Distant (e.g., bacteremia, endocarditis, brain abscess)

Consider CT chest, echocardiogram, additional imaging based upon sx (e.g., abd CT)

Wrong dx or missed additional process (e.g., PE, CHF, vasculitis, *etc.*)

Consider echocardiogram, serologies (e.g., ANCA, ANA), lower extremity US to r/o DVT and/or CT angiography if renal function allows & clinical scenario consistent to evaluate for PE

Nosocomial superinfection (e.g., VAP, *Clostridium difficile,* central venous catheter infxn)

Consider changing indwelling catheters, check stool *C. difficile,* RUQ US to r/o acalculous cholecystitis, amylase/lipase in consideration of pancreatitis

Adverse reaction to medication (e.g., drug fever, anaphylaxis)

Consider discontinuing unnecessary antibiotics and/or changing class of abx

Prevention:

Consider vaccination with pneumococcal & influenza vaccines at hospital discharge or in the outpatient setting (as most pt with pneumonia requiring ICU admission will likely be candidates for vaccination)

Smoking cessation resources should be offered to pt who smoke

ACUTE RESPIRATORY DISTRESS SYNDROME

AMEEKA PANNU, MD • DANIEL S. TALMOR, MD, MPH

Introduction

Acute respiratory distress syndrome (ARDS) was 1st described by Ashbaugh et al., & is characterized by severely impaired gas exchange resulting in significant hypoxemia (Ashbaugh DG, et al. *Lancet.* 1967;2:319–323). Prevalence of ARDS is 10.4% in ICU admissions worldwide with mortality as high as 46.1% in those with severe dz (Bellani G, et al. *JAMA.* 2016;315:788–800).

PATHOPHYSIOLOGY

Common predisposing conditions include sepsis, pneumonia, aspiration, pancreatitis, shock & trauma

Direct or pulmonary ARDS results from direct lung injury whereas indirect or extra pulmonary ARDS may develop from other inflammatory dz states

Types of ARDS	
Direct ARDS	**Indirect ARDS**
Pneumonia	Sepsis
Aspiration	Acute pancreatitis
Inhalational injury	Burns
Pulmonary contusion	Severe polytrauma
Fat embolism	Transfusion-related acute lung injury (TRALI)
Amniotic fluid embolism	Cardiopulmonary bypass

There are 3 distinct pathologic stages of ARDS

Exudative: in early ARDS there is increased alveolar capillary permeability with neutrophil extravasation into the alveoli, resulting in diffuse alveolar damage & loss of pulmonary compliance

Fibroproliferative: beginning 1–2 wks after the onset of ARDS, some patients develop a fibroproliferative phase in the lung

Fibrotic: Patients who survive the initial dz have varying levels of residual pulmonary fibrosis (Steinberg KP, et al. *N Engl J Med.* 2006;354(16):1671–1684).

Diagnosis

ALI/ARDS was defined by the 1994 American–European Consensus Conference Criteria (AECC) for ALI & ARDS (Bernard GR, et al. *Am J Respir Crit Care Med.* 1994;149:818–824); the Berlin criteria have since come into use

Gattinoni et al. described that CT scans in ARDS show nonhomogenous lungs with areas of consolidation, ground glass opacities & normal aeration (Gattinoni L, et al. *Am J Respir Crit Care Med.* 2001;164:1701–1711).

The Berlin Definition of ARDS was formulated in 2012 & accounts for the use of PEEP in its diagnostic criteria (ARDS Definition Task Force, et al. *JAMA.* 2012;307:2526–2533).

Characteristics of ARDS	
Timing	Within 1 week of known insult or new/worsening respiratory sx
Chest imaging	Bilateral opacities (on chest x-ray or CT scan)
Origin of edema	Respiratory failure not explained by cardiac failure or fluid overload
Oxygenation: Mild	PaO_2/FiO_2 between 200–300 mm Hg with PEEP or CPAP >5 cm H_2O
Moderate	PaO_2/FiO_2 between 100-200 mm Hg with PEEP or CPAP >5 cm H_2O
Severe	PaO_2/FiO_2 <100 mm Hg with PEEP or CPAP >5 cm H_2O

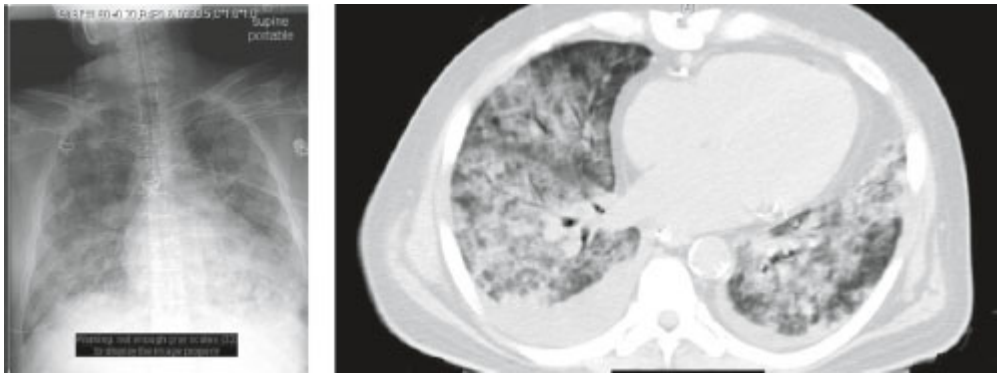
ARDS can coexist with CHF & clinical judgment is needed to differentiate between the 2

A focused echocardiogram in the ICU setting can be helpful in ruling out left atrial HTN as the cause of pulmonary edema

Bronchoscopy may be a useful diagnostic or therapeutic aid esp. if an infectious cause is suspected but should be used cautiously as it may worsen hypoxemia or hypercarbia

IMAGING

Figure 19-1. Chest Radiogram and CT Image of a Lung with ARDS



The chest x-ray shows bilateral patchy infiltrates which can progress to consolidation as dz progresses

The CT scan typically shows bilateral infiltrates, areas of dependent atelectasis, & small pleural effusions with some areas of undamaged lung tissue in the nondependent regions

Gattinoni et al. coined the term “baby lung” for these uninjured areas & postulated that lower tidal volume ventilation would prevent excessive mechanical forces on these areas of undamaged lung (Gattinoni L, Pesenti A. *Intensive Care Med.* 2005;31:776–784).

Treatment

The prevention of ventilator-induced lung injury (VILI) remains the mainstay of therapy

Prevention of Ventilator Induced Lung Injury

The primary goal in lung protective ventilation is to prevent stress of undamaged alveolar units

The 4 potential mechanisms of alveolar damage in pt with ARDS are:

Barotrauma: excessive airway pressure resulting in pneumothorax

Volutrauma: overdistention of alveoli from high tidal volume ventilation

Atelectrauma: shearing force on alveoli from opening during inspiration & collapse on expiration

Biotrauma: the release of proinflammatory cytokines from excessive mechanical forces on the lung

Ventilation Strategy

In 2000, the National Heart, Lung & Blood Institute funded ARDS Network published a landmark study showing improvement in mortality with lung protective ventilation, specifically lower tidal volume ventilation, 6 cc/kg ideal body wt & plateau pressure limits of 30 mm Hg (The Acute Respiratory Distress Syndrome Network. *N Engl J Med.* 2000;342(18):1301–1308).

The ARDSNet data show that low tidal volume ventilation is protective & demonstrated an absolute reduction in mortality of 9%

It remains debated whether pressure-controlled ventilation reduces barotrauma as compared to volume-controlled ventilation; a meta-analysis did not show a mortality benefit in the former vs. the latter (Rittayamai N, et al. *Chest.* 2015;148(2):340–355). In addition, no significant benefit has been shown of using airway pressure release ventilation or high-frequency oscillatory ventilation modes.

Positive End-Expiratory Pressure

Positive end-expiratory pressure (PEEP) helps recruit atelectatic lung tissue & prevents the development of further atelectasis; thereby improves ventilation–perfusion matching

Although increased PEEP decreases hypoxemia it did not appear to improve survival in several trials

Alternative methods of setting PEEP include using the lower inflection point of the pressure–volume curve, the stress index or titrating PEEP to a positive transpulmonary pressure estimated using an esophageal balloon catheter

Permissive Hypercapnia

Mechanical ventilation strategies that minimize tidal volume & plateau pressure can result in alveolar hypoventilation

Increased PaCO2 with resultant respiratory acidosis is accepted among ARDS pts to prioritize minimizing VILI

Positioning

In ARDS pt, prone positioning ventilation results in better oxygenation than supine positioning (Guérin C, et al. *N Engl J Med.* 2013;368(23):2159–2168).

In addition to improved oxygenation, prone positioning is thought to decrease VILI

Prone positioning poses logistical challenges & is contraindicated in pt with unstable spine fx & intracranial HTN among others (Guérin C, et al. *N Engl J Med.* 2013;368:2159–2168).

Supportive Therapy

Neuromuscular blockade & sedation:

Cisatracurium infusion for 48 hrs in ARDS pt was associated with decreased in-hospital mortality in a meta-analysis (Alhazzani W, et al. *Crit Care.* 2013;17:R43) following a landmark study by Papazian et al. (*N Engl J Med.* 2010;363(12):1107–1116).

Neuromuscular drug blockade is thought to benefit these pts by decreasing pt-ventilator dyssynchrony, minimizing work of breathing, & decreasing inflammation for an overall improvement in oxygenation

Risk of worsening ICU-associated myopathy & diaphragmatic weakness remain a concern; however, the meta-analysis above did not show an increased incidence of myopathy likely due to the short duration of cisatracurium infusion

Theoretically, sedatives early in the dz course can make mechanical ventilation easier; however, no studies thus far have demonstrated a mortality benefit

Fluid management:

Conservative fluid management is beneficial. Positive fluid balance & increased extravascular lung water is associated with poor outcomes (National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network, et al. *N Engl J Med.* 2006;354(24):2564).

Diuretics and/or hemodialysis may be beneficial in pt with volume overload

Nutrition:

Tube feeds with increased fat & decreased carbohydrates theoretically result in less carbon dioxide production & decrease in respiratory acidosis

Pharmacologic Therapy

Anti-inflammatory agents/steroids:

Although inflammation is thought to be involved in the pathogenesis of ALI/ARDS, anti-inflammatory therapies have been studied & have shown equivocal survival benefit

In 2006, the ARDSNet Late Steroid Rescue Study looked at this & showed no survival benefit. In fact, the study showed increased mortality when steroids were started 14 days after dz onset (Ware LB, et al. *N Engl J Med.* 2000;342(18):1334–1349).

Steroids are currently not recommended as they have not consistently shown a survival benefit & present possible side effects to pt

NSAIDs, statins, surfactant administration, ketoconazole have been studied & have shown no survival benefit in ALI/ARDS

Nitric oxide:

Inhaled nitric oxide has been shown to improve oxygenation in ARDS pt but a recent meta-analysis did not find it decreased mortality in either mild, moderate, or severe ARDS (Adhikari NK, et al. *Crit Care Med.* 2014;42:404–412).

Antiplatelet therapy:

Platelet activation is a key component of ALI/ARDS pathophysiology

In pt already on anti-platelet medications, Erlich et al. showed a decreased incidence of developing ARDS (Erlich JM, et al. *Chest.* 2011;139:289–295).

Rescue Therapies

Recruitment Maneuvers

A typical recruitment maneuver is an attempt at reexpanding atelectatic lung tissue by applying a constant positive pressure of about 30–40 mm H_2O for 60 s

The routine use of recruitment maneuvers is not supported in the literature for ALI/ARDS pt

Extracorporeal Membrane Oxygenation

Used in severe cases of ARDS, however it remains unclear which pt are likely to benefit from ECMO

Ongoing trials will determine if there is any survival benefit

Outcomes

Recognition of ARDS by clinicians continues to be a challenge & while appropriate dx is more likely in more severe dz, under-recognition remains a barrier to recommended management (Bellani G, et al. *JAMA*. 2016;315:788–800).

Although there have been advances in supportive therapy for these pt, mortality continues to be high & correlates to severity of dz with the study above noting an in-hospital mortality up to 40% (Bellani G, et al. *JAMA*. 2016;315:788–800).

Herridge et al. found that 5 yrs after surviving ARDS the survivors had normal to near-normal results on their pulmonary function test, but had significant exercise limitation with a decreased physical quality of life. As expected, younger pt had a greater rate of recovery than older ones, but neither group returned to normal predicted levels of physical function at 5 yrs (Herridge MS, et al. *N Engl J Med.* 2011;364:1293–1304).

Conclusion

ARDS is characterized by heterogenous lung parenchyma with consolidation leading to significant impairment in gas exchange

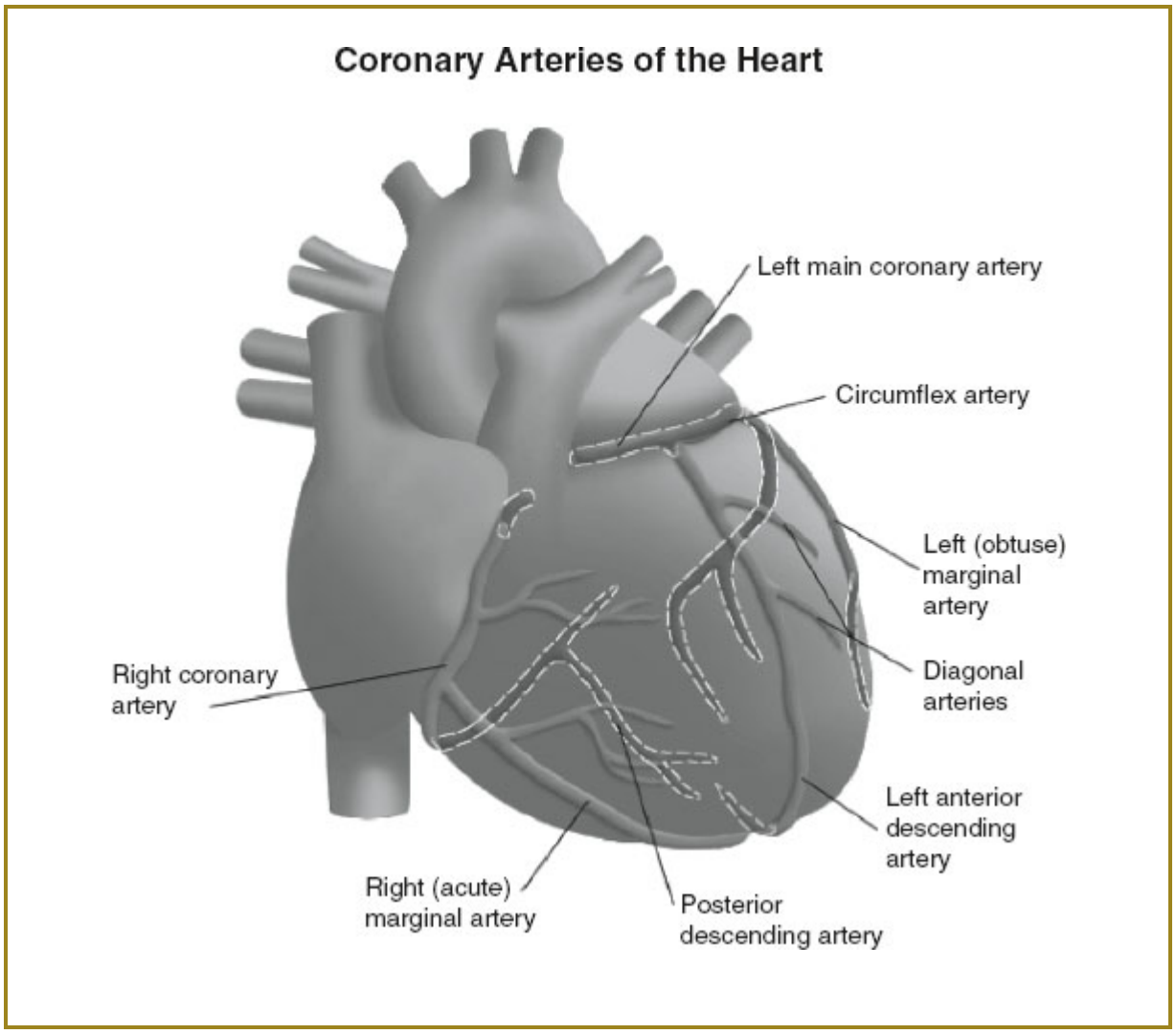
The mainstay of treatment for ARDS is lung-protective ventilation combined with supportive intensive care

Given complex interplay between body habitus, lung mechanics, & hemodynamic status, care should be personalized whenever possible

The management of ARDS related to infxn (pneumonia) or sepsis should prioritize the timely & appropriate treatment of those infectious issues (see Chapter 23 for the specifics of the management of infections & sepsis)

CARDIOVASCULAR CONDITIONS IN THE ICU—ACUTE CORONARY SYNDROMES AND OTHER COMMON CARDIAC PROBLEMS

PATRICK R. LAWLER, MD, MPH • DAVID A. MORROW, MD, MPH



Chest Pain

Ddx (cardiovascular causes, pulmonary causes, GI causes, musculoskeletal causes, other)

Cardiovascular causes: acute coronary syndrome (ACS) (unstable angina, MI), pericarditis, HTN emergency, aortic dissection, ruptured aortic aneurysm

Pulmonary causes: pneumonia, pleuritis, pneumothorax, PE, pulmonary HTN

GI causes: GERD, esophageal spasm, Mallory–Weiss, peptic ulcer disease (PUD), pancreatitis, biliary dz

Musculoskeletal/other causes: costochondritis, herpes zoster, anxiety/panic attack.

HTN Emergencies

Elevated BP (SBP >180 or DBP >120 mm Hg) causing clinical manifestations/end-organ damage

HTN urgency: Elevated BP that (by definition) is asymptomatic

Etiologies: essential HTN, medication nonadherence, stroke, drugs (cocaine, amphetamines), renovascular dz, endocrine (pheochromocytoma), vasculitis, eclampsia/preeclampsia

Work-up: hx of HTN, med compliance, illicit/OTC drug use. ROS for HA, visual changes, chest pain, back pain, SOB, orthopnea, PND. Exam: bilateral BPs, JVP, rales, s3/s4, renal or flank bruits, peripheral pulses, funduscopic exam, mental status & neurologic exam.

Studies: electrolytes, renal function, unstable angina (UA), ECG, CXR, cardiac biomarkers. Possibly renal US, metanephrines, renin/aldosterone.

Management: requires ICU admission. Decrease MAP by 10-20% in the 1st 1 hr. Then decrease BP down gradually with goal to reduce by 25% overall by 24 hrs. Initially avoid more rapid drops in BP to allow for end-organ autoregulation. Monitor UOP, renal function, mental status.

Possible therapeutic agents: IV labetalol, nicardipine, nitroprusside (be careful in renal/liver dysfunction), hydralazine, enalaprilat, nitroglycerin; if suspicion for cardiac ischemia or aortic dissection give β-blocker before vasodilator

Acute Coronary Syndromes

"Typical" angina defined by presence of all 3 of following: substernal discomfort, exertional, relieved by rest or nitro (Diamond GA, Forrester JS. *N Engl J Med.* 1979;300:1350–1358); "atypical" if ⅔ present.

Exam (key findings): check bilateral blood pressure to assess for aortic dissection. JVP. Pulmonary edema. New S4; new MR; underlying AS; HF (S3); femoral & carotid bruits, distal pulses (to assess for PAD); assess reproduction of pain from palpation

Electrocardiography: critical to obtain serial tracings.

Dx of ischemia or infarction requires ECG changes in 2+ contiguous leads. (Nikus K, et al. *J Electrocardiol.* 2010;43:91–103)

Ddx of ST elevation: MI, LVH, LBBB, LV aneurysm, myopericarditis, early repolarization, hyperkalemia, Brugada pattern, Takatsubo cardiomyopathy. (Wang K, et al. *N Engl J Med.* 2003;349:2128–2135)

Localization of the infarct: Anterior (V1–V4); apical/low lateral (V5, V6); Inferior (II, III, aVF), III > II suggests RCA as culprit compared to LCx; High lateral (I, aVL); posterior (inverse of V1–V3). (Zimetbaum PJ, Josephson ME. *N Engl J Med.* 2003;348:933–940)

Cardiac Biomarkers (Mohammed AA, et al. *Card Rev*. 2010;18(1):12)

Cardiac troponins preferred. CK–MB no longer recommended for dx of MI.
Look for rising and/or falling pattern to indicate acute myocardial injury.
For initial ACS dx, measure at presentation & 3–6 hrs.
Ddx of elevated troponin that is not ACS: recent MI, CKD/ESRD (chronic troponin elevations are common) (Lamb EJ, et al. *Am J Kidney Dis.* 2007;49:507–516), HTN emergency, HF decompensation or volume overload; CMP (infiltrative or dilated), trauma (blunt/cardioversion/ICD shocks, chest compressions), SAH, PE, pulmonary edema, myocarditis & myopericarditis, sepsis, systemic hypoperfusion.

Unstable Angina (UA) vs. Non-ST Elevation MI (Figure 20-1)

ACS represents acute mismatch of myocardial oxygen supply & demand, spanning presentations of: unstable angina → non-ST elevation MI (NSTEMI) → ST-segment elevation MI (STEMI).

Definition:
UA: acute myocardial ischemia *without* evidence of myocardial necrosis (biomarker negative). Angina that is new onset, crescendo, or at rest. There may or may not be ECG changes, & by definition cardiac biomarkers are negative. It is a clinical dx & diminishing in incidence with more sensitive assays for troponin.

NSTEMI: acute myocardial ischemia *with* evidence of myocardial necrosis (+ cardiac biomarkers) but without ST elevations.

Use Universal Definition of Myocardial Infarction Classification System	
Type 1	Spontaneous MI
Type 2	Secondary "demand" ischemia
Type 3	Sudden cardiac death with suspected MI
Type 4a	Periprocedural—PCI
Type 4b	Stent thrombosis
Type 5	Periprocedural—CABG

(Thygesen K, et al. *Circulation.* 2012;126:2020–2035)

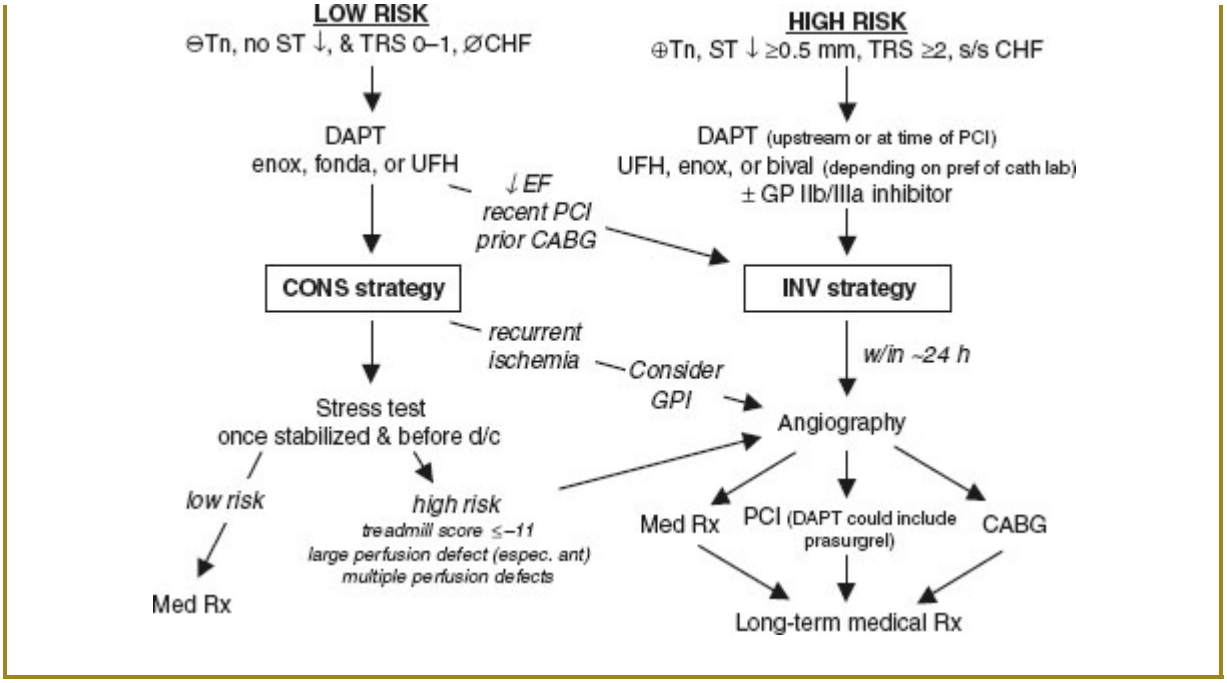
TIMI Risk Score for UA/NSTEMI (1 point per factor)
Age >65 yrs
3 or more risk factors for CAD (HTN, HL, DM, current smoking, FHx of CAD)
Prior coronary stenosis of 50%
ASA use in last 7 days (chronic use)
2 or more angina episodes in last 24 hrs
ST segment deviation of >0.5 mm (0.05 mV)
Elevated cardiac biomarkers (troponin or CK-MB)

(Antman EM, et al. *JAMA.* 2000;284:835–842)

TIMI Risk Score Interpretation	
Score	Rate of Death/MI/Revascularization in 14 days
0–1	5%
2	8%
3	13%
4	20%
5	26%
6–7	41%

(Antman EM, et al. *JAMA*. 2000;284:835–842)

Figure 20-1. Approach to UA/NSTEMI



(Figure adapted and significantly modified from Pocket Medicine by Sabatine, 4th ed.)

Therapeutics

Anti-Ischemics: Nitrates, β-Blockers, Calcium Channel Blockers, Morphine, Oxygen	
Agent	**Comment**
Nitrates, IV 20–200 μg/min gtt, SL 0.4 mg q5min × 3, topical 1–2 in paste)	↓ sx, no mortality change
β-Blockers e.g., metoprolol 5 mg IV q5min × 3, then 25–50 mg PO q6h titrated to HR 50–60 bpm.	↓ progression to MI (Yusuf S, Wittes J, Friedman L. *JAMA*. 1988;260:2259–2263). Contraindicated if HR <60, SBP <100, CHF, heart block, severe bronchospasm
Calcium channel blockers (nondihydropyridines alone, or dihydropyridines if administered with β-blockers)	Only if pt cannot tolerate β-blockers and persistent pain or tachycardia
Morphine 1–2 mg IV doses until pain relieved.	If persistent pain
Oxygen	Titrate to keep SaO_2 >90%
Statins	Survival benefit with high-intensity statin (e.g. atorvastatin 80 mg PO daily) (Cannon CP, et al. *N Engl J Med*. 2004;350:1495–1504)

Antithrombotics	
Agent	**Comment**
Unfractionated heparin 60 units/kg IV bolus (up to 4,000 units), then IV gtt at 12 units/kg (up to 1,000 units/h)	↓ death/MI approx 24% (Oler A, et al. *JAMA*. 1996; 276:811–815)
Enoxaparin 1 mg/kg SC b.i.d × 7 days or until PCI or hospital discharge (whichever comes 1st) (daily if CrCl <30)	↓ approx 10% death/MI compared to UFH (Petersen JL, et al. *JAMA*. 2004;292:89–96)
Fondaparinux 2.5 mg SC daily	Similar efficacy to enoxaparin, possibly less bleeding. (Fifth Organization to Assess Strategies in Acute Ischemic Syndromes Investigators, Yusuf S, et al. *N Engl J Med*. 2006;354:1464–1476). Not as monotherapy if PCI given catheter thrombosis risk. Not FDA approved in the US for use in ACS.
Bivalirudin 0.75 mg/kg IVB at time of PCI then 1.75 mg/kg/hr gtt	With PCI, bival alone similar outcomes to heparin & GP IIb/IIIa inhibitor combined with less bleeding (Stone GW et al. Bivalirudin during primary PCI in acute myocardial infarction. *N Engl J Med*.. 2008;358(21): 2218–2230)

Antiplatelets	
Agent	**Comment**
Aspirin 162–325 mg PO × 1, then 75–162 mg daily	50–70% ↓ in death or MI (Théroux P, et al. *N Engl J Med.* 1988;319:1105–1111)
Clopidogrel 300–600 mg × 1, then 75 mg/d. Requires 6 hrs to reach steady state	In addition to ASA, approx 20% ↓ in death/MI/stroke (Yusuf S, et al. *N Engl J Med.* 2001;345:494–502)
Prasugrel 60 mg × 1, then 10 mg/d	Given at time of coronary angiography if PCI is to occur. Approx 20% ↓ in death/MI stroke compared to clopidogrel, but more bleeding. Avoid if >75 yrs, hx CVA, wt <60 kg. (Wiviott SD. *N Engl J Med.* 2007;357(20):2001–2015). Reasonably preferred over clopidogrel (Class IIa)
Ticagrelor 180 mg × 1, then 90 mg b.i.d	More rapid & potent than clopidogrel. Approx 15% ↓ in death/MI/stroke compared to clopidogrel, but ↑ bleeding (Wallentin L, et al. *N Engl J Med.* 2009;361:1045–1057). Reasonably preferred over clopidogrel (Class IIa).
Cangrelor 30 µg/kg × 1, then 4 µg/kg/hr for at least 2 hrs or the duration of the PCI, whichever longer	IV ADP antagonist with rapid onset & offset. Reduces ischemic complications of PCI compared with clopidogrel (Bhatt DL, et al. *N Engl J Med.* 2013;368:1303–1313). Cost may limit use to selected pt.
GP IIb/IIIa inhibitors (eptifibitide, tirofiban). Infusions given up to 24 hrs post PCI.	May be considered in addition to other antiplatelet agents in high-risk ACS.

Angiography/Revascularization

Invasive strategy vs. *ischemia-guided* approach (Amsterdam JACC 2014):

Immediate invasive (within 2 hrs)	Refractory or recurrent (at low level) angina
	Signs or sx of HF or new or worsening MR
	Hemodynamic instability
	Sustained VT or VF
Ischemia-guided strategy	Low-risk score (e.g., TIMI [0 or 1], GRACE [<109])
	Low-risk Tn-negative women
	Pt/clinician preference in the absence of high-risk features
Early invasive (within 24 hrs)	None of the above, but GRACE risk score >140
	Rising troponin
	New ST depressions
Delayed invasive (within 25–72 hrs)	None of the above but diabetes mellitus
	Renal insufficiency (GFR <60 ml/min/1.73 m^2)
	LV systolic dysfunction (EF <0.40)
	Early postinfarction angina
	PCI within 6 mo or prior CABG
	GRACE risk score 109–140; TIMI score ≥2

Invasive strategy: Coronary angiography with the intent to perform revascularization

Ischemia-guided strategy: Noninvasive stress testing in low- & intermediate-risk pt once free of ischemia for a minimum of 12 to 24 hrs

ST-segment Elevation MI

(O'Gara PT, et al. *Circ*. 2013;127:529–555)

Dx: new ST segment elevation in 2 contiguous leads (or new LBBB) in setting of angina. New ST elevation defined at the J point in 2 contiguous leads with the cutpoints: ≥0.1 mV in all leads other than leads V2 to V3. In leads V2 to V3 ≥0.2 mV in men ≥40 yrs, & ≥0.25 mV in men <40 yrs, or ≥0.15 mV in women

Reperfusion: maximal benefit derived when reperfusion performed as early as possible. If avail., PCI should be performed within 90 min of 1st medical contact (FMC).

Primary PCI strategy: ~25% less death, 65% less reMI, 50% less strokes, & 95% less ICH compared with reperfusion with lytics (Keeley EC, et al. *Lancet.* 2003;361:13–20).

Transfer to PCI center is preferred if anticipated FMC-to-balloon time will be <120 min, if hemodynamically unstable, if contraindications to lysis, or if dx in doubt.

Lytic strategy (If primary PCI not avail.; target door-to-needle time 30 min)

Approx. 20% mortality decrease in AMI & approx. 10% mortality benefit in IMI compared to no reperfusion if done in <12 hrs.

Increased risk of ICH in elderly.

Absolute contraindications: prior ICH, intracranial neoplasm/aneurysm/AVM, stroke or head trauma within 3 mo, active bleeding or known bleeding diathesis, suspected aortic dissection.

Relative contraindications: uncontrolled HTN, ischemic stroke >3 mo prior, prolonged CPR (>10 min), trauma or major surgery in 3 wks, recent bleed or active PUD, noncompressible vascular punctures, pregnancy, current anticoagulation.

Adjunctive Antiplatelet Therapy

Strong evidence to support early initiation of dual antiplatelet therapy with aspirin & a platelet P2Y12 receptor blocker (dosing/approach as for NSTEMI)

For pt treated with lysis, clopidogrel is preferred over ticagrelor

Limited role for GP IIb/IIIa agents pre-PCI, no role with lysis

Anticoagulants

Unfractionated heparin: No clear mortality benefit in PCI, but used routinely. Increased vessel patency when used with fibrin-specific lytics.

LMWH: Preferred with lytic strategy but rarely used during primary PCI.

Bivalirudin: Decreased death & bleeding, but more early stent thrombosis compared to heparin & GP IIb/IIIa inhibitors (Stone GW, et al. *N Engl J Med.* 2008;358:2218–2230).

Other Medications Used to Treat STEMI

β-Blockers: approx. 20% decrease arrhythmic death or reinfarction, but increased risk of precipitating hypotension (Chen ZM, et al. *Lancet.* 2005;366:1622–1632). Start with oral dosing in 1st 24 hrs if not high risk of shock. Contraindicated if HR <60, SBP 100, CHF, high-grade heart block, severe bronchospasm.

ACE-inhibitors: approx. 10% mortality benefit seen with anterior MI, if pulmonary edema, or EF <40% (*Lancet* 1994;343:1115–1122).

Angiotensin receptor blockers (ARBs): similar to ACE-I efficacy (Pfeffer MA. *N Engl J Med*. 2003;349(20):1893–1906. Epub 2003 Nov 10).

Other **adjunctive meds:** similar to NSTEMI with nitrates, statins, oxygen, morphine as above. Concern that morphine may diminish pharmacodynamics of P2Y12 inhibitors.

Eplerenone should be considered in pt with HF or reduced EF & diabetes who are tolerating a β-blocker & ACEI.

Intra-aortic Balloon Pump

Consider for hemodynamic compromise or refractory angina

Deflates in systole, reducing aortic volume, & creates a vacuum effect thereby reducing afterload

Inflates during diastole improving coronary perfusion

Indications: cardiogenic shock, mechanical complications of MI (VSD, pap muscle rupture), refractory ischemia or VT/VF, facilitation of revascularization, critical valvular dz as a bridge to surgery. No mortality benefit in pt with shock (Thiele H, et al. *N Engl J Med* 2012;367:1287–1296) but may still offer temporary hemodynamic stabilization.

Contraindications: severe aortic insufficiency, aortic pathology (dissection, aneurysm, intramural hematoma), severe PAD, uncontrolled bleeding.

Complications: vascular trauma/leg ischemia, platelet destruction & hemolysis, bleeding, infxn, renal injury if malpositioned.

Temporary Ventricular Assist Devices (Spiro J, et al. *Curr Cardiol Rep.* 2014;16:544) **& VA ECMO** (Lawler PR, et al. *Circulation.* 2015;131:676–680; Discussed in Chapters 21 & 25)

Inferior Myocardial Infarction (IMI)

(Berger PB, et al. *Circulation.* 1990;81:401–411)

Heart block (<20%). Rx sinus bradycardia, type I 2nd degree (Wenckebach), or 3rd degree heart block with narrow escape with atropine, epi, isoproterenol, temporary pacing.

RV infarct associated with hypotension, elevated JVP, Kussmaul sign. Rx with optimization of preload with goal RA pressure 10–14 (usually requires IVF) (Berisha S, et al. *Br Heart J.* 1990;63:98–102); maintain AV synchrony (Bowers TR, et al. *N Engl J Med.* 1998;338:933–940); pulmonary vasodilators (e.g., NO), management of acute RV failure (Green EM, Givertz MM. *Curr Heart Fail Rep.* 2012;9:228–235).

Complications of Myocardial Infarction

(Ng R, et al. *J Intensive Care Med*. 2013;28:151–165)

See table. Account for <15% of mortality after STEMI; declining in the era of early primary PCI.

Risk factors: age, female gender, large MI, late presentation/revascularization

When concerned: obtain STAT echo, repeat angiography +/- PA catheter insertion (with O_2 saturation run looking for shunt). May need urgent surgical evaluation.

Early Complication	Clinical Features	Treatment
Cardiogenic shock	Immediate post-MI. Hypotension, elevated JVP, elevated PCWP, low CO	Inotropes, IABP, pVAD, revascularization
Free wall rupture (or pseudoaneurysm)	~5 days post-MI. Sudden hypotension to tamponade to PEA arrest	Emergent surgery, pericardiocentesis (may worsen status)
VSD	~5 days post-MI; new murmur	IABP, vasodilators, inotropes, surgery, transcatheter closure in selected pt
Papillary muscle rupture (acute severe MR)	~5 days post-MI; new MR murmur (although may not be audible in acute MR)	Vasodilators, IABP, surgery

Late Complications

LV thrombus: 10–40% anterior MI. Increased embolization risk. Rx with anticoagulation 3–6 mo.

Pericarditis: 2 types – *early,* 2–4 days post-MI pericardial rub/effusion, pleuritic CP, ECG changes. Rx with ASA (up to 650 mg q4h) > colchicine > tylenol > steroids > other NSAIDs; *late* (Dressler syndrome): late autoimmune carditis, rarer in reperfusion era. Similar rx to acute pericarditis.

LV aneurysm: occurs days to weeks post-MI, persistent ST elevation. Risk factors: large/anterior MI, steroids, NSAIDs. Apical dyskinesis/aneurysm increases risk of LV thrombus. Can compromise pump function or cause arrhythmia.

Electrical Complications

Atrial fibrillation: (10–15%).

VT/VF: VT/VF prior to reperfusion does not have significant long-term prognostic value, most effective treatment is β-blockers (reduces arrhythmic death [Randomised trial of intravenous atenolol among 16027 cases of suspected acute myocardial infarction: ISIS-1, First International Study of Infarct Survival Collaborative Group. *Lancet.* 1986;2:57–66.]) or lidocaine/amiodarone; increased mortality with class IC (Echt DS, et al. *N Engl J Med.* 1991;324:781–788).

Bradyarrhythmias: range from sinus bradycardia to complete heart block. May require emergent pacing.

Complete heart block associated with IMI typically has narrow complex escape rhythm with rate ~50–60 bpm & can often be monitored carefully without insertion of temp pacemaker unless there is hemodynamic compromise, often atropine responsive.

Heart block associated with AMI (bifascicular or complete heart block) usually requires emergency temp pacemaker placement (asystole risk)

Cardiomyopathy/Shock/Heart Failure

Cardiomyopathies

Dilated CMP

Defined as ventricular dilation with decreased contractility.

Etiologies: ischemic, valvular, HTN, idiopathic, myocarditis: viruses (echovirus, coxsackievirus, HIV), bacterial, fungal, rickettsial, Chagas, giant cell, Toxic: alcohol, athracyclines, radiation, cocaine; Autoimmune: peripartum, collagen vascular dz, sarcoid; Metabolic: hypothyroid, pheochromocytoma, acromegaly, thiamine or selenium deficiency; tachycardia induced, familial

Work-up: hx, ischemia evaluation (noninvasive or angiography), labs (TFTs, iron studies, HIV), consider: cardiac MRI, endomyocardial bx (particularly new fulminant)

Treatment: Standard heart failure therapy.

Genetic Hypertrophic CMP

Excessive LV and/or RV hypertrophy

Ddx includes hypertensive heart dz or infiltrative process (Lawler PR. *Circulation.* 2014; 129(16):1703–1711.)

Pathology: mutations in sarcomere encoding genes. Myofibril disarray on pathology.

Pathophysiology:

Subaortic outflow obstruction: narrowed tract from hypertrophied septum & systolic anterior motion of the mitral valve. Worsened with increased contractility or decreased preload.

Mitral regurgitation due to SAM.

Diastolic dysfunction from increased chamber stiffness

Ischemia: small vessel dz & subendocardial ischemia

Arrhythmias

Physical exam: systolic crescendo–decrescendo murmur that increases with emptying the LV (with Valsalva or standing, decreases with squatting & handgrip).

Studies:

ECG: LVH, Q waves, large T-wave inversions.

Echo: severe LVH (can be asymmetric), SAM, MR.

MRI: hypertrophy & patchy late gadolinium enhancement

Catheterization: subaortic LV pressure gradient; Brockenbrough–Braunwald–Morrow sign: decrease in pulse pressure post extrasystolic beat.

Treatment:

Drug therapy to reduce inotropy, palpitations (β-blockers, CCBs, disopyramide). Maintain adequate intravascular volume. If refractory with obstruction, surgical myomectomy vs. alcohol septal ablation.

ICDs to prevent sudden death if high risk.

Family counseling & genetic screening.

Restrictive CMP (Lawler PR. *Circulation.* 2014;129(16):1703–1711)

Impaired ventricular filling due to decreased compliance.

Etiology: idiopathic fibrosis, autoimmune (scleroderma, PM/DM), infiltrative dz (amyloid, sarcoid, hemachromatosis), storage dz (Fabry's, Gauchers, etc.), Loffler endocarditis, radiation, anthracyclines, serotonin (carcinoid, drugs), metastatic cancer

Pathology: decreased myocardial compliance → normal EDV, but increased pressure → increased filling pressure

Exam: elevated JVP, Kussmaul sign, S3/S4, MR/TR. Congestive hepatopathy, ascites, edema.

Diagnostic Studies:

Echo: LVH, atrial enlargement, significant diastolic dysfunction

Cath: atria: prominent x & y descents; Ventricles: dip & plateau. Concordance of LV/RV pressure during respiratory cycle (compared to constriction with discordance).

Treatment: volume control. Maintain sinus rhythm. Treat underlying condition.

Valve Diseases

Mitral Stenosis

Etiology: mostly rheumatic (<80%) > other (endocarditis, mitral annular calcification, myxoma, thrombus, autoimmune valvulitis)

Pathophysiology: elevated LA pressure, pulmonary HTN, AF

Exam: high-pitched opening snap, low pitched diastolic rumble, loud S1, presystolic accentuation (if in sinus rhythm).

Treatment: indicated in severe MS with sx, consider if pulmonary HTN. Percutaneous valvulotomy preferred if valve anatomy is amenable (Wilkins score) & there is not significant MR. Otherwise surgery.

Medical management: Na restriction, β-blockers or calcium channel blockers to slow HR & allow for adequate LV diastolic filling, anticoagulation for large LA or AF.

Mitral Regurgitation

Etiology: functional vs. structural

Structural: myxomatous degeneration (MVP), endocarditis, rheumatic, valvulitis, congenital, anorectic drugs

Functional: dilated CMP & annular dilation or papillary muscle displacement, ischemic papillary dysfunction, ruptured chordae

Clinical: acute → pulmonary edema, hypotension; chronic → DOE, orthopnea, PND, AF.

Exam: holosystolic murmur at apex, radiates to axilla, increases with handgrip, & decreased with Valsalva.

Anterior leaflet abnormality: murmur heard at spine

Posterior leaflet abnormality: murmur heard at sternum

Treatment:

Acute MR: vasodilators, inotropes, IABP. Often need urgent surgery

Chronic MR: surgical repair better than replacement if possible. Indications if symptomatic or asymptomatic if EF <60% or LV dilation (LVESD >4.0 cm), consider in pulmonary HTN, or new AF.

Aortic Stenosis

Etiology: Calcific (most common in >70 yrs), bicuspid valve (most common <70 yrs), rheumatic (usually with AI & mitral valve dz involvement).

Pathophysiology: increased afterload from pressure overload causes concentric hypertrophy

Clinical: angina, syncope, heart failure, acquired vWD in approx 20% (Heyde syndrome).

Natural hx: slowly progressive, but may have a rapidly progressive course as severity progresses (esp. in calcific degenerative etiology). Need for AVR becomes urgent once sx develop in setting of severe obstruction angina—5-yr mean survival; syncope—3-yr mean survival; heart failure—2-yr mean survival.

Physical exam: harsh systolic crescendo–decrescendo murmur at upper sternal border; radiates to sternal notch, carotids, apex (can sound like MR = Gallavardin effect).

Murmur increases with leg raise, decreases with Valsalva or standing.

Signs of severity: late-peaking murmur, soft A2, small & delayed carotid upstrokes (parvus & tardus).

Spectrum of Disease in Aortic Stenosis			
Stage	Mean Gradient (mm Hg)	Valve Area (cm^2)	Peak Velocity (m/s)
Mild	<25	>1.5	<3.0
Moderate	25–40	1.0–1.5	3.0–4.0
Severe	>40	<1.0	>4.0

Treatment is surgical AVR or transcathether valve implantation (TAVI) for symptomatic severe AS, asymptomatic severe AS with decreased EF, or very severe AS (Nishimura RA. *J Am Coll Cardiol.* 2014;63(22):2438–2488).

Medical management: gentle diuresis, avoid excess preload reduction. Avoid venodilators & negative inotropes.

Balloon aortic valvuloplasty (BAV): <50% increase in AVA, with >50% restenosis rate at 6–12 mo. Often used as bridge to AVR or through another complicated illness.

Aortic Insufficiency

Etiology: leaflet abnormalities (bicuspid valve, endocarditis, rheumatic) or root dilation (HTN, aortic aneurysm/dissection, Marfan's, syphilis)

Pathophysiology: volume loading & increased LVEDP causes ventricular dilation

Clinical manifestations: angina, orthopnea, dyspnea, left heart failure

Exam: increased pulse pressure, early diastolic murmur (often with crescendo–decrescendo systolic murmur), many eponymous signs that are not associated with prognosis

Echo: severity based on size of regurgitant jet (vena contracta >0.6 cm, regurgitant. volume >60 ml, regurgitant. fraction >50%, ERO ≥0.3 cm^2) & presence of flow reversal in descending aorta. Also assesses LV size & function.

Treatment:

Acute: surgery usually urgently/emergently needed as it is poorly tolerated. Start therapy with IV afterload reduction (nitroprusside) & inotropes. Increased HR is better as less time for diastolic regurgitation.

Chronic: risks of progression to sx & LV dysfunction are both related to LV dimensions.

Surgery: symptomatic severe AI, asymptomatic severe AI + EF <50% or LV systolic diameter >50 mm, asymptomatic severe AI undergoing other cardiac surgery.

Medical therapy: vasodilators (ACE-I, nifedipine, hydralazine/nitrates)

Acute AI: often aortic dissection or endocarditis. Urgent surgery usually required. Until surgery, need afterload reduction, but IABP contraindicated.

Prosthetic Valves

Mechanical

Bileaflet (St. Jude) tilting discs, ball & cage.

Very durable (20–30 yrs), but thrombogenic & require anticoagulation.

Consider in younger pt (<65 yrs) or if already have indication for anticoagulation

Bioprosthetic

Bovine pericardial or porcine heterograft, homograft

Less durable, but minimally thrombogenic. Do not require anticoagulation.

Used in older pt or if contraindication to anticoagulation.

Exam: crisp valve closure sounds (louder with mechanical valves). Soft-flow murmur though prosthesis due to small, normal pressure gradients. Worrisome if absent sounds or regurgitant murmurs.

Anticoagulation: Risk of valve thrombosis MVR > AVR & risk is highest early after implantation before endothelialization.

Warfarin: low-risk mech AVR: INR 2–3 (consider 2.5–3.5 for 1st 3 mo); mechanical MVR or high-risk AVR (with prior VTE, AF, low EF, hypercoagulability): INR 2.5–3.5.

ASA for bioprosthetic valves alone & with warfarin in mechanical valves.

Bridging: warfarin should be stopped 48–72 hrs early with IV UFH when INR <2 until 4–6 hrs before surgery; postop restart UFH & warfarin ASAP.

Pericardial Tamponade

(Roy CL, et al. *JAMA*. 2007;297:1810–1818)

Definition: hemodynamic insufficiency caused by cardiac compression due to fluid trapped in the pericardial space.

Etiologies: pericarditis, iatrogenic, malignancy, idiopathic, MI, ESRD, CHF, collagen vascular dz, TB, other infxns

Pathophysiology: increased pericardial pressure → compression of heart → decreased venous filling → decreased CO.

Diastolic pressure elevated in all chambers & equalize

Dx & clinical assessment:

Sign/sx: dyspnea, tachycardia, increased pulsus paradoxus, elevated JVP, hypotension (Beck triad: hypotension, JVD, quiet heart sounds).

Pulsus paradoxus: exaggeration of normal respiratory ventricular interdependence causing decreasing LV stroke volume with inspiration. If inspiratory fall in BP >10 mm Hg, consistent with tamponade. Many conditions can have elevated pulsus paradoxus (severe obstructive lung dz, PE), & can be absent in volume depletion, ASD, pulmonary HTN, & LV noncompliant states.

Diagnostics:

ECG: low voltage, electrical alternans; CXR with large cardiac silhouette

Echocardiogram: pericardial effusion, dilated IVC, septal shift, diastolic chamber collapse, exaggerated respirophasic changes in transvalvular velocities.

Treatment: volume & inotropes, then pericardiocentesis. Remember, tamponade caused by pericardial pressure rising above RA pressure. Often relieved by simply increasing RA pressure allowing for nonurgent performance of pericardiocentesis.

Pericardiocentesis (also see Chapter 46) (Kirkland LL, et al. *Crit Care Clin.* 1992;8:699–712)

Indications

Treatment for clinically significant pericardial tamponade, occasionally diagnostic

Contraindications/Considerations

Uncorrected bleeding diatheses in nonemergent setting
Always have cardiac surgical backup

Complications

Atrial or ventricular puncture, atrial or ventricular laceration, cardiac arrhythmias, vasovagal reaction, pneumothorax, gastric or bowel perforation, acute pulmonary edema

Cardiogenic Shock and Tailored Heart Failure Therapy

Shock

Hemodynamic Profiles of Shock				
Subtype	**CVP**	**PCWP**	**CO/CI**	**SVR**
Hypovolemic	Low	Low	Low	High
Cardiogenic	High	High	Low	High
Distributive (Septic/Anaphylactic)	Low	Low	Normal/high	Low
RHF or PE	High	Low to normal	Low	High
Tamponade	High	High	Low	High

PA Catheters (see Chapter 2)

Rationale:

C.O. = SV × HR. Stroke volume depends on preload (LVEDV) & afterload (SVR).

LVEDV is not easily measureable. However, using a balloon-tipped catheter & measuring pressure beyond the balloon tipped when balloon is wedged in PA gives PCWP.

With no flow, PCWP = alveolar pressure = LA pressure = LVEDP, which is proportional to LVEDV. PA diastolic pressure will equal PCWP if no "obstruction" (no transpulmonary gradient) from PA to LA (e.g., arteriolar constriction, severe bronchoconstriction leadings to arteriolar constriction)

Assumptions fail when:

Catheter tip in area where PCWP does not equal alveolar pressure (if not in West lung zone 3—lung zones can change with changes in pt position)

Obstruction between PCWP & LV: mediastinal or lung fibrosis, pulmonary vein stenosis, MS.

Abnormal compliance of LV so that LVEDP is not proportional to LVEDV

Common uses of PA catheters:

Narrowing DDx: type of shock, mechanism of pulmonary edema, RV vs. LV failure

Dx: pulmonary HTN, restrictive cardiomyopathy, tamponade, intracardiac shunt, MR/TR

Management: volume status, pressors, cardiogenic shock, complicated MI, postcardiac/thoracic surgery, pHTN

Complications of PA catheters: RBBB, ventricular arrhythmia, PA rupture, pulmonary infarct, infxn, catheter knotting.

Efficacy:

No routine benefit to PAC in high-risk surgery or ARDS (Wheeler AP, et al. *N Engl J Med.* 2006;354:2213–2224).

No benefit from routine use for tailored heart failure therapy for decompensated CHF (Binanay C, et al. *JAMA.* 2005;294:1625–1633).

Placement & waveforms: see Chapter 2

CO: can be measured using Fick equation or thermodilution.

Thermodilution: saline injected into RA. Change in temp over time measured at distant thermistor is integrated. Inaccurate if low CO or severe TR.

Fick method: oxygen consumption = CO × arteriovenous (AV) oxygen difference

CO (l/min) = oxygen consumption (l/min)/[(AVO_2 difference)(10)(1.34 ml/g)(Hgb g/dl)].

Can estimate oxygen consumption using wt-based formula. Optimal to measure but rarely done.

Resistances:

SVR = (MAP – RA)/CO

PVR = (PA mean – PCWP)/CO

1 Wood unit = 80 dyn·s/cm^5

Hemodynamic considerations:

All quantitative measurements should be made at end expiration.

Positive pressure ventilation inverts respirophasic variation (RA pressure increases with positive pressure inspiration).

Measure RA & PCWP at the end of diastole, i.e., at the end of the a wave.

Remember to account for PEEP (generally subtract ½ of PEEP)

Decompensated Heart Failure/Tailored Therapy

Definitions/General Considerations:

Definition: sx (often dyspnea) from rapid accumulation of fluid due to increased LVEDP or from diminished CO

Precipitants: myocardial ischemia/infarction, dietary or pharmacologic nonadherence, uncontrolled HTN, arrhythmia, endocarditis, valvulopathy, tamponade, myocarditis, fluid overload, high-output state (anemia, systemic infxn, hyperthyroidism, etc.), toxins (EtOH, cocaine, etc.), iatrogenic (anthracyclines, steroids, etc.), infxn

Most common hospitalizing dx.

Low output (decreased CO) vs. high output (increased SV, increased CO)

Left heart failure (pulmonary edema/congestion) vs. Right heart failure (JVD, edema, ascites, hepatomegaly)

Systolic (insufficient CO so cannot perfuse organs) vs. Diastolic (impaired ventricular filling)

History, Exam, Labs, Radiographs

4 Major Hemodynamic Profiles		
	No Congestion	**Yes Congestion**
Adequate perfusion (warm)	"Warm and dry" Outpatient management	"Warm and wet" Majority of pt Rx with diuretics +/– vasodilators
Low perfusion (cool)	"Cool and dry" Rx in ICU	"Cool and wet" Rx with inotropes & vasodilators; tailored & advanced therapy (ICU)

Source: Nohria A, et al. *J Am Coll Cardiol.* 2003;41:1797–1804.

Evidence for low perfusion: narrow pulse pressure (pulse pressure proportion <25%), pulsus alternans, cool forearms & calves, drowsy/obtunded, poor tolerance of ACE-I & β-blockers, hyponatremia, worsening renal function

Evidence for congestion:

Left sided: dyspnea, orthopnea, PND, S3, rales (often not present because of lymphatic adaptation)

Right sided: elevated JVP, loud P2 (if pulmonary HTN), right-sided S3, increased TR, edema, ascites, anorexia, HJR

RA pressure in mm Hg = JVP (in cm water)/1.3

CXR signs: pulmonary edema, pleural effusions (L > R), cardiomegaly.

BNP/NTproBNP: useful when dx is uncertain

Treatment of Acute Decompensated Heart Failure				
Address Etiology	**Hemodynamics**	**Volume Status**	**Oxygenation**	**Optimize Chronic Therapy**
• Treat precipitant & etiology (such as ischemia, arrhythmia, etc.). • Address life-threatening conditions (STEMI, malignant arrhythmias, etc.)	• Vasodilators to ↓ afterload • Inotropes if low output (may need to cut or stop β-blockers during acute decompensation)	• Sodium restriction • IV diuretics initially give predictable bioavailability • May need combination of loop & thiazide diuretics for multiple mechanisms • Convert to oral diuretics when able • Follow daily wt & I/Os.	• Oxygen • Morphine to ↓ work of breathing & some venodilation • May need NIPPV, or eventually, mechanical ventilation	• Transition once stable of IV agents & euvolemic • Move toward long-acting agents with evidence (ACE-I/ARB, β-blockers, aldosterone antagonists, etc.)

Heart Failure with Preserved EF

DDx: HTN/LVH, HCMP, infiltrative CMP (amyloid, hemachromatosis, sarcoid, etc.), restriction, scar, noncompaction

Findings: S4 (not in AF), LVH (not required for dx)

Treatment goals:

No specific evidence-based treatment, address underlying etiology

Optimize volume & reduce congestion with diuretic

Rhythm control: prevent tachycardia, prolong diastole, & maintain sinus rhythm (to preserve atrial kick)

Cardiogenic Shock/Tailored Therapy

Cardiogenic shock definition: SBP <80 or 90 mm Hg, CI <2.2 l/min/m^2, PCWP >18 mm Hg

Tailored therapy with PA catheter to guide treatment based on hemodynamics; catheter-directed strategy not shown to improve outcomes (Binanay C, et al. *JAMA.* 2005;294:1625–1633), however principles are useful to consider in treating decompensation

Hemodynamic goals of tailored therapy: MAP >60 mm Hg, CI >2.2, PCWP 14–18 mm Hg, CVP 8–12 mm Hg, SVR <800.

Approach to Tailored Therapy		
Fluid (Preload) Optimization	**SVR (Afterload) Optimization**	**CI (Inotropy) Optimization**
• PCWP high: diuresis +/– inotropes • PCWP low: crystalloid or colloid • Some pts in cardiogenic shock have low PCWP & need fluid. • Clues to hypovolemia include hypotension on positive pressure ventilation & pulse pressure variation. • Consider higher PCWP goals in LVH, HOCM, infiltrative dz	• SVR >1,200: vasodilators such as nitroprusside • Occasionally in pt with ↑ SVR, vasodilators actually raise the MAP. • Besides vasodilators, an IABP also lowers SVR.	• If CI <2.2: try to augment CI by optimizing PCWP & SVR. • If still not at goal, may need inotropes

Pacemakers and Defibrillators

Pacemaker Nomenclature

Single chamber PPM: single RV or RA lead only.

Dual Chamber PPM: when atrial-ventricular synchrony still possible. RA & RV leads.

Cardiac resynchronization therapy (CRT) (also called biventricular PPM): RV & LV leads (in cardiac veins via coronary sinus). Indicated in heart failure with wide native QRS, preferably LBBB.

Pacemaker Codes: A: atrial, V: ventricular, I: inhibition, D: dual, R: rate modulation			
1st Letter	**2nd Letter**	**3rd Letter**	**4th Letter**
Chamber(s) paced	Chamber(s) sensed	Response to sensing	Rate modulation

Common Examples

VOO: asynchronous ventricular pacemaker. Magnet placed over permanent PPM reverts to VOO (or occasionally DOO), although programing can be changed. Often required for operations involving electrocautery (VOO prevents over-sensing).

VVI: ventricular demand pacing; output in ventricle inhibited by sensed native QRS complex in ventricle. Mode used in temporary pacing.

DDDR: Most common mode for permanent dual chamber devices. For chronotropic incompetence/AV block. Allows AV synchrony if the native complexes are not too bradycardic or conducted too slowly. Rate responsive to increase HR with activity.

Indications for Permanent Pacing (PPM) (Epstein AE, et al. *Circulation.* 2008;117(21):e350–e408)

Symptomatic bradycardia in general.

AV block: symptomatic 3rd or 2nd degree block. Asymptomatic 3rd degree block or type II 2nd degree block is questionable. Type I 2nd degree block does not require intervention.

Sinus dysfunction: Sinus bradycardia or pausing with sxs. Chronotropic incompetence.

Indications for Temporary Pacing

Generally the same indications as for PPM

Symptomatic bradycardias (such as sinus brady, acquired AV block, post-MI, syncope). Variable progression to PPM depending on if indication is permanent.

Most common situations for temporary pacing that do not require PPM:

Acute bradycardia or AV block: postsurgical or traumatic conduction system dz, Lyme, toxic, medication, endocarditis, periprocedural (alcohol septal ablation, etc.).

Overdrive pacing: for recurrent polymorphic VT to prevent R on T phenomena.

Acute MI & conduction block.

Cardiac Resynchronization Therapy (CRT)

Pacing of both ventricles (via RV lead & coronary sinus lead for LV) with goal of restoring ventricular–ventricular synchrony.

Indications for CRT: certain pt with LVEF <35% & symptomatic ischemic & nonischemic CMP, QRS >120 ms (preferably LBBB) despite optimal medical therapy.

Implantable Cardioverter-Defibrillators (ICDs) (Myerburg RJ. *N Engl J Med.* 2008;359:2245–2253)

Goal: to terminate VT/VF with burst pacing or shock & prevent sudden death.

Unlike PPMs, ICDs are programmed for bradycardia & tachycardia, but ICDs also have back-up pacing functions.

Most often, if ICD senses tachyarrhythmia there are several responses: antitachycardia pacing to attempt to terminate rhythm without shock or series of shocks.

Indications for ICD:

Secondary prevention: survivors of VT/VF arrest, unstable VT/VF without reversible cause, structural heart dz, & VT.

Primary prevention: life expectancy >1 yr, LVEF <30% or LVEF 30–35% & NYHA II-III or LVEF 35–40% & inducible VT/VF. Also for certain pt with HCMP, Brugada, sarcoid, Long QT, Chagas, congenital heart dz with risk factors.

Device Complications

Implantation: tamponade, hematoma, pericarditic pain, pneumothorax.

Later Complications:

Failure to pace: from battery failure, lead fx/dislodgement, increased pacing threshold.

Failure to sense: from lead dislodgement or increasing thresholds (e.g., lead fibrosis)

PPM mediated tachycardia: reentrant tachycardia initiated by early beat conducted retrograde (V-A conduction) where it is sensed & triggers paced beat, thus causing reentrant circuit.

PPM syndrome: palpitations, heart failure, cannon A-waves, from loss of AV synchrony or interventricular synchrony.

Device infxn: pocket infxn or lead infxn requiring removal of system.

Inappropriate shocks: can cause serious psychiatric distress & possibly myocardial injury (Sweeney MO. *Circulation.* 2010;122:2638–2641). Place magnet over system to disable shock therapies.

Pharmacology of Cardiovascular Drugs (also see Chapter 25)

Inotropes and Vasopressors

Drug	α	β-1	β-2	dopa	Other	CO/CI	SVR	MAP	HR
Dopamine (low dose)	0	+	0	++	0	↑	↔	↔	↔/↑
Dopamine (medium dose)	+	++	+	++	0	↑	↔/↑	↔/↑	↑
Dopamine (high dose)	++	++	+	++	0	↑↑	↑↑	↑↑	↑↑
Dobutamine	0/+	+++	++	0	0	↑↑	↓	↔/↓	↑
Milrinone	0	0	0	0	PDEi	↑↑	↓	↔/↓	↔/↑
Epinephrine	+++	+++	++	0	0	↑	↑↑	↑↑	↑↑
Norepi-nepherine	+++	+++	0	0	0	↑	↑↑	↑↑	↑
Phenylephrine	+++	0	0	0	0	↓	↑↑	↑↑	↔
Isoproterenol	0	+++	+++	0	0	↑	↔/↓	↔	↑↑
Vasopressin	0	0	0	0	V1,V2	↔	↑↑	↑↑	↔

Inotropes

Generally used in decompensated heart failure/cardiogenic shock.

Milrinone: phosphodiesterase inhibitor. Causes increased inotropy & vasodilation. BP effect is variable. Some pulmonary vasodilation. Proarrhythmic. Bolus not recommended in HF.

Dobutamine: nonselective β-agonist. Increased inotropy/chronotropy. Generally less vasodilation than milrinone. BP effect variable. Also proarrhythmic.

Antihypertensives

β-Blockers

Mechanism via inhibition of β-receptors on cell surface.

Uses: HTN, angina, chronic systolic heart failure, rate control, antiarrhythmics

Multiple classes based on mechanism:

β-1 selective: metoprolol, atenolol, etc.

Nonselective: nadolol, propranolol

Combined α & β-blockers: carvedilol, labetalol

Miscellaneous: carvedilol, bisoprolol, metoprolol (sustained release) improve mortality in chronic systolic heart failure.

Side effects: hypotension, bradycardia/heart block, negative inotropy, fatigue/lethargy, sexual impotence.

Calcium Channel Blockers

2 classes: dihydropyridines & non-dihydropyridines

Dihydropyridines: amlodipine, nifedipine, etc. Function peripherally. Use in HTN, coronary spasm/Reynaud's, PAH. Adverse reaction: LE edema.

Nondihydropyridines: verapamil, diltiazem. Function at level of heart, but also lower BP. Use as antianginals, rate controlling agents. Adverse reactions: negative inotropes, heart block/bradycardia, hypotension.

Angiotensin Converting Enzyme Inhibitors (ACE-I)/Angiotensin Receptor Blockers/Renin antagonists/Aldosterone antagonists:

Interrupt renin–angiotensin–aldosterone system at different levels.

Cause small decrease in GFR & increase serum K.

Uses: HTN, post-MI, chronic heart failure, prevent progression of renal dz

Adverse reactions: renal failure, hyperkalemia, hypotension, cough (ACE-I only, not ARBs or aldosterone antagonists). Avoid ACE-I in bilateral renal-artery stenosis.

Nitrates

Administered in many ways (PO, SL, transdermal, IV).

Venodilators & antianginals.

Uses: angina, HTN (although much more powerful on venous dilation than arterial dilation), vasospasm.

Adverse reactions: hypotension, headache. Tachyphylaxis achieved quickly.

Diuretics

All cause natriuresis. Can be used in conjunction with each other if different classes.

Thiazides (HCTZ, chlorthalidone, metolazone, etc.): function in distal convoluted tubules.

Loops (furosemide, bumetanide, torsemide, etc.): function at Loop of Henle

Carbonic anhydrase inhibitors: acetazolamide

α-Blockers

Used for HTN, BPH. Particularly useful in pheochromocytoma prior to initiating β-blockade (to prevent unopposed symbol α agonism).

Adverse effects: orthostatic hypotension. Central effects.

Others

Nitroprusside: direct arterial dilator. Most effect anti-HTN. Cyanide or thiocyanate toxicity with prolonged use (more rapidly if liver or kidney dysfunction).

Hydralazine: direct arterial dilator. Anti-HTN. Decreases mortality in combo with nitrates in heart failure. Can cause autoimmune (Lupus-like, antihistone antibodies) reaction.

Clonidine: centrally acting symbol α-agonist. Rebound HTN with withdrawal.

Antiplatelets/Anticoagulants

Antiplatelets Agents

Different mechanisms in preventing platelet activation/aggregation. Primary adverse effect of all agents is bleeding.

ASA: Mechanism: Irreversibly blocks thomboxane A2 mediated platelet aggregation via actions on COX enzymes.

Used in stable atherosclerosis (CAD, PAD, stroke prevention), ACS, post-PCI.

Long-functional half-life.

Thienopyridines: clopidogrel, prasugrel. Irreversible ADP receptor antagonists. Oral administration. Require loading dose. Used in ACS, post-ACS, post-PCI, CVA prevention.

Ticagrelor: reversible P2Y12 receptor antagonist. Use will be in ACS, post-PCI. Half-life ~12h.

Cangrelor: IV, very short-acting, IV P2Y12 receptor antagonist.

GP IIb/IIIa inhibitors: IV infusions. 3 agents avail. Use in ACS & to facilitate PCI.

Antithrombotics

All balance benefit of anticoagulation with risk of bleeding.

Heparins: UFH/LMWH. Avail. IV (UFH) or as subcutaneous injection (LMWH). Useful in atrial fibrillation, ACS, facilitating PCI, venous thromboembolism, mechanical valves.

UFH requires titration to aPTT. Reversible with protamine. Short half-life (90 min).

LMWH generally needs no titration. Wt-based dosing. Contraindicated in renal failure. Can be monitored with anti-Xa levels. Not reversible & longer half-life. Can be self-administered.

All associated with HIT although risk lower for LMWH.

Warfarin: Inhibits vitamin K dependent clotting factor (II, VII, IX, X) generation.

Oral. Requires aPT (INR) monitoring. Slow to become therapeutic.

Anti-Xa inhibitors:

IV agents: fondaparinux"

Non-vitamin K antagonist oral anticoagulants (NOACs):

Direct thrombin inhibitor: dabigatran

Anti-Xa inhibitors ("Xa" in name): rivaroxiban, apixaban, and edoxaban

Indicated for non-valvular AF and DVT/PE (rivaroxiban and edoxaban)

In AF, less bleeding and less hemorrhagic stroke (Ruff, et al. *Lancet*. 2014;383(9921):955–962. https://www.ncbi.nlm.nih.gov/pubmed/24315724) compared w/ warfarin

Specific reversal agents in development (idarucizumab approved for dabigatran reversal); otherwise partial reversal with non-specific hemostatic agents including prothrombin complex concentrates and recombinant factor VIIa (dialysis partially effective for dabigatran)

Thrombin inhibitors:

IV agents: argatroban, bivalirudin, hirudin, lepirudin

Can be used in place of heparins or to treat HIT.

Antiarrhythmics

Vaughan-Williams classification created 4 classes of antiarrhythmics.

Class I agents: sodium channel blockers

Class II agents: β-blockers

Class III agents: potassium channel blockers

Class IV agents: calcium channel blockers

Commonly Used ICU Antiarrhythmics (also see Appendix & Chapter 9)

Amiodarone: class III agent. Long half-life. Useful with atrial & ventricular arrhythmias. Most effective agent for maintaining sinus rhythm in atrial fibrillation/flutter. IV or PO avail. IV formulation has more β-blocker properties. Causes thyroid, liver, lung, eye toxicity. Typical load for VT/VF is 8–10 g cumulative before switching to maintenance dosing (4–5 g for atrial dysrhythmias).

Lidocaine: class Ib agent. Useful for VT (particularly ischemic VT or post-MI). IV formulation. Hepatic metabolism & renal excretion. Levels should be monitored. Toxicity includes nonspecific CNS effects, & eventually seizures.

Procainamide: class Ib agent. Particularly useful if in bypass tract-dependent arrhythmias (WPW).

Sotalol: combined class II/III (β-blocker/potassium blocker). Useful for VT & atrial fibrillation. Needs careful QTc monitoring.

Ibutilide: class III agent. Particularly useful for chemical cardioversion from atrial fibrillation. Pretreat with magnesium. Monitor QTc.

EXTRACORPOREAL MEMBRANE OXYGENATION AND VENTRICULAR ASSIST DEVICES

GAURAV BUDHRANI, MD • JAMES M. BLUM, MD

Introduction to ECMO

Extracorporeal life support (ECLS) also known as extracorporeal membrane oxygenation (ECMO) is a modified form of cardiopulmonary bypass for patients (pt) experiencing severe pulmonary or cardiac failure

Dates back to the early 1970s, but remained largely unused because at the time there was no evidence to support a survival benefit for patients in severe respiratory failure vs. conventional management

There has been a resurgence in ECMO as of the 2009–2010 H1N1 influenza pandemic

Essentials of Circuit Configuration (Figure 21-1)

Principles: removal of circulating venous blood into venous inflow cannula, passage externally through a pump to a membrane oxygenator for carbon dioxide & oxygen exchange, temp management, & then return into systemic circulation via outflow cannula

Venovenous (VV) approach for pt with respiratory failure

Venoarterial (VA) approach for pt with cardiac failure with or without respiratory failure

Sweep gas flow essentially determines carbon dioxide clearance

Circuit flow is the main driver for oxygenation

Centrifugal pump using rotating impellers to propel blood to oxygenator

Oxygenator: series of hollow fibers through which sweep gas flows internally, & blood externally, to allow for gas exchange

Modes of Perfusion		
	Venovenous (VV)	**Venoarterial (VA)**
Anatomy	Blood removed & returned to venous system	Blood removed from vein & returned to an artery
BP	Determined by native CO & SVR	Determined by pump flow & native SVR
Oxygenation	Yes, can provide full support	Yes, can provide full support
CO_2 removal (ventilation)	Yes, can provide full support	Yes, can provide full support
Cardiac support	None	Yes, can provide full support

Common Terms and Definitions

Rated flow: flow rate of venous blood (vO_2 sat 75%) that can be maximally oxygenated to a vO_2 sat 95% in a min, as measured at the membrane lung outlet

Flow rate of the membrane lung should be > the required flows for maximum pt support

Suspect an oxygenator problem if the postmembrane O_2 sat <95% at flows < maximal rated flow with pre-oxygenator saturation >70%

Sweep gas: gas applied to the membrane oxygenator

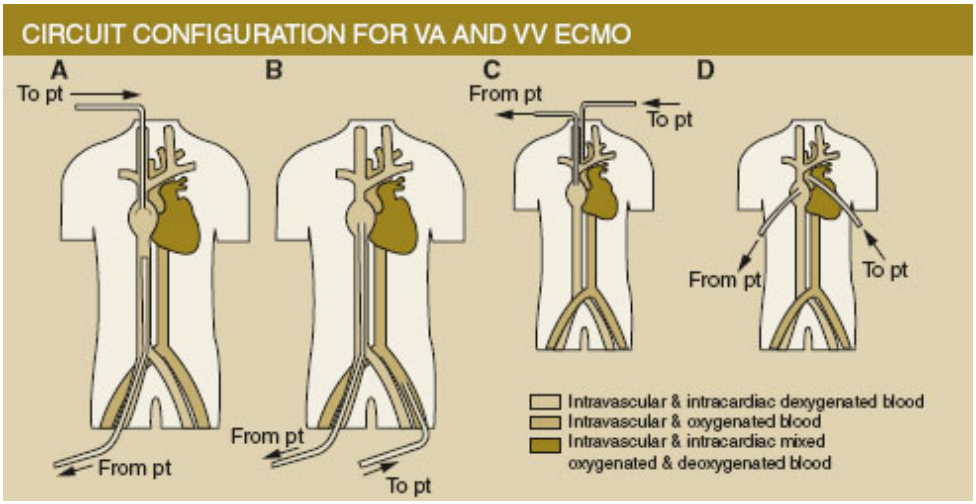
Commonly O_2 or carbogen (95% O_2 + 5% CO_2)

Sweep gas rate controls CO_2 clearance

Priming solution: solution used to fill the circuit prior to cannulation

Commonly crystalloid, albumin, or PRBCs

Figure 21-1. Example of VV and VA Cannulation. (A) VV ECMO (B) VA ECMO, Femoral Cannulation (C) VA ECMO, Carotid Cannulation (D) VA ECMO, Thoracic Cannulation.



Indications for Initiation of ECMO

Consider ECMO at 50% mortality prediction. It is generally indicated at 80% mortality risk for many circumstances (ELSO)

VV-ECMO: hypoxemic respiratory failure due to any cause, hypercarbic respiratory failure, bridge to lung transplantation, surgeries requiring apnea, severe air leak

ARDS/hypoxemic respiratory failure: P/F ratio <150 with Murray Score 2–3 correlates with 50% mortality. P/F ratio <100 with Murray score 3–4 despite optimal care correlates with 80% mortality risk (ELSO)

Carbon dioxide retention on mechanical ventilation despite high ventilating pressure (plateau pressure >30 cm H_2O) with or without pH <7.15

To help prevent intubation in a pt expecting lung transplantation

Any sudden cardiac or respiratory collapse that is unresponsive to optimal care can be considered

VA-ECMO: refractory cardiogenic shock that persists despite adequate volume resuscitation or use of vasopressors & inotropes +/– intra-aortic balloon pump counterpulsation (ELSO)

Typical causes: massive PE, refractory cardiac arrest, fulminant myocarditis, bridge-to-heart transplantation or ventricular assist device placement, primary graft failure following heart transplantation, acute myocardial infarction, or peripartum cardiomyopathy

Septic shock with myocardial dysfunction can be an indication

Contraindications for Initiation of Extracorporeal Life Support Organization (ELSO) (http://www.elso.org/Portals/0/IGD/Archive/FileManager/989d4d4d14cusersshyerdocumentselsoguidelinesforadultrespiratoryfailure1.3.pdf)

The data regarding absolute & relative contraindications is not well-studied & there is a limited consensus around the named relative contraindications & their applications.
(http://www.elso.org/Portals/0/IGD/Archive/FileManager/989d4d4d14cusersshyerdocumentselsoguidelinesfo
radultrespiratoryfailure1.3.pdf and http://www.acc.org/latest-in-cardiology/articles/2015/07/14/09/27/indications-and-complications-for-va-ecmo-for-cardiac-failure)

Strong contraindications:

Mechanical ventilation ≥7 days

CNS catastrophes: significant anoxic brain injury, diffuse axonal injury, massive intracranial hemorrhage, or herniation

Irreversible pulmonary condition that is not amenable to lung transplantation

Death within 3 hrs of intubation

ARDS not severe enough to meet usual inclusion criteria

Unrecoverable heart & not a candidate for heart transplant or vetricular assist device (VAD)

Chronic severe organ dysfunction: examples include emphysema, cirrhosis, renal failure

Compliance: psychosocial, financial, or cognitive concerns particularly when considering bridge to device or transplant.

Prolonged CPR without adequate tissue perfusion

Relative contraindications:

Age over 70

Immunocompromised state: solid-organ or stem-cell transplant, solid-organ or hematologic malignancy, chronic immunosuppressive therapy, HIV/AIDS, & inherited immunodeficiency syndromes

Chronic CNS deficit or CNS status unknown

High risk for anticoagulation

Multiorgan dysfunction syndrome

Anticoagulation:

Heparinize (50–100 units/kg) for cannula placement

Heparin gtt to maintain ACT >1.5 × normal

Ventilator settings:

Oxygenation & ventilation primarily accomplished by the membrane lung
Follow pre- & postmembrane lung gases
Ventilator settings should focus on resting the lung, esp. in pt with respiratory failure or inflammation → low RR, plateau <30, FiO_2 <0.3, PEEP to prevent atelectasis without compromising venous return
If possible, allow spontaneous respirations

Expected Oxygen Saturations: Determined by Cannulation Type and Location			
	VV	**Peripheral VA**	**Central VA**
Anatomy	Returned oxygenated blood enters venous system & mixes with systemic deoxygenated venous blood	Returned oxygenated blood flows retrograde from femoral artery & mixes in the midaorta with desaturated systemic blood pumped through the native heart	Returned oxygenated blood flows into proximal aorta
Expected SaO_2	If little or no native lung function, expect SaO_2 ≥80% & SvO_2 >60%	Variable, depending on where mixture in the aorta occurs & where blood is sampled	Close to 100%
Special concerns	Due to the lower expected SaO_2, must maintain adequate CO & Hct for sufficient tissue oxygen delivery	Beware of inadequate oxygenated perfusion of coronary & cerebral arteries. Expect more proximal aortic mixing with higher pump flows	Knowing cannula location is critical. Unusual cannula placements can affect management in emergencies (e.g., cardiac arrest in a PA–Aortic cannulated pt → R heart support for adequate preload is essential!)

Weaning:
Start weaning trials once the required cardiac and/or pulmonary support provided by ECLS is <30%
Method of weaning highly variable depending on type of ECLS support & underlying dz

Common Problems			
	VV	**Peripheral VA**	**Central VA**
Hypotension	Hypovolemia Pneumothorax Cardiac tamponade Low SVR **Low native CO**	Low pump flow **Hypovolemia** (look for circuit "chugging") Cannula malposition Cardiac tamponade Pneumothorax Low SVR	Same as peripheral VA
HTN	High SVR state	High SVR state—consider adding vasodilators (e.g., nitroprusside, esmolol, etc.) High pump flow Cannula malposition—measure at multiple sites, upper & lower extremity	Same as peripheral VA
Hypoxia	**High native CO:** higher blood flows through the native diseased lungs Malfunctioning membrane lung (e.g., clotting) Required flows are > the membrane lung's rated flow Low pump flows Cannula malposition	**High adrenergic state**—pain, agitation, iatrogenic (vasopressors) causing high native CO **Cannula malposition**—sample at multiple sites **High native CO:** results in more distal mixing of oxygenated & deoxygenated blood in the aorta. Can add an additional RA return cannula (VVA), change to central cannulation, ↑ pump flows, or ↓ native CO (e.g., esmolol gtt) Low pump flow **Hypovolemia**—membrane clotting	**High adrenergic state**—pain, agitation, iatrogenic (vasopressors) causing high native CO **High native CO:** consider adding agents to ↓ native inotropy (e.g., esmolol gtt) Low pump flow Membraneclotting
Hypercarbia	Malfunctioning membrane lung (e.g., clotting) High native CO Low pump flow	Same as VV	Same as VV

Hematologic:

Bleeding: most common problem with ECLS

Minimize unnecessary procedures (e.g., venipuncture, ETT suctioning, etc.)

Ensure anticoagulation is within the appropriate range

If uncontrolled hemorrhage, can consider reversal of anticoagulated state with FFP, platelets, & antifibrinolytics (e.g., Amicar) & turning off the heparin gtt but risk of circuit clotting increases

Thrombocytopenia:

Ddx: drug effect, underlying disorder, splenic/liver sequestration after platelet activation from exposure to the ECLS circuit, heparin induced thrombocytopenia (HIT)

Consider argatroban gtt if suspicion for HIT is high

Hemolysis:

Causes: membrane inlet suction pressure <−100 mmHg; pump clots; high flows through a small return cannula (outlet pressure >300 mmHg); occlusions in the return circuit

Circuit clotting:

No action required for clots <5 mm

Exchange circuit or replace the circuit section with the clot

Check ACT levels; consider AT3 deficiency & FFP transfusion for recurrent clotting despite appropriate heparin dosage

Inadequate venous drainage:

Replace cannula with a larger cannula

Place additional venous cannula in a separate location

Catastrophes:

Air entrainment or O_2 emboli: (1) stop pump & clamp cannulas/lines near the pt, institute support settings; (2) locate source of air entrainment (e.g., drainage vs. return line, membrane lung)

Check cannulation site of the drainage cannula for leaks

Check connectors & stopcocks in the circuit tubing

Check other IV lines in the pt

Keep systemic BP greater than the sweep gas pressure; keep the membrane lung below pt level

Power failure:

Should automatically revert to the backup battery (30–60 min energy supply)

Turn off unessential, high-energy components of the circuit (e.g., heated water bath)

Identify cause of the power failure

If unable to restore power and/or battery fails, use the manual hand crank

Unintentional decannulation:

Stop pump, clamp lines close to pt, & apply pressure to the original cannulation site

Initiate backup ventilator settings

Ischemic/embolic events:

Limb ischemia from peripheral cannulation

Coronary or cerebral ischemia from inadequate oxygenation with peripheral VA ECLS

Inadequate flows for organ perfusion (e.g., renal failure)

Embolic events due to inadequate anticoagulation

Ventricular Assist Devices

Introduction to VADs (Keon WJ, et al. *Can J Cardiol.* 1996;12(10):1017–1030; Frederick A., et al. *A Practical Approach to Cardiac Anesthesia*. Lippincott Williams & Wilkins; 2008)

Use of Ventricular Assist Devices (VADs) has continued to increase over the past 2 decades. They are designed to assist a failing ventricle with mechanical support.

Devices are avail. for either implanted permanent support or temporary support through an extracorporeal pump.

Permanent devices are only approved for left ventricular support (except total artificial heart [TAH]) & can be used as either a bridge to transplant or a destination therapy, meaning the pt will not get a transplant.

Indications of LVED: for Severe Cardiogenic Shock & Hemodynamic Compromise as a Bridge to Transplant or for Ongoing Support as "Destination" Therapy

Physiologic Benefits

Decreased myocardial work & O_2 consumption

Decreased myocardial wall tension

Increased ventricular unloading

Increased CO

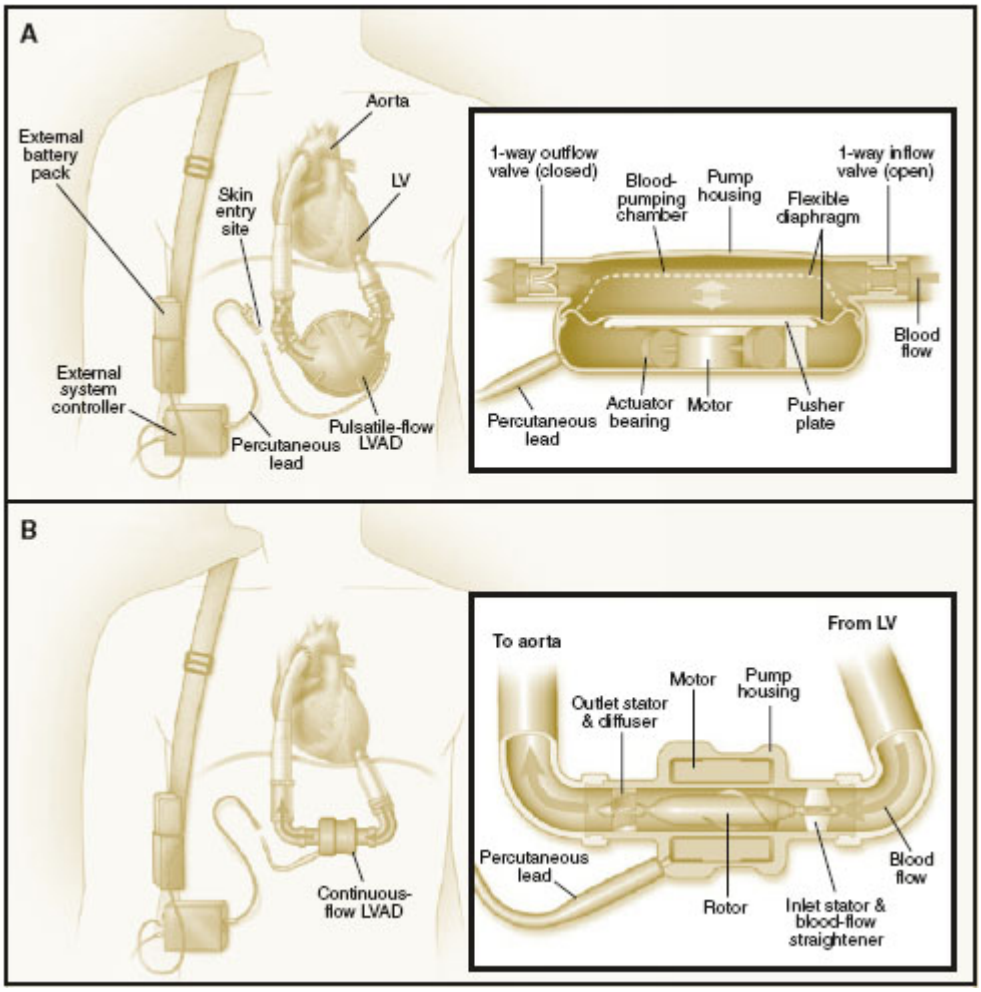
Components/Types (Figure 21-2)

Composed of cannulas (inflow cannula to the pump, outflow cannula returning blood to the pt), pump (pulsatile or continuous flow pumps), & a power supply

Used in parallel to the native heart; does not require excision of the diseased ventricles, as with TAHs

Types of VADs		
Types	**Cannulation Sites**	**Notes**
LVAD (LV assist device)	Inflow cannula: LV apex Outflow cannula: ascending aorta	LA can be cannulated for the inflow cannula for short-term therapy only given risk of LV thrombus formation from blood stasis
RVAD (RV assist device)	Inflow cannula: RA or RV Outflow cannula: PA	Significantly lower risk of RV thrombus formation with RA cannulation
BiVAD (Biventricular assist device)	Combination of the LVAD & RVAD	Provides complete cardiovascular support

Figure 21-2. Example of LVAD Devices. (A) Pulsatile-Flow LVAD and (B) Continuous-Flow LVAD.



(Slaughter MS, et al. *N Engl J Med.* 2009;361:2241–2251)

Types of VAD Pumps			
Pump Type	**Valves**	**Comments**	**Examples**
Pulsatile (a) volume displacement	Inflow & outflow valves	More afterload insensitive	Abiomed BVS 5,000 Heartmate XVE (Thoratec) PVAD/IVAD (Thoratec) Worldheart (Novacor)
Continuous flow (a) axial flow (b) centrifugal flow	None	Pros: smaller, easier implantation Cons: • No palpable pulses or arterial waveform (e.g., out of hospital arrest) w/ full support • Afterload sensitive; e.g., poor RVAD flow w/ ↑ PVR • Poor preload can cause "device regurgitation" due to lack of valves	HeartMate II (Thoratec) Incor (Berlin Heart) Jarvik 2,000 (Jarvik Heart) CentriMag Hemopump Impella (see below)

PVAD, paracorporeal ventricular assist device; IVAD, implantable ventricular assist device.

Management

Hematology:

Requires chronic systemic anticoagulation & antiplatelet therapy after initial postop period

If transfusions are indicated for transplant candidates, consider leuko-reduced PRBCS to minimize alloantibody formation

Right heart function in LVAD pt:

Critical to maintain right heart function in LVAD-only pt

May require inotropes, chronotropes, systemic vasoconstrictors, & pulmonary vasodilators

Follow CVP & PA pressure as markers of R heart failure & RV afterload

LVAD effect on valvular dysfunction or patent foramen ovale (PFO):

May worsen preexisting AI (aortic insufficiency) by decreasing left ventricular end diastolic pressure (LVEDP) from unloading in the setting of increasing systolic BP (SBP)

May unmask or worsen PFOs (Right atrial pressure (RAP) > Left atrial pressure (LAP) with L-sided unloading)

Arterial waveforms:

Arterial waveforms corresponding to ECG QRS in continuous flow VADs indicate native left ventricular function

Complications (Genovese EA, et al. *Ann Thorac Surg.* 2009;88:1162–1170)

High cumulative incidence of ≥1 significant adverse event in the acute (<60 days) postimplantation period

Early complications (post-operative day (POD) 0–10):

Arrhythmias

Ventricular arrhythmias particularly common given ventricular insertion site

Replete electrolytes; consider antiarrhythmic medications (e.g., amiodarone), cardioversion, & implantable cardioverter-defibrillator (ICD) placement depending on the arrhythmia's effect on VAD filling

Preexisting ICDs should NOT be deactivated after LVAD or RVAD placement

Refractory malignant arrhythmias may require conversion to BiVAD

Tamponade

Significant bleeding

Renal/hepatic injury

Late complications (POD 11–60)

Infxn, neurologic events, thromboembolism, reoperation

Device malfunction: suspect with poor device flow & TEE/TTE evidence of a nondecompressed, cannulated ventricle

Right heart failure: in patient with LV support only; suspect with poor device flow & TEE/TTE evidence of a decompressed LV

Minimally Invasive Interventions

Percutaneous VADs (Pulido JN, et al. *J Cardiothorac Vasc Anesth*. 2010;24(3):478–486)

Indications

Short-term (<14 days) therapy of cardiogenic shock
Bridge to procedure (e.g., longer-term VAD placement)
Cardiac support for complex percutaneous cardiac procedures

Types of Percutaneous VADs		
	Tandem Heart	**Impella**
Anatomy & placement	Transseptal left atrial-to-femoral arterial device Inflow/drainage cannula inserted in the femoral vein → RA → trans-septally → tip positioned in LA Outflow/return cannula inserted in the common femoral artery → advanced to common iliac artery	Femoral artery or R axillary artery insertion Positioned across the aortic valve with the distal inflow port in the LV & the proximal outflow port in the aorta Placed in cath lab
Flow dynamics	Continuous, low-speed, centrifugal pump Nonpulsatile flow	Axial flow rotary pump Nonpulsatile flow
Flow rates	Up to 4–5 l/min at 7,500 rpm	3 sizes (2.5, 3.5 & 5.0) that provide maximum 2.5 l/min, 3.5 l/min, or 5 l/min flows
Anticoagulation	Systemic anticoagulation w/ heparin gtt	Systemic anticoagulation w/ heparin gtt
Contraindications	Severe RV dysfunction or failure (when used as a L heart device) Severe AI VSD Severe PAD and/or femoral grafts Contraindications to anticoagulation IVC filter (relative)	Severely calcified AV +/– AS Prosthetic AV Severe AI Severe PAD
Efficacy over intra-aortic balloon pumps (IABPs)	RCTs show no mortality benefit over IABPs (Thiele H, et al. *Eur Heart J.* 2005;26(13):1276–1283; Burkhoff D, et al. *Am Heart J.* 2006;152(3):469)	RCTs & meta-analysis showed improved hemodynamics but no proven mortality benefit compared to IABPs (Seyfarth M, et al. *J Am Coll Cardiol.* 2008;52:1584–1588; Cheng JM, et al. *Eur Heart J.* 2009;30:2102–2108)
Complications	CVAs; vascular injury; limb ischemia; hemorrhage; hemolysis, thrombocytopenia Catheter migration Paradoxical embolism: secondary to transseptal approach Cardiac tamponade	CVAs; vascular injury; limb ischemia; hemorrhage; hemolysis, thrombocytopenia Catheter migration: LV overload if proximal port is too deep or aortic valve leaflets are unable to coapt cardiac tamponade

Intra-aortic Balloon Pump (Bolooki H. Clinical Application of Intra-Aortic Balloon Pump, 3rd Edition, Wiley-Blackwell, 1998) (Figure 21-3)

Indications

Supports short-term LV failure refractory to maximum medical inotropic support (e.g., acute cardiogenic shock, failure to wean from intraoperative CPB, acute MI/unstable angina)

Temporizing measure until cardiac recovery or as a bridge to other procedures (e.g., transplant, complex/high-risk PTCA, VAD, etc.)

Improves myocardial O_2 supply & demand balance

Improves coronary perfusion by diastolic augmentation (increase diatolic BP [dBP] & decrease LVEDP) → increases coronary perfusion pressure (CPP)

CPP = dBP – LVEDP

Systolic unloading: decrease MVO_2 by decreasing systolic aortic pressure → decreased LV afterload & decreased LVEDP

Strong Contraindications

Severe AI: diastolic balloon inflation → increase AI → LV distension → decrease CPP, increase myocardial O_2 consumption

Relative Contraindications

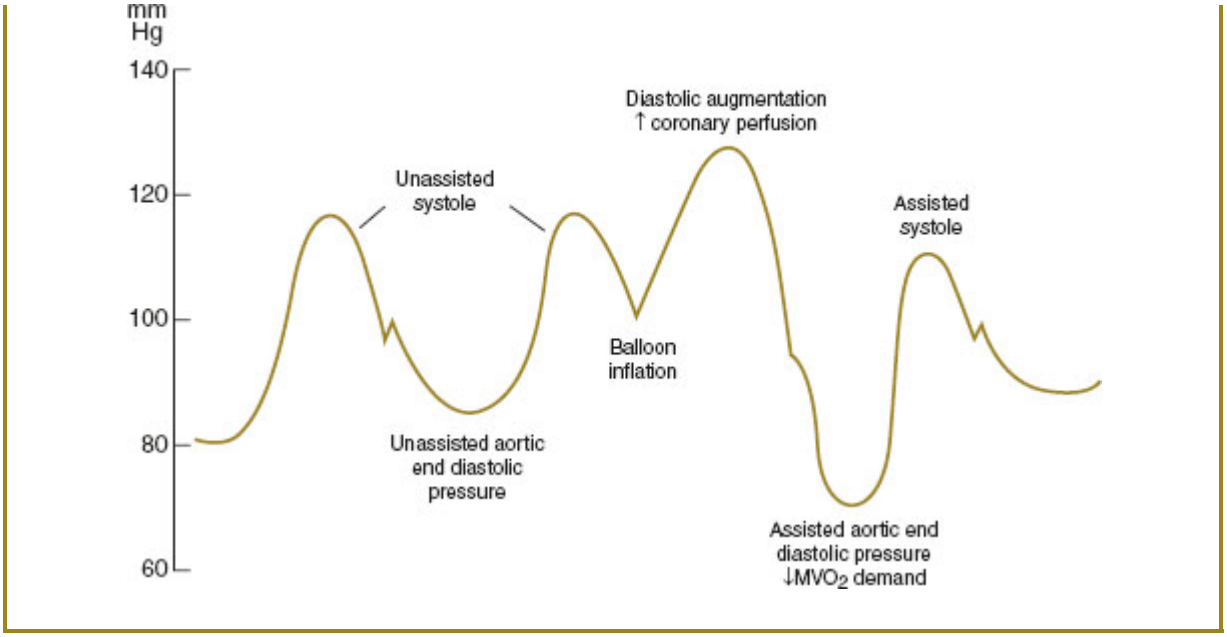
Sepsis

Severe vascular dz (e.g., Abdominal or Thoracic Aortic Aneurysm (AAA, TAA), femoral grafts for vascular dz, etc.)

Severe LV failure

Irregular, rapid rhythms → makes IABP synchrony more difficult

Figure 21-3. Aortic Pressure Waveforms of IABP.



Equipment/Components

Placed intraoperatively, in the cath lab, or at the bedside emergently via the femoral artery

Other insertion locations: ascending aortic arch, subclavian artery, axillary artery, iliac artery

Verify placement with TEE, fluoroscopy or CXR

On CXR, tip should be at the anterior 2nd intercostal space & 1st lumbar vertebra

Balloon is threaded to the descending aorta, with the tip just distal to the L subclavian artery takeoff & proximal to the renal arteries

Helium (30–50 ml) used as the inflating gas due to low density, rapid diffusion coefficient

Management

Balloon inflation & deflation:

Synchronized to the QRS or more commonly, to an arterial waveform

Balloon inflation: timed to aortic dicrotic notch or immediately after the ST–T wave

Balloon deflation: timed to the beginning of the systolic upstroke or the start of the R wave = beginning of systole

Markers of a correctly timed IABP:

Augmented dBP should be greater than unassisted systolic peak pressure

The augmented dBP is often falsely displayed as the computed sBP from a peripheral arterial line → follow MAPs in pt with IABPs instead

Augmented end-dBP (aka ballooned aortic end-diastolic pressure) should be *lower* than the unassisted end-dBP

Assisted peak sBP should be *lower* than the unassisted peak sBP

Anticoagulation:

Discuss anticoagulation plan with surgeon for postop pt (they may already be fully anticoagulated)

If no contraindications, start heparin gtt with goal PTT 1.5–2 × normal

Positioning:

Keep the limb with the inserted IABP straight

Weaning:

Maximum support is a 1:1 ratio of IABP-supported beats to native cardiac beats

Start weaning when the pt is no longer requiring maximum medical inotropic support and/or underlying issue has resolved

Gradually decrease the IABP ratio from 1:1 → 1:2, 1:3, 1:4, etc., & monitor the hemodynamic response

To prevent thrombus formation, the IABP is not turned off in situ unless the pt is anticoagulated

Complications

Improperly timed inflation/deflation:

Early balloon inflation or late balloon deflation → increase LV afterload & decrease LV ejection as LV ejects against an inflated balloon

Late balloon inflation → decrease diastolic augmentation → suboptimal coronary perfusion

Early balloon deflation → decrease LV unloading

Vascular injury:

Aortic dissection or rupture; aortic arch injury

Limb ischemia

Mesenteric ischemia

Balloon malfunction:

Balloon migration: occlusion of renal or L subclavian arteries

Balloon entrapment

Resistance to balloon catheter removal due to incomplete balloon deflation (clots in or malfunction of the gas lumen) or a kinked central catheter

Treatment: confirm dx with angiography, may require surgical removal; literature reports of successful removal after instilling & aspirating tPA, streptokinase, or urokinase into the driving gas line

Gas emboli:

Balloon rupture → suspect if there is blood in the driving gas line, low balloon pressure alarm, loss of diastolic augmentation → immediately stop the IABP → examine &, if needed, replace the balloon, head CT, *can consider hyperbaric chamber for massive He emboli, if avail.*

Air emboli from the pressure monitoring port at the tip of the balloon can cause CVAs given the port's location near the carotid arteries

Infection

Hemorrhage

HEMATOLOGY, FLUID AND ELECTROLYTE MANAGEMENT

YASSER EL KOUATLI, MD • LENA M. NAPOLITANO, MD, FACS, FCCP, MCCM

Anemia in the ICU

Anemia is common in ICU patients (pt), with >90% of pt with anemia on ICU day 3

Anemia persists after ICU discharge, with >50% of pt still anemic 6 mo after ICU discharge

Etiologies of anemia in the ICU include blood loss related to daily phlebotomy, hemodilution due to crystalloid fluid resuscitation, renal replacement therapies, renal dz, hemorrhage, occult blood loss from the GI tract, bone marrow suppression due to dz, drug-induced anemia, & nutritional deficiencies such as iron, folate, & vitamin B12 deficiency

In ICU pt with anemia & chronic kidney dz, treatment with erythropoietin-stimulating agents (ESAs) is indicated, with target Hgb concentrations no higher than 9 g/dl. Adjunctive iron treatment should be strongly considered, as optimal response to ESAs requires supplemental iron

In most ICU pt, the etiology of anemia is "anemia of inflammation" or "anemia of chronic dz (ACD)"

Anemia of inflammation develops via 3 mechanisms: (1) impaired iron regulation, (2) shortened red blood cell (RBC) life span, & (3) reduced rate of erythropoiesis related to inappropriate erythropoietin response

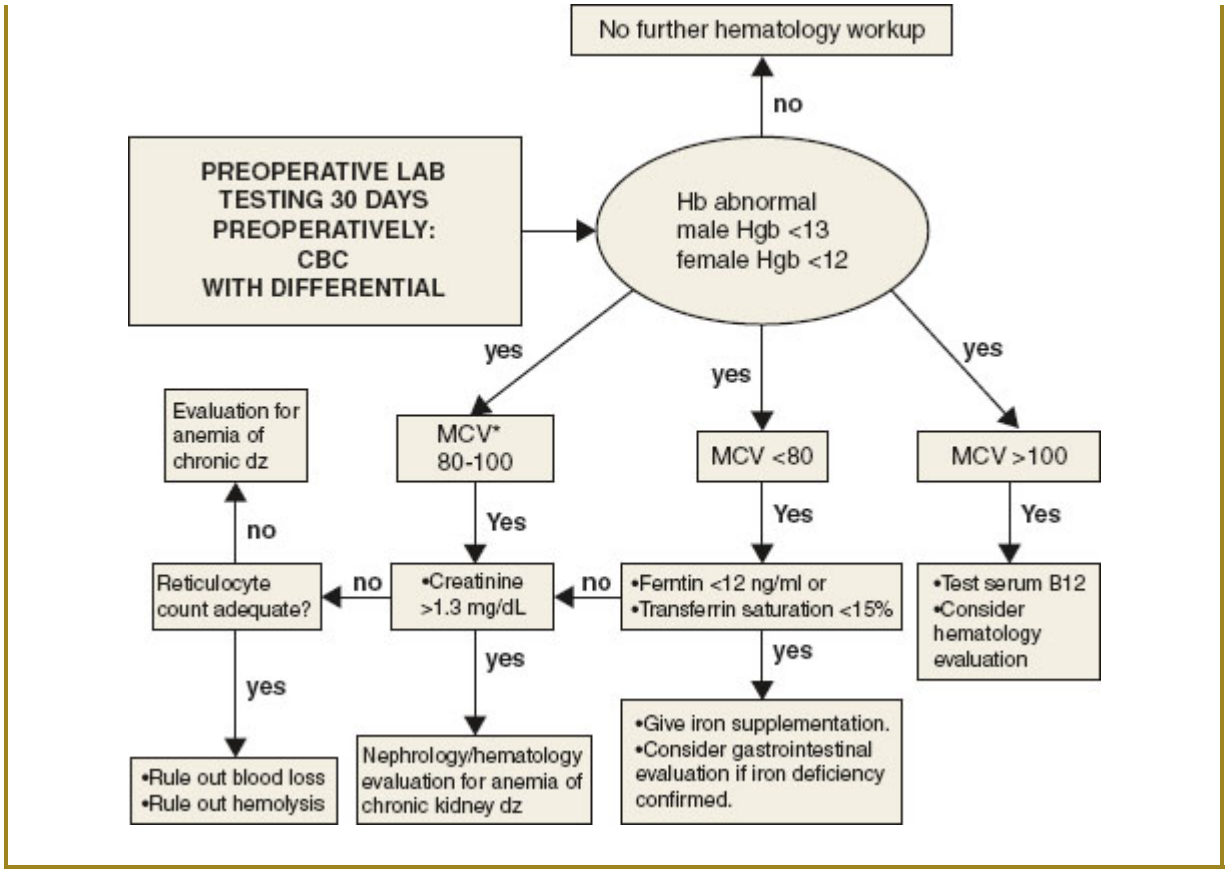
Hepcidin is the main iron regulatory hormone, made primarily in hepatocytes, & causes functional iron deficiency, hypoferremia, & iron-restricted erythropoiesis despite normal iron stores by blocking enteral iron absorption & shuttling iron into macrophages where it is unavailable for erythropoiesis

Hepcidin concentrations are high in anemia of inflammation & ACD (Hayden SJ, et al. *Am J Respir Crit Care Med.* 2012;185(10):1049–1057)

Anemia: Clinical Approach to Diagnostic Evaluation

ICU pt with anemia should undergo a diagnostic evaluation as for any pt with anemia (Fig. 22-1)

Figure 22-1. Diagnostic Evaluation of Anemia



(From Goodnough LT, et al. *Anesth Analg.* 2005;101(6):1858–1861)

Determination of the causative factors for anemia will allow appropriate anemia management which will aid in avoiding RBC transfusion solely for the treatment of anemia

Anemia and Diagnosis of Iron Deficiency in the ICU

Iron deficiency is difficult to diagnose in ICU pt since most will have high ferritin levels related to inflammation. In these pt, check zinc protoporphyrin which will be high in iron deficiency

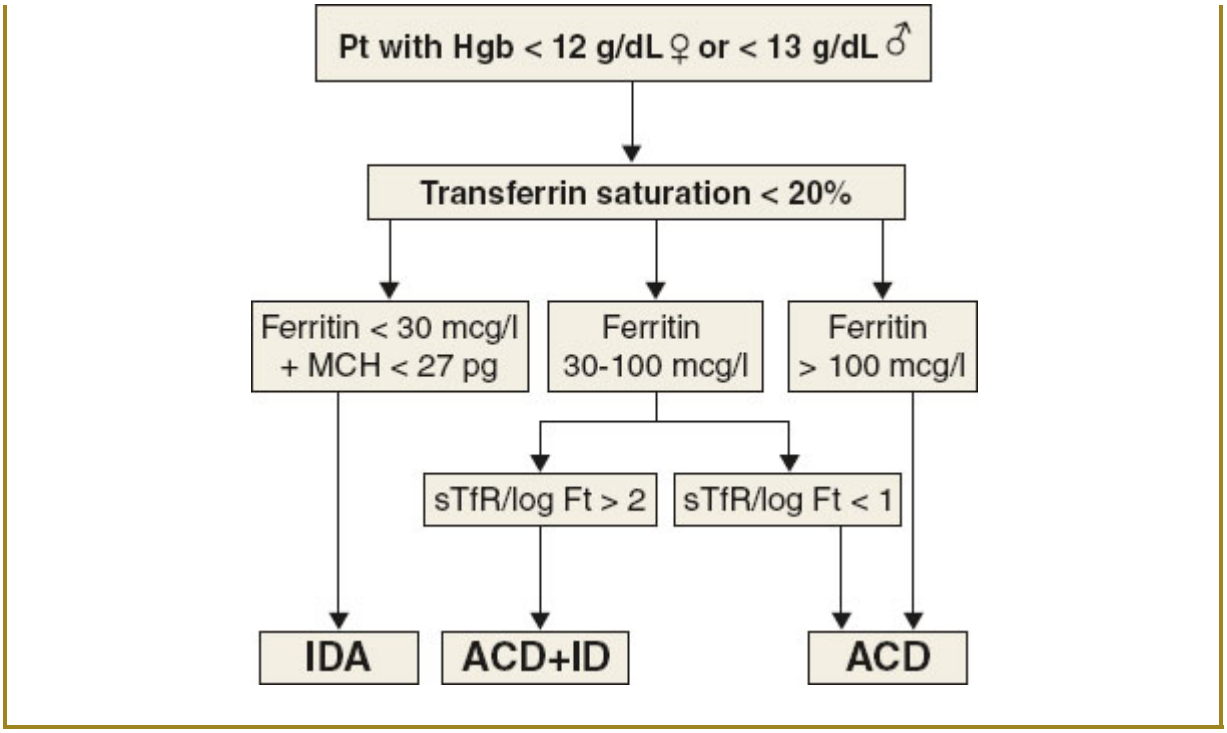
In the presence of inflammation true iron deficiency is defined by a ferritin <100 ng/ml & a TSAT <20% (TSAT [transferrin saturation] is calculated by dividing the serum iron by the total iron-binding capacity [TIBC]), whereas functional iron deficiency is defined by ferritin >100 ng/ml & a TSAT <20% (Fig. 22-2).

Total iron deficit (TID) can be calculated using the Ganzoni formula: TID (mg) = wt (kg) × (ideal Hgb – actual Hgb) (g/dl) × 0.24 + depot iron (500 mg)

According to this formula, a person weighing 70 kg with a Hgb level of 9 g/dl would have a body iron deficit of about 1,400 mg. Following the administration of oral iron, it takes 2–2.5 wks for the Hgb to start rising, 2 mo for it to return to normal levels, & 6 mo for iron stores to be replete

In anemia of inflammation or ACD, enteral iron absorption is problematic due to high hepcidin concentrations which block enteral iron absorption, & IV iron should be considered

Figure 22-2. A Simplified Algorithm for the Diagnosis of Iron Deficiency Anemia



ACD, anemia of chronic disease; Hgb, hemoglobin; IDA, iron deficiency anemia; MCH, mean corpuscular hemoglobin; sTFR, serum transferrin receptor.
(Modified from Weiss G, Goodnough LT. *N Engl J Med.* 2005;352(10):1011–1023; From Muñoz M, et al.
J Clin Pathol. 2011 Apr;64(4):287–296)

Transfusion and Transfusion Triggers in the ICU

Red Blood Cell Transfusion

RBC transfusion is common in ICU pt, with 40–50% receiving RBC transfusion during the ICU stay

The Transfusion Requirements in Critical Care (TRICC) Trial confirmed that ICU pt 30-day mortality was not different in pt randomized to a restrictive (transfuse if Hgb <7 g/dl) or liberal (transfuse if Hgb <10 g/dl) transfusion strategy (Hebert PC, et al. *N Engl J Med.* 1999 Feb 11;340(6):409. Erratum in: *N Engl J Med.* 1999 Apr 1;340(13):1056)

Indications

RBC transfusion for stable ICU pt without acute cardiac ischemia: guidelines recommend transfusion when Hgb <7 g/dl (see Guideline Executive Summary below)

For ICU pt with acute cardiac ischemia: transfuse RBCs if Hgb <8 g/dlz

Summary of Recommendations from Guidelines for RBC Transfusion in Adult Trauma and Critically Ill Patients

A. Recommendations Regarding Indications for RBC Transfusion in the General Critically III Patient

1. RBC transfusion is indicated for pt with evidence of hemorrhagic shock. (Level 1)
2. RBC transfusion may be indicated for pt with evidence of acute hemorrhage & hemodynamic instability or inadequate oxygen delivery. (Level 1)
3. A "restrictive" strategy of RBC transfusion (transfuse when Hgb <7 g/dl) is as effective as a "liberal" transfusion strategy (transfusion when Hgb <10 g/dl) in critically ill pt with hemodynamically stable anemia, except possibly in pt with acute myocardial ischemia. (Level 1)
4. The use of only Hgb level as a "trigger" for transfusion should be avoided. Decision for RBC transfusion should be based on an individual pt's intravascular volume status, evidence of shock, duration & extent of anemia, & cardiopulmonary physiologic parameters. (Level 2)
5. In the absence of acute hemorrhage RBC, transfusion should be given as single units. (Level 2)
6. Consider transfusion if Hgb <7 g/dl in critically ill pt requiring mechanical ventilation (MV). There is no benefit of a "liberal" transfusion strategy (transfusion when Hgb <10 g/dl) in critically ill pt requiring MV. (Level 2)
7. Consider transfusion if Hgb <7 g/dl in resuscitated critically ill trauma pt. There is no benefit of a "liberal" transfusion strategy (transfusion when Hgb <10 g/dl) in resuscitated critically ill trauma pt. (Level 2)
8. Consider transfusion if Hgb <7 g/dl in critically ill pt with stable cardiac dz. There is no benefit of a "liberal" transfusion strategy (transfusion when Hgb <10 g/dl) in critically ill pt with stable cardiac dz. (Level 2)
9. RBC transfusion should not be considered as an absolute method to improve tissue oxygen consumption in critically ill pt. (Level 2)
10. RBC transfusion may be beneficial in pt with acute coronary syndromes (ACS) who are anemic (Hgb ≤8 g/dl) on hospital admission. (Level 3)

B. Recommendations Regarding RBC Transfusion in Sepsis

1. There are insufficient data to support Level 1 recommendations on this topic.
2. The transfusion needs for each septic pt must be assessed individually since optimal transfusion triggers in sepsis pt are not known & there is no clear evidence that blood transfusion increases tissue oxygenation. (Level 2)

C. Recommendations Regarding RBC Transfusion in Patients at Risk for or with Acute Lung Injury (ALI) and ARDS

ALI & ARDS are common clinical sequelae of massive transfusion. Prior studies have suggested that RBC transfusion is associated with respiratory complications, including ALI & ARDS that remains even after adjusting for potential confounders.

1. There are insufficient data to support Level 1 recommendations on this topic.
2. All efforts should be initiated to avoid RBC transfusion in pt at risk for ALI & ARDS after completion of resuscitation. (Level 2)
3. All efforts should be made to diagnose & report transfusion-related ALI (TRALI) to the local blood bank because it has emerged as a leading cause of transfusion-associated morbidity & mortality, despite under-dx & under-reporting. (Level 2)
4. RBC transfusion should not be considered as a method to facilitate weaning from MV. (Level 2)

D. Recommendations Regarding RBC Transfusion in Patients with Neurologic Injury and Diseases

1. There are insufficient data to support Level 1 Recommendations on this topic.
2. There is no benefit of a “liberal” transfusion strategy (transfusion when Hgb <10 g/dl) in pt with moderate-to-severe traumatic brain injury. (Level 2)
3. Decisions regarding blood transfusion in pt with subarachnoid hemorrhage (SAH) must be assessed individually since optimal transfusion triggers are not known & there is no clear evidence that blood transfusion is associated with improved outcome. (Level 3)

E. Recommendations Regarding RBC Transfusion Risks

1. There are insufficient data to support Level 1 Recommendations on this topic.
2. RBC transfusion is associated with increased nosocomial infxn (wound infxn, pneumonia, sepsis) rates independent of other factors. (Level 2)
3. RBC transfusion is an independent risk factor for MOF & SIRS. (Level 2)
4. There is no definitive evidence that prestorage leukocyte depletion of RBC transfusion reduces complication rates, but some studies have shown a reduction in infectious complications. (Level 2)
5. RBC transfusions are independently associated with longer ICU & hospital length of stay, increased complications, & increased mortality. (Level 2)
6. There is a relationship between transfusion & ALI & ARDS. (Level 2)

F. Recommendations Regarding Alternatives to RBC Transfusion

1. There are insufficient data to support Level 1 recommendations on this topic.
2. Recombinant human erythropoietin (rHuEpo) administration improves reticulocytosis & hematocrit & may decrease overall transfusion requirements. (Level 2)
3. Hgb-based oxygen carriers (HBOCs) are undergoing investigation for use in critically ill & injured pt but are not yet approved for use in the United States. (Level 2)

G. Recommendations Regarding Strategies to Reduce RBC Transfusion

1. There are insufficient data to support Level 1 recommendations on this topic.
2. The use of low-volume adult or pediatric blood sampling tubes is associated with a reduction in phlebotomy volumes & a reduction in blood transfusion. (Level 2)
3. The use of blood conservation devices for reinfusion of waste blood with diagnostic sampling is associated with a reduction in phlebotomy volume. (Level 2)
4. Intraoperative & postoperative blood salvage & alternative methods for decreasing transfusion may lead to a significant reduction in allogeneic blood usage. (Level 2)
5. Reduction in diagnostic lab testing is associated with a reduction in phlebotomy volumes & a reduction in blood transfusion. (Level 2)

From Napolitano LM, et al. *Crit Care Med.* 2009;37(12):3124–3157.

Technical aspects

ABO-Rh compatibility: RBC serology requires transfusion from pt with compatible ABO & Rhesus groups. In pt with multiple transfusion subgroup (A1, A2) & other groups (MN, K, D, L) compatibility becomes necessary

Crossmatched blood should be used unless unavailable or in emergent situations

Temp: rewarming blood products is a necessity as they are refrigerated for storage

Room temp is acceptable for slow & low-volume transfusions but using a blood warmer is necessary to prevent hypothermia if higher volume of blood products are transfused

Tubing & filters: blood tubing with a filter should be used for transfusions, the use of microfilters (pores of 30–40 micron) has not been associated with reduced complications

Monitoring during transfusions: pt vital signs including temp should be monitored during & after completion of RBC transfusions

In patients with bleeding or hemorrhagic shock:

Use uncrossmatched blood (Type O)—if hemodynamic instability due to hemorrhagic shock
Substitute type-specific blood—for type O as soon as possible (in order to minimize exposure to anti-A & anti-B antibodies in type O blood)
Transfusion rate depends on bleeding rate, do not rely on Hgb

Complications

Citrate toxicity: metabolic alkalosis & hypoCa+ with low levels of ionized calcium in pt with impaired liver function or after massive transfusions
Electrolytes: low ionized calcium, hyperkalemia
Transfusion-related febrile reactions
Anaphylactoid reactions
Immunomodulation: with increased risk for infxns
Graft vs. host dz
Hemolytic reactions
Transfusion-related acute lung injury (TRALI)
Infxn: by contamination from donor (decreasing incidence) or contamination from manipulation (highest risk of infxn with the transfusion of platelets stored at room temp)
Hypothermia
Overall pt outcomes: many recent studies demonstrated worse outcomes in pt that were transfused in a critical care setting & perioperatively

Fresh Frozen Plasma (FFP) Transfusion (Roback JD, et al. *Transfusion.* 2010;50(6):1227–1239)

Indications

FFP should be transfused to pt requiring massive transfusion

The optimal amount of FFP required in massive transfusion pt is controversial. The guidelines recommend plasma: RBC ratio of 1:2 or more during massive transfusion. Use coagulation studies & clinical evidence of bleeding as a guide

There is no recommendation for or against transfusion of plasma to pt undergoing surgery without massive transfusion

FFP should be transfused in pt with Warfarin therapy–related intracranial hemorrhage but could not recommend for or against transfusion of plasma to reverse Warfarin anticoagulation in pt without intracranial hemorrhage

The guidelines suggested against plasma transfusion for other selected groups of pt, including those with liver dz, Hemophilia (A&B), other factor deficiency & antithrombin deficiency in a situation requiring anticoagulation with heparin

Technical aspects

Same technical aspects include using crossmatched plasma for transfusions in order to avoid a reaction between pt red blood cells & donor antibodies

ABO compatibility required, Rh compatibility not required

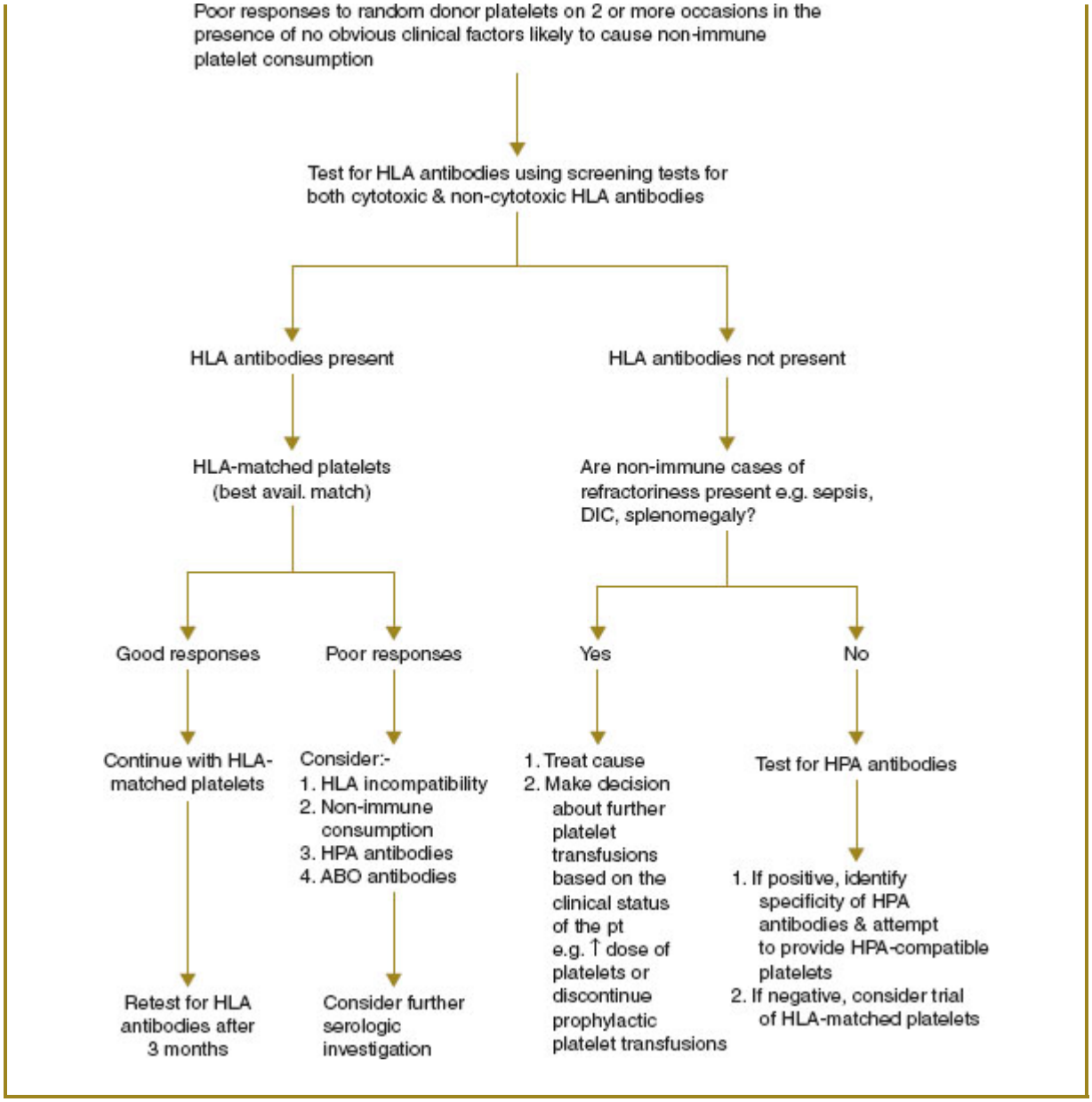
Complications

Identical to RBC transfusion keeping in mind that citrate content is higher in FFP & potassium transfer is not an issue

TRALI has a higher incidence with plasma transfusions (particularly from multiparous female donors). Of note, the American Red Cross now only provides FFP from male donors to reduce the risk of TRALI

Platelet Transfusion (Kaufman RM, et al. *Ann Intern Med.* 2015;162:205–213)

Figure 22-3. Diagnostic Evaluation for Thrombocytopenia Refractory to Platelet Transfusion



Indications and Contraindications

Recommend prophylactic platelet transfusions (single apheresis unit or equivalent) in pt at risk of bleeding, for platelet count ≤10 × 10^9/l

Therapeutic platelet transfusions are required in hemorrhage to keep platelet count >100 × 10^9/l required to create stable clot & minimize rebleeding

Suggest platelet transfusion for pt having elective central venous catheter placement with platelet count <20 × 10^9/l

Suggest platelet transfusion for pt having elective diagnostic lumbar puncture with platelet count <50 × 10^9/l

Suggest platelet transfusion for pt having major elective nonneuraxial surgery with platelet count <50 × 10^9/l

Contraindications to platelet transfusions include thrombotic thrombocytopenic purpura (TTP) & heparin-induced thrombocytopenia (HIT)

Technical aspects

Same as RBC transfusion with the necessity for ABO compatibility but RhD-negative platelet concentrates should be given, when possible, to RhD-negative pt & women in particular

Complications

Technical issues (related to platelet unit contamination & infxn risk), platelet function (deep VT) & immune effects (alloimmunization & hemolysis from residual ABO antibodies)

Some ICU pt will be refractory to platelet transfusions, defined as failure to achieve an appropriate increment after receiving 2 consecutive transfusions with fresh ABO-compatible platelets (Fig. 22-3)

Measurement of platelet count 30 & 60 min following platelet transfusion will determine response.

Cryoprecipitate Transfusion (Nascimento B, et al. *Br J Anaesth.* 2014;113(6):922–934)

Indications

Hypofibrinogenemia in the setting of massive hemorrhage

2nd-line therapy for von Willebrand dz & hemophilia A (factor VIII deficiency)

Technical aspects
Same as all blood products but ABO compatibility is not necessary.

Complications
Similar to all blood products & in case of large volume of ABO-incompatible cryoprecipitate is used, the recipient may develop a positive DAT &, very rarely, mild hemolysis.

Massive Transfusion

Defined as ≥10 units RBC transfusion in 24 hrs
Associated with high mortality rates

Adverse Effects of Massive Transfusion

HypoCa+; blood ionized calcium concentrations should be measured since calcium depletion occurs secondary to citrate chelation; calcium replacement should be administered intravenously (see table below)

Calcium Preparations and Their Use

Solution	Elemental Calcium	Unit Volume	Total Elemental Calcium	Osmolarity
10% Calcium chloride	27 mg (1.36 mEq)/ml	10 ml Ampule	270 mg/10 ml	2,000 mOsm/l
10% Calcium gluconate	9 mg (0.46 mEq)/ml	10 ml Ampule	90 mg/10 ml	680 mOsm/l
10% Calcium chloride continuous infusion	2.45 mg/ml	5 Amps/ 500 ml NS	1,350 mg/550 ml	200 mOsm/l
10% Calcium gluconate continuous infusion	0.82 mg/ml	5 Amps/ 500 ml NS	450 mg/550 ml	67 mOsm/l

Transfusion reaction (given cumulative risk of clerical errors)
Hyperkalemia (secondary to hemolysis in stored blood)
Transfusion-related immunomodulation (TRIM)—increased risk for infxn
Transfusion-related acute lung injury (TRALI)
Transfusion-associated circulatory overload (TACO)

Strategies to Reduce Complications Associated with Massive Transfusion

Massive transfusion protocols should be established with standardized policies to reduce complications related to transfusion therapy

Strategies to Reduce Transfusion-Related Complications	
Complication	**Strategies to Reduce Complication**
Hypothermia	Warm the room Surface warm the pt with heating blankets, heating lamps Heat & humidify inspired gases for ventilators Warm all IV fluids & blood products administered
Coagulopathy	Transfuse RBC: FFP in 1:1 ratio Check coagulation testing, including fibrinogen Transfuse cryoprecipitate if fibrinogen concentration low
Thrombocytopenia	Transfuse platelets to keep platelet count >100,000 (100 × 109/l) to form stable clot
Electrolyte abnormalities	Measure blood potassium, calcium, & magnesium concentrations Replete electrolytes to normal values as indicated
Acid–base disorders	Sodium bicarbonate or THAM for severe met acidosis with hemodynamic instability or renal failure
TRALI	Use restrictive transfusion strategy once hemorrhage controlled Use FFP from men or nulliparous women
TACO	Discontinue crystalloid fluid resuscitation Consider IV diuretic use

Once definitive hemorrhage control has been achieved & the pt is hemodynamically stable, a restrictive approach to transfusion should be implemented, with RBC transfusion for Hgb <7 g/dl

Venous Thromboembolism and Pulmonary Embolism, Prevention Strategies

VTE includes both deep vein thrombosis (DVT) & PE

Critically ill pt are at increased risk of developing VTE; untreated PE has a mortality rate of 25%

Risk factors that predispose ICU pt to VTE include factors common in the general medical population (cancer, surgery, trauma) as well as factors acquired in the ICU (e.g., sedation, immobility, MV, platelet transfusion, vasopressor use, dialysis-dependent renal failure)

VTE risk increases with age

DVT complications include postthrombotic syndrome, phlegmasia cerulean dolens (venous gangrene)

Complications associated with ICU-acquired VTE increase morbidity, mortality length of stay, & costs

Without thromboprophylaxis, VTE incidence ranges from 15% to 60%

Systematic implementation of VTE ppx significantly reduces this rate

All ICU pt should be evaluated on ICU admission for the appropriate VTE ppx therapy

The American College of Chest Physicians (ACCP) publishes guidelines for VTE ppx in ICU

ACCP Guideline Recommendations for Thromboprophylaxis in ICU Patients

For critically ill pt, we suggest using LMWH or LDUH thromboprophylaxis over no ppx (grade 2C)

For critically ill pt who are bleeding, or are at high risk for major bleeding, we suggest mechanical thromboprophylaxis with GCS (grade 2C) or IPC (grade 2C) until the bleeding risk decreases, rather than no mechanical thromboprophylaxis. When bleeding risk decreases, we suggest that pharmacologic thromboprophylaxis be substituted for mechanical thromboprophylaxis (grade 2C) (Kahn SR, et al. *Chest.* 2012;141(2)(suppl):e195S–226S)

Diagnostic Tests for VTE and PE

Venous duplex us of the 4 extremities is the best diagnostic test for VTE in ICU pt

D-dimer assay has high sensitivity (98%) & modest specificity (50%)—is useful for excluding DVT & PE, but not useful for confirming dx. Should not be used in surgical, pregnant or cancer pt

In ICU pt with possible PE, computed tomographic pulmonary angiography (CTPA) is indicated

If normal CXR & contraindication to CTPA (1st trimester pregnancy, IV contrast allergy, impaired renal function), then V/Q scan is useful. If abnormal CXR, steroid/antihistamine pretreatment for IV contrast allergy. If severe allergy, wt risks & benefits of empiric therapy for VTE

Transthoracic echocardiography (TTE) findings of right ventricular strain or dysfunction may be suggestive of PE but are not diagnostic of PE, it may be helpful for ICU pt unable to travel to radiology (Stein PD, et al. *N Engl J Med.* 2006;354(22):2317–2327)

Treatment of VTE and PE

Treatment of VTE or PE is systemic anticoagulation for 3-mo duration (grade 1B)

For systemic anticoagulation, oral anticoagulants (dabigatran, rivaroxaban, apixaban, or edoxaban) are suggested over vitamin K antagonist (grade 2B), except in pt with cancer where LMWH is suggested over VKA or other oral therapies (grade 2C)

For pt with absolute contraindication to anticoagulation, inferior vena cava filter is indicated

Pt with TTE findings consistent with massive PE or with significant cardiovascular compromise should receive either direct or systemic thrombolysis

Pt with cardiopulmonary arrest from suspected PE, consider immediate catheter-assisted thrombus removal, systemic or direct thrombolysis, extracorporeal membrane oxygenation (ECMO), or surgical thrombectomy (Kearon C, et al. *Chest.* 2016;149(2):315–352)

Heparin-Induced Thrombocytopenia (HIT)

HIT is an anticoagulant-induced *prothrombotic* disorder

HIT is an immune-mediated adverse drug effect characterized by platelet activation, hypercoagulability & increased risk of thrombosis, both venous & arterial

HIT is caused by platelet-activating heparin-dependent antibodies of immunoglobulin G class

HIT should be considered when the platelet count falls to <150 × 10^9/l (or by >50% from baseline) between days 5 & 14 of exposure to any heparinoid product

Rapid-onset HIT can occur if heparin is given to a pt who already has circulating HIT antibiotics, usually due to heparin given in the last 5–100 days

Thrombocytopenia in HIT is usually moderate – mean platelet count 60 × 10^9/l

Thrombocytopenia in HIT usually recovers within a few days of heparin discontinuation

Reported mortality rate with HIT ranges between 10% & 20%

A high index of suspicion is required for early recognition of HIT

A clinical scoring system is used to identify pt with HIT, called the "4 Ts"

Clinical Scoring System Used to Diagnose HIT: The "Four T's"

	Points (0, 1, or 2 for each of the 4 Categories): Maximum Score = 8		
	2	1	0
Thrombocytopenia	>50% platelet decrease to nadir ≥20	30–50% platelet ↓, or nadir 10–19, or >50% decrease secondary to surgery	<30% platelet ↓, or nadir <10
Timing* of onset of platelet ↓ (or other sequelae of HIT)	Days 5–10 or ≤day 1 with recent heparin (past 30 days)	>Day 10 or timing unclear; or <day 1 with recent heparin (past 31–100 days)	<Day 4 (no recent heparin)
Thrombosis or other sequelae	Proven new thrombosis, skin necrosis, or acute systemic reaction after IV unfractionated heparin bolus	Progressive or recurrent thrombosis, erythematous skin lesions, suspected thrombosis (not proven)	None
Other causes of platelet decrease	None evident	Possible	Definite

*1st day of immunizing heparin exposure considered day 0. Pretest probability score: 6–8 indicates high; 4–5, intermediate; & 0–3, low. Adapted from Warkentin TE. *Circulation.* 2004;110:e454–e458.

Once HIT is strongly suspected in a critically ill pt, all of the following should occur:

Principles of Treatment for Suspected or Confirmed HIT: The "Six A's"	
Two "Do's"	1. Avoid & discontinue all heparin (including low–molecular-wt heparin)
	2. Administer an alternative non-heparin anticoagulant; recommend a direct thrombin inhibitor (DTI)
Two "Don'ts"	3. Await platelet recovery before initiation of warfarin anticoagulation
	4. Avoid platelet transfusions
Two Diagnostics	5. Anti-PF4/heparin antibody test for confirmation
	6. Assess for lower extremity deep VT

Non-Heparin Anticoagulants for HIT Treatment

Drug	Mechanism	Approved for HIT	Half-Life	Monitoring	Dosing	Clearance
Fondaparinux	long-acting AT3-dependent inhibition of factor Xa	Not approved for HIT treatment in U.S.	Long (24 hrs); avoids potential for rebound hypercoagulable state	Direct (anti-Xa levels): accurate drug levels obtained	Not established for HIT, but consider 7.5 mg once daily (prophylaxis dose is 2.5 mg daily)	Renal
Danaparoid	long-acting AT3-dependent inhibition of factor Xa	Not approved for HIT, not avail. in U.S., Approved for HIT in Canada, Europe, Australia, New Zealand, & Japan	Long (17–20 hrs) avoids potential for rebound hypercoagulable state	Direct (anti-Xa levels): accurate drug levels obtained	Bolus: 2,250 U IV only in life- or limb-threatening thrombosis; infusion, 400 U/hr × 4 hrs, then 300 U/hr × 4 hrs, then 200 U/hr IV, subsequently adjusted by anti-Xa levels (target, 0.5–0.8 anti-Xa U/ml)	Renal
Argatroban	Direct thrombin inhibitor (DTI)	Approved for HIT treatment in U.S.	Short (40–50 min); potential for rebound hypercoagulable state	Indirect (APTT): risk for DTI underdosing due to APTT elevation for non-DTI factors	No bolus; initial rate, 0.5–2 mcg/kg/min (adjust to APTT); Reduce in liver dz	Hepatobiliary
Lepirudin	DTI	Approved for HIT treatment in U.S.	Short (80 min); potential for rebound hypercoagulable state	Indirect (APTT): risk for DTI underdosing due to APTT elevation for non-DTI factors	No bolus; initial rate, 0.10 mg/kg/hr (adjust to APTT); reduce dose for renal dysfunction	Renal
Bivalirudin	DTI	Not approved for HIT treatment in U.S.	Short (25 min); potential for rebound hypercoagulable state	Indirect (APTT): risk for DTI underdosing due to APTT elevation for non-DTI factors	Not established; no bolus; initial dose, 0.15–0.20 mg/kg/hr has been suggested	Enzymic metabolism

APTT, activated partial thromboplastin time.
Adapted from Warkentin TE, et al. *Chest*. 2008;133:340S–380S.

Comparison of Selected Thrombocytopenic Disorders That Should Be Considered When Evaluating a Patient for Heparin-Induced Thrombocytopenia (HIT). Common Clinical Manifestations Focus on Thrombotic versus Hemorrhagic Symptoms. Comments Include Relationships to Other Disorders and/or Drugs That Need to Be Considered. HIT Has Also Been Reported to Occur Concomitantly in Patients with Antiphospholipid Syndrome or Disseminated Intravascular Coagulation

Disorder	Common Clinical Manifestations	Useful Clinical Laboratory Analyses	Comments
Heparin-induced thrombocytopenia (HIT)	>50% present with thrombosis; VT > arterial	Anti-heparin/PF4 antibody testing (ELISA, functional assays)	Temporal relationship with heparin or LMWH therapy
Antiphospholipid syndrome (APS)	Recurrent venous and/or arterial thromboembolic complications; recurrent fetal loss	Anticardiolipin antibody & anti-β_2-glycoprotein 1 antibody testing (ELISA); lupus anticoagulant testing	Autoimmune disorder, either primary or associated with other rheumatologic conditions (e.g., lupus); in some cases, may be drug-induced (e.g., procainamide)
Disseminated intravascular coagulation (DIC)	Hemorrhagic or thromboembolic events predominate, depending on underlying cause & clinical course	PT, PTT, thrombin time, fibrinogen, D-dimer	May be acute (e.g., associated with sepsis, obstetric complications, severe trauma) or chronic (e.g., associated with cancer, aortic aneurysm). DIC can complicate severe HIT
Thrombotic thrombocytopenic purpura (TTP)	Neurologic manifestations may include stroke, TIA, altered mental status, seizures; other sx include fever, renal insufficiency	Microangiopathic hemolytic changes on blood film, elevated LDH, decreased ADAMTS13 levels	Associated with severe ADAMTS13 deficiency due to inhibitors in most pt; may be seen in pt taking ticlopidine or clopidogrel, or with other drugs (e.g., cyclosporine, tacrolimus, mitomycin). Microangiopathy can also be seen in severe HIT with associated DIC
Drug-induced thrombocytopenia (non-heparin)	Petechiae, purpura, & other hemorrhagic sx with severe thrombocytopenia	Isolated thrombocytopenia, may be severe	Associated with multiple drugs (e.g., abciximab, quinine, multiple abx)
Posttransfusion purpura (PTP)	Hematoma, ecchymoses, purpura	Severe thrombocytopenia that begins approx. 5 days after blood product use	Temporal relationship to transfusion therapy; most common in multiparous females. The timing of PTP approx. 1 week after surgery can mimic HIT

LMWH, low–molecular-wt heparin; DIC, disseminated intravascular coagulation; ELISA, enzyme-linked immunosorbent assay; TIA, transient ischemic attack; PT, prothrombin time; PTT, partial thromboplastin time; LDH, lactate dehydrogenase; ADAMTS13, a disintegrin & metalloproteinase with thrombospondin components-13.
From Ortel TL. *Hematology Am Soc Hematol Educ Program*. 2009:225–232.

Do not wait for lab confirmation of HIT prior to initiation of a direct thrombin inhibitor (DTI)—this is associated with increased risk for thrombosis & adverse outcome

HIT dx is confirmed with either a positive anti-PF4/polyanion-IgG enzyme immunoassay (EIA) or a positive platelet activation assay (i.e., serotonin-release assay, SRA)

Once platelet count has normalized, warfarin should be initiated with a low maintenance dose (specifically, no loading dose) & overlapped with the non-heparin anticoagulant until the target international normalized ratio (INR) has been reached & for a minimum of 5 days

The duration of warfarin therapy should be standard for venous thromboembolism (VTE), for a minimum of 3 mo with consideration for a more extended course depending on clinical circumstances related to the thromboembolic event. (Napolitano LM, et al. *Crit Care Med.* 2006;34:2898–2911)

Hypercoagulable States and Coagulopathies

Hypercoagulable States

Hypercoagulable states should be considered in ICU pt who develop venous or arterial thrombosis

Hypercoagulable states can be inherited or acquired

Acquired thrombophilia is related to risk factors or predisposing conditions for thrombosis, including surgery, trauma, malignancy, central venous catheter, use of oral contraceptives, & others

Inherited thrombophilia is a genetic tendency to VTE

Factor V Leiden is the most common cause of inherited thrombophilia, accounting for 40–50% of cases

The prothrombin 20210A gene mutation, & deficiencies in protein S, protein C, or antithrombin account for most of the remaining cases of inherited thrombophilia

Diagnostic Testing for Hypercoagulable States

CBC
Activated protein C (APC) resistance test
Prothrombin 20210A mutation
Antithrombin III activity
Protein C activity
Protein S activity
ELISA anti-PF4 antibody (for HIT dx)
Cardiolipin antibody (IgG & IgM)
β_2-Glycoprotein-1 antibody (IgG & IgM)
Lupus anticoagulant
Homocysteine levels
Factor VIII activity
Fibrinogen (Clottable)
Fibrinogen antigen
Plasminogen activity
Hexagonal phospholipid neutralization
Dilute Russel's viper venom
Aspirin and/or Plavix resistance (VerifyNow rapid assay)

Treatment of Hypercoagulable States

Initial treatment of venous or arterial thrombosis in an ICU pt is systemic anticoagulation

Antithrombin, protein C, or protein S deficiency carries VTE recurrence rates of 5–15% per year, a relative increase of 2.5 compared with rates in the absence of thrombophilia

Pt heterozygous for factor V Leiden or the prothrombin G20210A mutation are much less prone to VTE recurrence with a relative risk of 1.3–1.4; VTE recurrence rates are 5-fold greater with homozygosity or double heterozygosity

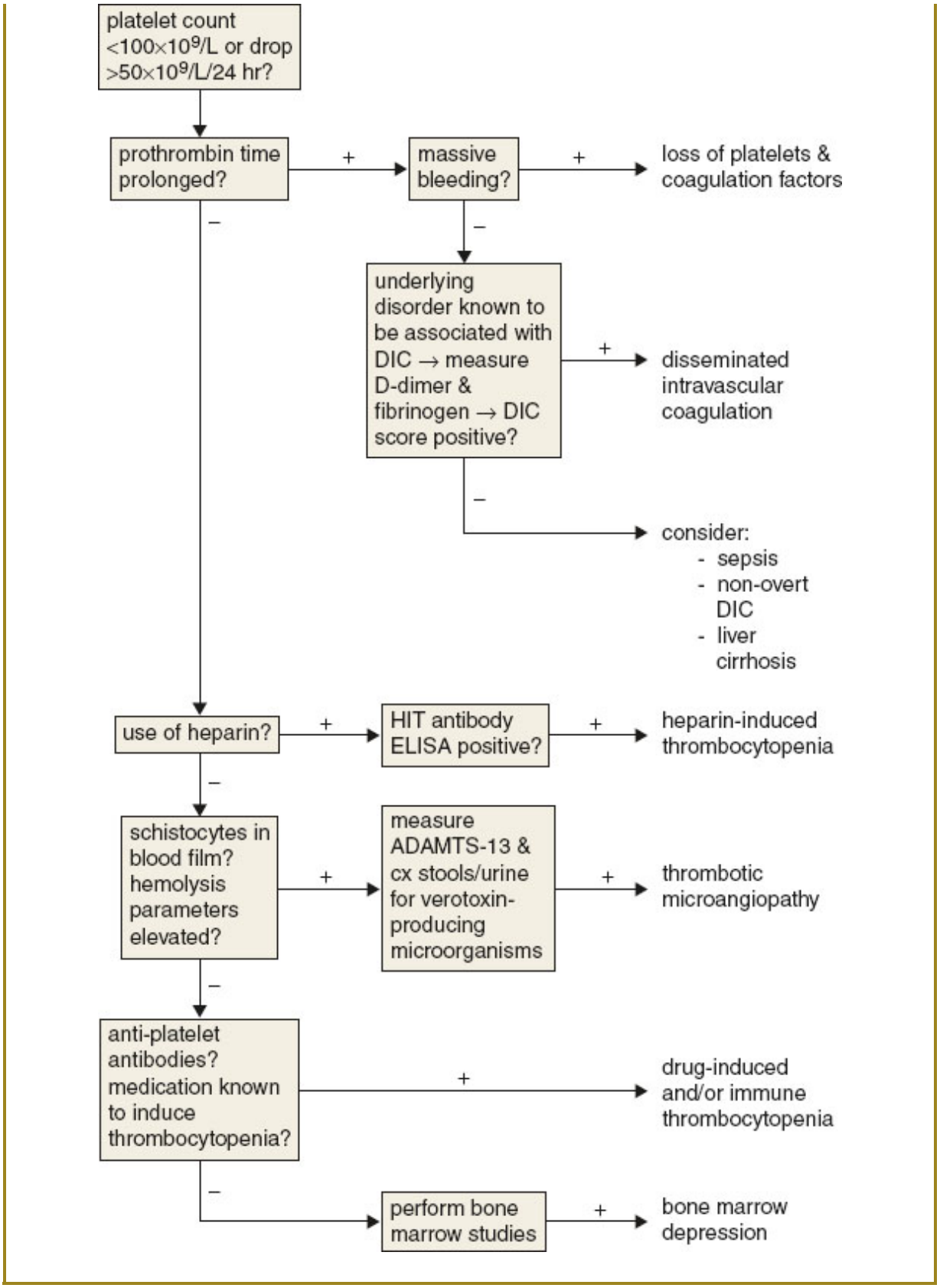
A mild/moderate increase in homocystein level is associated with a 2.5 increased risk for recurrent VTE

Long-term anticoagulant therapy is recommended in selected high-risk hypercoagulable states after a 1st spontaneous VTE episode in antithrombin, protein C or protein S deficiency, & for pt homozygous or doubly heterozygous for factor V Leiden and/or the prothrombin mutation

For pt with lower risk for recurrence, they are treated with anticoagulation for 6 mo, & then imaging for residual thrombosis or D-dimer testing are performed at the end of anticoagulant therapy, & the results are used to determine likelihood of VTE recurrence

Coagulopathies

Differential Diagnostic Algorithm for Coagulation Abnormalities in the ICU


platelet count <100×10⁹/L or drop >50×10⁹/L/24 hr?
prothrombin time prolonged?
+
massive bleeding?
+
loss of platelets & coagulation factors
–
–
underlying disorder known to be associated with DIC → measure D-dimer & fibrinogen → DIC score positive?
+
disseminated intravascular coagulation
–
consider:
- sepsis
- non-overt DIC
- liver cirrhosis
use of heparin?
+
HIT antibody ELISA positive?
+
heparin-induced thrombocytopenia
–
schistocytes in blood film? hemolysis parameters elevated?
+
measure ADAMTS-13 & cx stools/urine for verotoxin-producing microorganisms
+
thrombotic microangiopathy
–
anti-platelet antibodies? medication known to induce thrombocytopenia?
+
drug-induced and/or immune thrombocytopenia
–
perform bone marrow studies
+
bone marrow depression

DIC, disseminated intravascular coagulation; ELISA, enzyme-linked immunosorbent assay; HIT, heparin-induced thrombocytopenia.
From Levi M, Opal SM. *Crit Care.* 2006;10(4):222.

ICU pt with coagulation defects have a 4- to 5-fold increased risk for bleeding compared to pt with a normal coagulation status

Disseminated intravascular coagulation (DIC) is a syndrome caused by systemic intravascular activation of coagulation with formation of microvascular thrombi with clotting factor consumption, & occurs in pt with infxn, malignancy, trauma, amniotic fluid embolism & others

DIC manifests as prolonged plasma clotting times, thrombocytopenia, reduced plasma fibrinogen concentration, raised plasma fibrin-degradation products, & sometimes microangiopathic hemolysis

The most frequent cause of DIC is sepsis, with reduced protein C concentrations resulting in decreased endogenous fibrinolysis

ICU pt with severe sepsis or septic shock may manifest abnormalities in coagulation testing, but plasma should not be transfused unless the pt has evidence of clinical bleeding (Surviving Sepsis Guidelines 2008)

Pt with sepsis-induced DIC may progress to purpura fulminans, a rapidly progressive thrombotic disorder with hemorrhagic infarction of the skin & dermal vascular thrombosis

Protein C concentrations should be measured in pt with purpura fulminans

Meningococcal & Pneumococcal sepsis are common causes of purpura fulminans & DIC

Treatment of DIC is supportive with aggressive treatment of the underlying cause of the DIC

Treatment of bleeding in DIC requires blood component replacement therapy with plasma, platelets & cryoprecipitate

Hemostatic Resuscitation for Acute Traumatic Coagulopathy

Hemorrhage is a major cause of trauma deaths & coagulopathy exacerbates hemorrhage

Trauma pt with severe hemorrhage have early fibrinolysis in addition to coagulopathy

Uncontrolled hemorrhage in trauma leads to the lethal triad of acidosis, hypothermia, & coagulopathy

Prompt reversal of coagulopathy using "hemostatic resuscitation" with early use of blood component therapy is advocated as the optimal practice for pt requiring massive transfusion

Most severely injured pt are coagulopathic at hospital admission, before resuscitation interventions

An emerging consensus for hemostatic resuscitation in pt requiring massive transfusion is as follows:

Expedite the control of hemorrhage to prevent consumptive coagulopathy & thrombocytopenia & reduce the need for blood products

Limit isotonic crystalloid infusion to prevent dilutional coagulopathy & thrombocytopenia

Hypotensive resuscitation (SBP, 80–100 mm Hg) until definitive hemorrhage control is established

Transfuse blood products in a 1:1:1 ratio of RBCs/FFP/platelets (1 5-pack of pooled platelets counted as 5 units)

Frequent lab monitoring (arterial lactate to assess adequacy of resuscitation, ionized calcium, & electrolytes)

It is recognized that increased early use of plasma is associated with increased risk for acute lung injury (ALI-TRALI) & acute respiratory distress syndrome (ARDS), but is associated with decreased mortality

ELECTROLYTES

Sodium and Total-Body Water

Sodium & total-body water are intimately related issues. Clinical assessment of pt with hypernatremia or hyponatremia should include an assessment of their total volume status (Fig. 22-4).

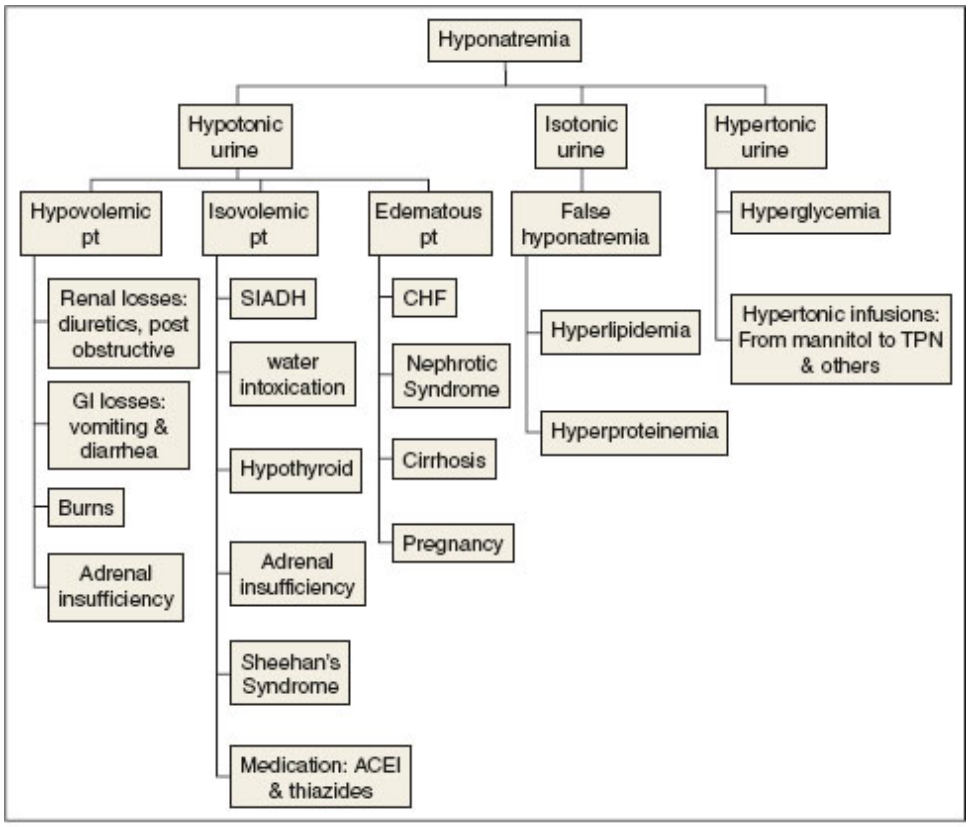
For details on hyponatremia & hypernatremia & their workup, see Chapter 24.

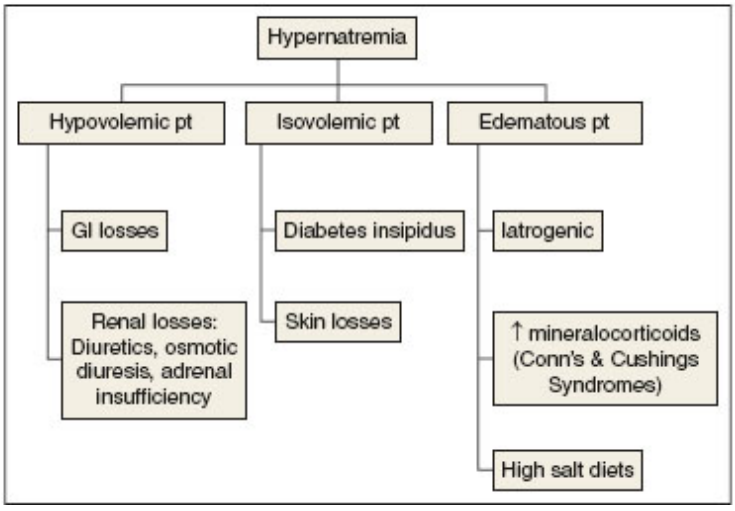
Comparison of Hemostatic Testing Found with Common Medications and Disease States in Critically Ill Patients

Condition	PT	aPTT	Fibrinogen	FDP	Platelets	BT	TT
UFH	Normal or prolonged[a]	Prolonged	Normal	Normal	Normal	Normal	Prolonged
LMWHs	Normal or prolonged[a]	Normal or minimally prolonged	Normal	Normal	Normal	Normal	Normal or minimally prolonged
Direct factor Xa inhibitors	Normal or prolonged[a]	Normal or minimally prolonged	Normal	Normal	Normal	Normal	Normal
Direct thrombin inhibitors	Prolonged	Prolonged	Normal	Normal	Normal	Normal	Prolonged
Coumadin	Prolonged	Normal or prolonged[b]	Normal	Normal	Normal	Normal	Normal
Vitamin K deficiency	Prolonged	Prolonged	Normal	Normal	Normal	Normal	Normal
Hepatic insufficiency	Prolonged	Normal or prolonged	Low or normal	Normal or elevated	Low	Normal or prolonged	Prolonged
DIC	Normal or prolonged	Normal or prolonged	Normal or low	Elevated	Low	Prolonged	Prolonged
Dilution	Prolonged	Prolonged	Low or normal	Normal	Low	Normal or prolonged	Normal or prolonged
von Willebrand dz	Normal	Prolonged	Normal	Normal	Normal	Prolonged	Normal
Lupus anticoagulant	Normal or prolonged	Prolonged	Normal	Normal	Normal	Normal	Normal
Thrombocytopenia	Normal	Normal	Normal	Normal	Low	Normal or prolonged	Normal

BT, bleeding time; DIC, disseminated intravascular coagulation; FDP, fibrin degradation product; LMWH, low–molecular-wt heparin; TT, thrombin time; UFH, unfractionated heparin.
[a]At supratherapeutic dosages.
[b]Early in coumadin treatment.
From Wheeler AP, Rice TW. *Chest.* 2010 Jan;137(1):185–194.

Figure 22-4. Differential Diagnosis of Hyponatremia & Hypernatremia





Potassium

Hypokalemia—Etiology

Inadequate intake (<40 mEq/d)
Increased excretion
Diarrhea, laxative abuse
Renal losses
Loop, thiazide diuretics
Metabolic alkalosis (vomiting, nasogastric drainage)
Osmotic diuresis (uncontrolled diabetes)
Nonreabsorbable anions (penicillin)
Magnesium depletion
Renal tubular acidosis (types 1 & 2)
Mineralocorticoid excess (i.e., primary hyperaldosteronism)
Congenital adrenal hyperplasia (i.e., Liddle, Gitelman, Bartter syndromes)
Intracellular shifts
Metabolic alkalosis
Drugs
β-Adrenergic agonists
Bronchodilators, decongestants, tocolytic agents, theophylline, caffeine
Insulin
Delirium tremens
Hyperthyroidism
Familial hypokalemic periodic paralysis
Barium poisoning

Hypokalemia—Clinical Significance

Hypokalemia is well tolerated in otherwise normal individuals; it is associated with an increased incidence of life-threatening cardiac arrhythmias in pt with cardiac dz. Severe hypokalemia <2.5 mEq/l can cause rhabdomyolysis &, when the value is less than 2.0 mEq/l it can cause an ascending paralysis with eventual respiratory arrest.

Hypokalemia—EKG Findings

Flattened T-wave, prominent U-wave.

Hypokalemia—Treatment

Dx & treatment of the underlying cause is essential; Repletion under EKG monitoring in situations where intracellular potassium shifts are not in play;

intense repletion is dangerous & should be avoided.

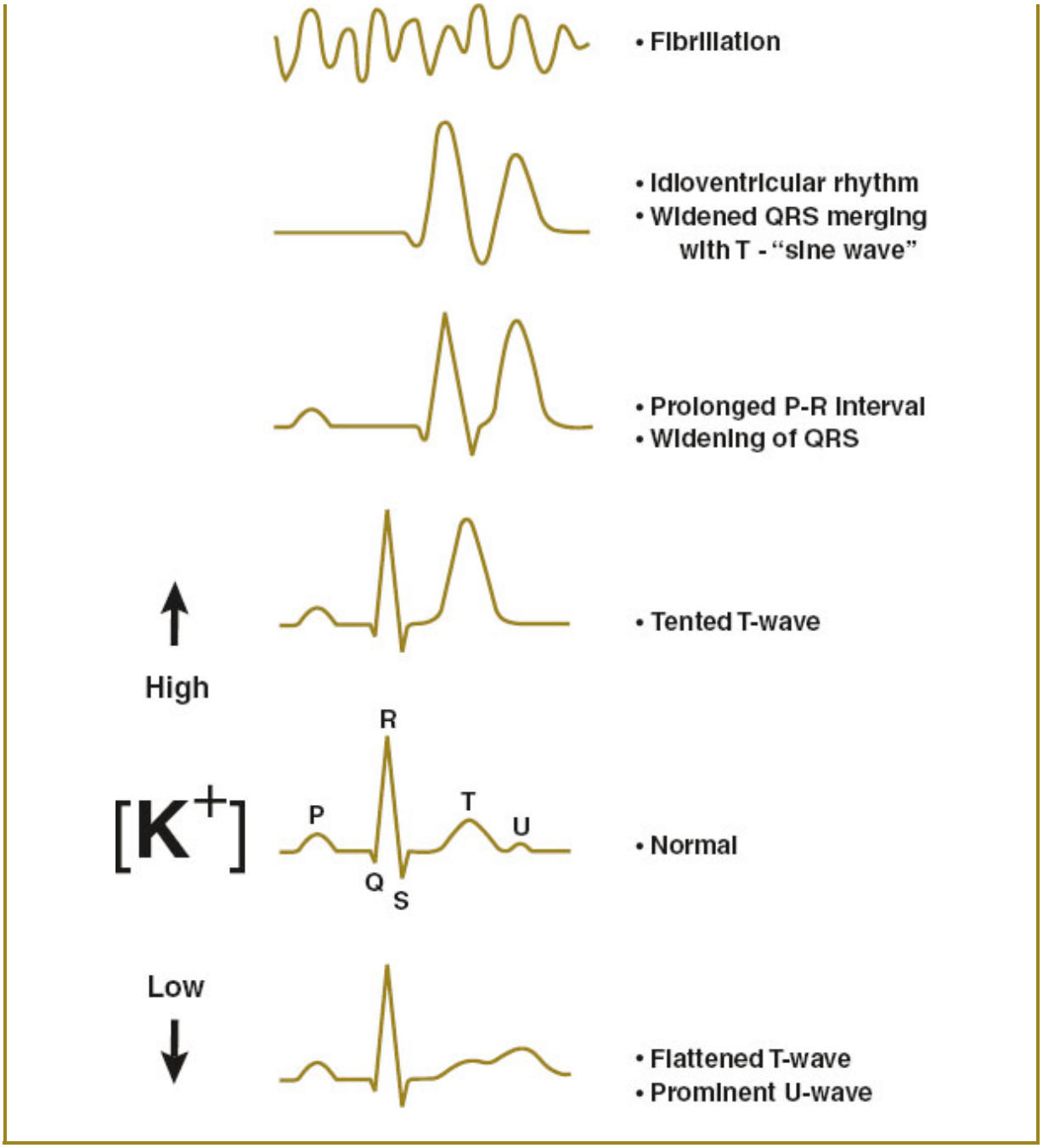
Hyperkalemia—Etiology

Factitious
Thrombocytosis (platelets >1,000,000/mm^3)
Leukocytosis (WBC >100,000/mm^3)
Hemolysis
Repeated fist clenching with tourniquet in place
Impaired K+ excretion
Renal insufficiency or failure
Mineralocorticoid deficiency
Addison dz
Hyporenin hypoaldosteronism (type 4 renal tubular acidosis)
Heparin-induced inhibition of aldosterone synthesis
Hereditary enzyme deficiencies
Pseudohypoaldosteronism
Drugs
K+-sparing diuretics (Spironolactone, amiloride, & triamterene)
ACE inhibitors
Angiotensin receptor blockers, NSAIDs, β-blockers, digoxin, heparin (see above), succinylcholine, cyclosporine, tacrolimus, trimethaprime, pentamidine
Transcellular shifts
Metabolic or respiratory acidosis
Familial hyperkalemic periodic paralysis
Release into the blood stream
Rhabdomyolysis
Burns
Trauma
Thrombocytosis
Hemolysis
Extremely high white cell counts
Iatrogenic: excessive replacement is a very frequent cause of hyperkalemia

Hyperkalemia—Clinical Significance

Hyperkalemia is asymptomatic, but impairs normal cardiac conduction, ECG changes: peaked T-waves, widening of QRS (sinusoidal wave forms), can progress to asystole or ventricular fibrillation (Fig. 22-5).

Figure 22-5. ECG Changes due to Hyper- & Hypokalemia



Treatments for Hyperkalemia		
Emergency	**Response Time**	**Duration**
Cardiac conduction abnormal		
Calcium gluconate or chloride[a] (10 ml of 10% solution)	Immediate	15–30 min
Serum [K^+] >6.5 mEq/l or rising		
Glucose (50 ml of 50% solution) plus regular insulin 10 U	10–20 min	2–3 hrs
Albuterol 10–20 mg by inhaler over 10 min	20–30 min	2–3 hrs
$NaHCO_3^-$, only if met acidosis present	Delayed	
Kayexalate 15–30 g with sorbitol		
By mouth	4–6 hrs	—
As retention enema	1 hr	—
Loop diuretic (IV)	1 hr	—
Hemodialysis	15–30 min	—

[a]IV calcium should not be given in the setting of digoxin toxicity.

Hyperkalemia—Treatment

Regardless of the cause, therapy to lower serum K should be initiated immediately if the concentrations are greater than 5.5 mEq/l or if the ECG shows signs of conduction abnormalities.

Strategies for the management of hyperkalemia (for the specific interventions & their mode of action see table below):

I. Stabilize membranes (calcium)

II. Drive K+ back into cells (insulin, bicarbonate, β-agonists)

III. Decrease total-body K+ (sodium polystyrene, loop diuretics, hemodialysis)

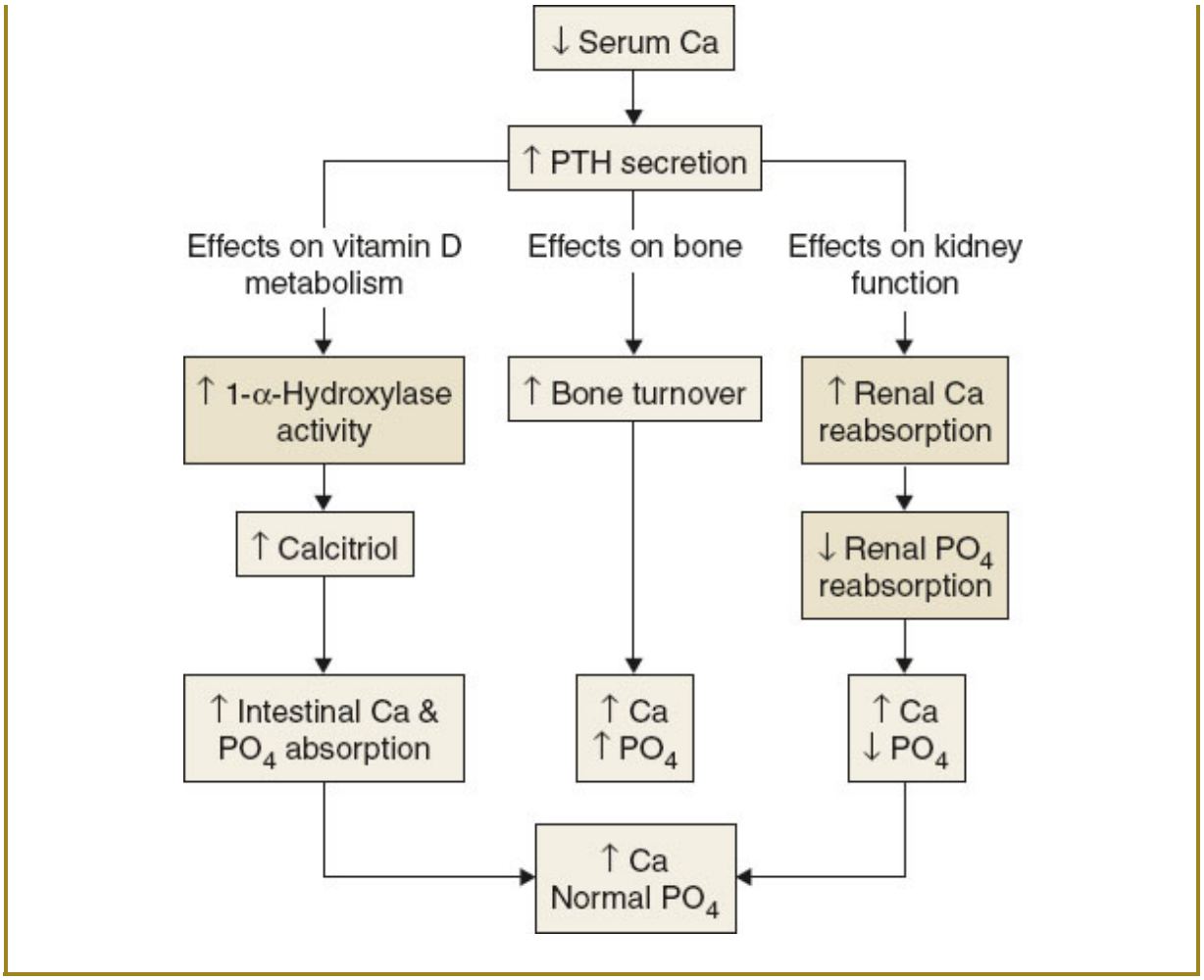
Interventions effective for the treatment of hyperkalemia:

Mechanisms of Interventions Used for the Treatment of Hyperkalemia				
Mechanism	**Intervention**	**Dose**	**Onset**	**Comments**
Stabilize membranes	Calcium gluconate Calcium chloride	1–2 amps IV	<5 min	Transient effect
Drive potassium into cells	Insulin	Regular insulin 10 units IV with 1–2 amps of D50		Especially when hyperglycemia related
	Bicarbonate	1–3 amps IV	15–30 min	
	β-2 Agonists	Albuterol 10–20 mg inhaled	30–90 min	
Remove potassium	Cation exchange resin	Sodium polystyrene (Kayexalate) 30–90 g PO or PR	1–2 hrs	Risk of intestinal necrosis with sorbitol formulation
	Diuretics	Furosemide 40 mg IV or more	30 min	Unclear utility in short term
	Renal replacement therapy	Hemodialysis		

Adapted from Sabatine MS. Pocket Medicine, 4th ed, 2011, page 117.

Calcium (Fig. 22-6)

Figure 22-6. Effects of Hypocalcemia on Calcium & Phosphate Homeostasis



Hypercalcemia

Total calcium >10 mg/dl & ionized calcium >1.3 mmol/l.

Hypercalcemia—Clinical Manifestations

Depends on the magnitude of hypercalcemia & the rate of rise in serum calcium

GI sx: nausea, vomiting, constipation, & abd pain

Neurologic sx: difficulty concentrating, fatigue, lethargy, & muscle weakness

Renal sx: Nephrogenic diabetes insipidus & renal failure with volume depletion

Cardiovascular sx: HTN & shortening of the QT interval. Severe arrhythmias are rare

Hypercalcemia—Etiology

Malignancy
Local osteolytic hypercalcemia
Humoral hypercalcemia of malignancy (PTH-related peptide)
Hematologic malignancies (ectopic calcitriol synthesis)
Hyperparathyroidism, thyrotoxicosis, pheochromocytoma, granulomatous dz
Drug induced
Vitamin D
Thiazide diuretics
Estrogens & antiestrogens
Androgens (breast cancer therapy)
Vitamin A
Lithium
Immobilization
Total parenteral nutrition
Milk-alkali syndrome
Kidney dz (acute & chronic, usually from medications)

Hypercalcemia—Treatment

General Measures: volume repletion with saline to counteract the kidney's increase of its tubular reabsorption of sodium to maintain normovolemia. This is associated with increased tubular reabsorption of calcium

Diuretics: Loop diuretics, particularly furosemide because they increase urinary calcium excretion

Bisphosphonates: Currently the treatment of choice for malignancy associated hypercalcemia due to their inhibitory action on bone resorption (zoledronate, pamidronate)

Steroids: Glucocorticoids have been used in the past to treat hypercalcemia, esp. in pt with hematologic malignancies. Today their use is restricted to the treatment of hypercalcemia due to ectopic production of $1,25(OH)_2D$

Hemodialysis

Hypocalcemia

Total calcium <8.6 mg/dl & ionized calcium <1.12 mmol/l.

Hypocalcemia—Clinical Manifestations

Depends on the magnitude of hypoCa+ & the rate of fall in serum calcium

Neurologic sx: perioral numbness & carpopedal spasms of the hands & feet. In some pt, these spasms may progress to tetany

Chvostek & Trousseau signs. Chvostek sign is tested by tapping on the facial nerve near the temporal mandibular joint & watching for grimacing caused by spasm of the facial muscles. Trousseau sign is tested by inflating a BP cuff above the systolic blood pressure for 3 min & watching for spasm of the outstretched hand

Hypocalcemia—Etiology

Hypoalbuminemia has to be ruled out

Vitamin D deficiency

Hypoparathyroidism

Pseudohypoparathyroidism (hypoCa+ & hypophosphatemia but elevated PTH, indicating nonresponsiveness to PTH)

Tissue consumption of calcium:

Precipitation into, as in pancreatitis

Excess bone formation in some malignancies with blastic bone metastases

Following parathyroidectomy

Hypomagnesemia

Following acute hyperphosphatemia caused by rhabdomyolysis or tumor lysis syndrome, the phosphorus binds to calcium, leading to a drop in ionized calcium

Citrate infusion for renal replacement therapy or with blood & plasma transfusions

Sepsis (unclear mechanism)

Hypocalcemia—Treatment

IV calcium infusions are indicated only in the setting of symptomatic hypoCa+ & should not be given in the presence of hyperphosphatemia because of the risk of precipitation

Asymptomatic pt should be repleted with oral calcium. The amount of calcium absorbed will be increased if calcitriol is given with the calcium

Hypomagnesemia should be treated concomitantly

If appropriate, pt may be changed from loop diuretics to thiazides

Treatment of the underlying dz

Magnesium

Hypermagnesemia

Rare dx because of the kidney's high clearance of magnesium

Sx: lethargy & confusion, arrhythmias, & muscle weakness (pregnant pt treated with magnesium with serum levels of 4–6 mg/dl are usually asymptomatic)

Etiology: increased intake, decreased renal function, or lithium toxicity

Treatment: stopping the magnesium intake & adequate volume repletion

Hypomagnesemia

Common in both hospitalized & ICU pt

Sx: apathy, depression, delirium, seizures & paresthesias, tremors, general muscle weakness, ventricular arrhythmias, & increased susceptibility to Digoxin-related arrhythmias. Commonly is associated with other electrolyte abnormalities, including hypokalemia, hyponatremia, hypoCa+, & hypophosphatemia

Etiology

Reduced intake: starvation, alcoholism, prolonged postoperative state

Redistribution from extracellular to intracellular: insulin, parathyroidectomy, catecholamine excess states, acute pancreatitis, excessive lactation

Reduced absorption: specific or generalized malabsorption syndrome, extensive bowel resections, chronic diarrhea, laxative abuse.

Drug-induced losses: diuretics, aminoglycosides, digoxin, cisplatinum, & cyclosporine

Hormone-induced magnesuria: aldosteronism, hypoparathyroidism, hyperthyroidism

Renal losses due to polyuria: hypercalcemia, hyperglycemia extracellular fluid volume expansion

Phosphate depletion syndrome, alcohol ingestion

Treatment: hypomagnesemia should be treated with IV or oral supplementation

Phosphate

Hyperphosphatemia

Common causes include renal failure (decreased phosphate excretion), increased extracellular phosphate causes (tumor lysis syndrome, rhabdomyolysis, hemolysis), & increased phosphate reabsorption (hypoparathyroidism, acromegaly, treatment with bisphosphonates, or vitamin D)

Treatment for chronic condition: low phosphate diet & phosphate binders

Treatment for acute condition: saline infusion to increase phosphate excretion, hemodialysis

Hypophosphatemia

Common causes include chronic alcoholism, malnutrition, TPN with inadequate phosphate, & chronic ingestion of antacids. Monitor for refeeding syndrome in pt with malnutrition

Signs include myopathy, ileus, rhabdomyolysis, respiratory failure, cardiac failure, metabolic encephalopathy, confusion, seizures, delirium, & coma

If IV therapy is necessary in the symptomatic pt, the dose depends on the severity of hypophosphatemia. For moderate hypophosphatemia (i.e., levels between 1.25 & 2.5 mg/dl), 0.08 to 0.24 mmol/kg (maximum total dose of 30 mmol) may be given over 6 hrs; for more severe hypophosphatemia, 0.25–0.5 mmol/kg (maximum total dose of 80 mmol) may be given over 8–12 hrs

Fluid Resuscitation and IV Replacement Solutions

Crystalloids

Fluid resuscitation with isotonic crystalloid solutions is recommended in ICU pt with hypovolemic, hemorrhagic, or distributive shock

Some studies document that chloride-rich solutions (NS) are associated with increased risk for AKI and/or mortality, but the most recent RCT failed to confirm that finding (Young P, et al. *JAMA.* 2015;314:1701–1710).

Albumin resuscitation is indicated for pt with liver dz/ascites, nephrotic syndrome, & possibly septic shock (Caironi P, et al. *N Engl J Med.* 2014;370(15):1412–1421).

The Saline vs. Albumin Fluid Evaluation (SAFE) study demonstrated that in ICU pt, use of either 4% albumin or NS for fluid resuscitation resulted in similar 28-day mortality rates, outcomes (Finfer S, et al. *N Engl J Med.* 2004;350(22):2247–2256).

Albumin was associated with higher mortality rates in traumatic brain injury (TBI) pt in the SAFE study

Hypertonic saline is considered in severe TBI & intracranial HTN

Synthetic hydroxyethyl starch solutions should not be used for fluid resuscitation as multiple RCTs have documented increased risk of kidney injury

The Composition of Crystalloid and Colloid Resuscitation Fluids

	Lactated Ringer's (LR)	Normal saline (0.9 NS)	Half normal saline (0.45 NS)	D5W	3% NaCl	Albumin 5%	Hetastarch 6%
Sodium (Na^+)	130 mmol/l	154 mmol/l	77 mmol/l	–	513	150	154
Chloride (Cl^-)	109 mmol/l	154 mmol/l	77 mmol/l	–	513	150	154
Potassium (K^+)	4 mmol/l	–	–	–	–	–	–
Calcium (Ca^{++})	3 mmol/l	–	–	–	–	–	–
Lactate	28 mmol/l	–	–		–	–	–
Glucose	–	–	–	50 g; 278 mmol/l	–	–	–
pH	6.5	5.0	5.0	4.0	–	–	–
Osm	275 mosm/l	308 mosm/l	–	–	1,025 mosm/l	310 mosm/l	310 mosm/l
Tonicity	Isotonic	Isotonic	Hypotonic	Hypotonic	Hypertonic		
Cost	$1.26	$1.44	$1.26	$1.26	$1.28	$100	$27.30
Comments	Fluid choice for initial resuscitation	Alternative to LR; watch for hypernatremia, hyperchloremic acidosis	Common maintenance fluid, with or without dextrose	Fluid choice in hypernatremia Watch for hyponatremia	Risk of hypernatremia; consider in pt unresponsive to isotonic fluid	Indicated only in liver dz & nephrotic syndrome	No specific indication in ICU pt for fluid resuscitation; potential harm in sepsis

INFECTIOUS DISEASE, SEPSIS, AND THE SURVIVING SEPSIS GUIDELINES 2015

DAVID OXMAN, MD • ANKIT GUPTA, MD, MS • GYORGY FRENDL, MD, PhD

Evaluation of New Fever in the Critically Ill Patient

Fever is common in the ICU. About 50% of ICU patients (pt) experience a fever (temp >101°F) at least once during ICU course (Niven DJ, et al. *J Intensive Care Med.* 2012;27(5):290–297)

Majority of fevers, particularly low grade (<101.5°F) are benign & resolve without specific treatment. However, others may be due to life-threatening condition

Main objective is to distinguish infectious from noninfectious causes (see the below table)

Approach to dx should be tailored to pt & avoid unnecessary tests

Pt with fever & signs of sepsis, or those at high risk of infxn (e.g., immunocompromised pt) need early empiric abx treatment

Selected Causes of ICU Fever	
Infectious	**Noninfectious**
Catheter-related bloodstream infxn	Postoperative state
Bacteremia	Blood transfusion
VAP	Drug fever
Sinusitis	Thromboembolic dz
UTI	Acalculous cholecystitis
Wound infxn	Cerebral hemorrhage
Endocarditis	ARDS
C. difficile colitis	Adrenal insufficiency
	Thyroid storm
	Vasculitis
	Pancreatitis
	Hematoma
	Gout
	Alcohol withdraw
	Tumor fever
	Burns

VAP, ventilator-associated pneumonia; UTI, urinary tract infxn; ARDS, acute respiratory distress syndrome.

Nosocomial Infections

Catheter-Related Blood Stream Infections (CRBSI)

Also see Chapter 8.

Epidemiology

Among most common of hospital-acquired infxns

Incidence decreasing due to increased awareness & prevention strategies

Pathogenesis

Microorganisms enter bloodstream via 1 of 4 mechanisms:

Colonization of the skin at the catheter entry site

Contamination of catheter hub or stopcock

Seeding of catheter through blood from infxn at distant site

Contamination of IV infusates

Short-term, noncuffed central venous catheters have highest rate of infxn but arterial catheters & peripherally inserted central venous catheters (PICC lines) also can cause infxn

Clinical Manifestations

Fever, rigors, hypotension, or other early signs of sepsis

Catheter entry sites & tunneled catheter tracts should be examined for erythema, local tenderness, or purulent drainage—but most often are normal

Microbiology of CRBSI

Staphylococcus aureus & coagulase-negative *Staphylococcus are* most common causative organisms

Assorted gram-negative bacteria, *Enterococci* (including vancomycin-resistant enterococci) & *Candida* species next most common organisms

Diagnosis

Always draw at least 2 sets of blood cx from different sites to avoid risk of falsepositive result due to skin contamination

Positive blood cx with typical organism & no other likely source of bacteremia suggests CRBSI

If source of bacteremia uncertain 2 tests further suggest catheter as source

"Differential time to positivity" (blood cx taken via catheter grows >120 min before peripherally drawn cx)

Semi-quantitative culture (cx) of tip with >15 CFU of bacteria

Treatment

Abx directed at typical pathogens should be started immediately & catheter should be removed

Gram-positive organisms, including MRSA, cause the majority of infxns & vancomycin is the 1st-line abx

In the immunocompromised, burn victim or unstable pt, empiric treatment should be broadened to cover typical nosocomial gram-negative organisms.

Fungal CRBSI, although increasing in incidence, is still relatively uncommon, & empiric antifungal coverage should be reserved for high-risk pt

Exchange of an infected catheter over a guidewire is *not* effective for managing CRBSI

Prevention

Preventing CRBSI

Use maximum barrier precautions for placement procedure—sterile gloves, surgical mask & gown, & sterile drapes

Cleanse skin with chlorhexidine instead of povidone–iodine

Access ports must be cleaned with an antiseptic immediately prior to use

Avoid femoral insertion site if possible

Subclavian site associated with a slightly lower risk of infxn than IJ catheterization.

When no longer essential for care remove catheter immediately

Ventilator-Associated Pneumonia (VAP)

Pathogenesis

Impaired cough reflex & mucociliary clearance
Aspiration of oropharyngeal or gastric contents
Hematogenous spread from distant sites
Inhalation of contaminated aerosols

Microbiology

Oropharynx normally colonized with streptococci & anaerobes, but mouth of critically ill pt colonized with gram-negative bacteria & *S. aureus*

Gram-negative organisms & *S. aureus* are the most common pathogens responsible for VAP. Drug-resistant organisms, such as *Pseudomonas aeruginosa, Klebsiella pneumonia,* & methicillin-resistant *S. aureus* (MRSA) also very common. Anaerobic bacteria, *Legionella* & viruses, such as herpes simplex virus, can cause VAP as well but are much less common

Diagnosis

No gold standard diagnostic test for VAP (American Thoracic Society; Infectious Diseases Society of America. *Am J Respir Crit Care Med.* 2005;171:388–416).

Clinical characteristics: fever, sputum production, leukocytosis, increased oxygen requirements, & new infiltrate on CXR suggestive of VAP, but not specific

Sampling of the lower respiratory tract for pathogenic organisms may increase diagnostic accuracy

Several methods exist: tracheal aspiration, nonbronchoscopic "mini-BALs" & fiberoptic bronchoscopy with bronchoalveolar lavage or a protected brush sampling

Clinical Pulmonary Infection Score (CPIS): prediction tool for dx of VAP (see table on next page)

Presence or absence of fever, purulent sputum, or leukocytosis, as well as the degree of hypoxemia, character of radiographic abnormalities, & microbiologic findings

Score of >6 suggests that pneumonia is present

Positive predictive value modest—~60%—& should not be overly relied upon. More useful to ruling out VAP in pt with low score

Clinical Pulmonary Infection Score			
	0 Point	**1 Point**	**2 Points**
Temp	≥36.5 or ≤38.4	≥38.5 or ≤38.9	≥39 or <36.5
White blood cell count	≥4,000 or ≤11,000	<4,000 or >11,000 *Band forms ≥50 percent add 1 additional point*	
Tracheal secretions	Absence of tracheal secretions	Presence of nonpurulent tracheal secretions	Presence of purulent tracheal secretions
Oxygenation	PaO_2/FiO_2 >240 or ARDS		PaO_2/FiO_2 ≤240 & no ARDS
CXR	No infiltrate	Diffuse infiltrate	Localized infiltrate
Progression of CXR (after 48–72 hrs)	No radiographic progression		Radiographic progression (if pulmonary edema & ARDS excluded)
Microbiology	Pathogenic bacteria in rare or few quantities or no growth	Pathogenic bacteria cultured in moderate or heavy quantity *Same pathogenic bacteria seen on Gram stain, add 1 additional point*	

Treatment

Treatment for VAP should begin as soon as it is suspected
Initial abx therapy should be broad & directed at typical organisms
After microbiologic data become avail., abx therapy should be tailored to specific pathogen & pt with alternative dx should have abx stopped

Exposure to unnecessary abx leads to colonization with drug-resistant organisms & makes future episodes of VAP more difficult to treat.

Prevention

Avoid intubation by using noninvasive positive pressure ventilation
Minimize duration of mechanical ventilation by limiting sedation & performing daily spontaneous breathing trials
Maintain head-of-bed elevation above 30°
Wash hands before physical exam, & limit respiratory circuit tubing changes
GI decontamination, continual subglottic suctioning, & silver-coated ET tubes promising but not recommended for routine use

Urinary Tract Infection

Often cited as most common ICU infxn but no consistent definition

Pyuria and/or bacteruria does not always indicate infxn—particularly in pt with indwelling urinary catheter

Deciding when a pt needs treatment is difficult

In general, abx treatment should be reserved for pt at high risk of complication from untreated UTI (e.g., neutropenic or kidney transplant pt) those with possible urinary flow obstruction, recent urinary instrumentation, & those with signs or sxs of sepsis

Majority of infxns caused by gram-negative bacteria (including multidrug-resistant organisms), enterococcus & candida species

Changing urinary catheter may transiently decrease bacteruria or candiduria but new catheter will almost always be rapidly recolonized

Clostridium Difficile Colitis

Presentation

Most common cause of hospital-acquired infectious diarrhea

Clinical signs include frequent loose stools (>3 per day), fever, & abd pain; may also present with ileus. Some pt may have mild clinical signs & no diarrhea

Leukocytosis, often extreme, frequently present

Typically there is recent exposure to abx. Nearly all abx can predispose to clostridium difficile infxn but fluoroquinolones, cephalosporins, & clindamycin are most often associated

Dx: Toxin assays

Enzyme immuno-assay (EIA): rapid result; tests for Toxin A & B; high specificity but only 75% sensitive

Stool PCR: rapid, highly sensitive & specific. Can be positive in asymptomatic carriers

EIA for GDH antigen—screening test; cannot differentiate between toxigenic & nontoxigenic strains

Cytoxin assay: labor intensive, slow, but highly specific

Treatment

Nonsevere dz: Metronidazole 500 mg PO/IV q8h

Severe dz: vancomycin 125–500 mg PO q6h (higher doses sometimes used)

Surgery: subtotal colectomy indicated for toxic megacolon, perforation or progressive dz not likely to respond to medical therapy alone

Principles for the Use of Antibiotics in the ICU

Severe acuity of illness often requires early broad spectrum empiric abx treatment before infxn identified

Many studies have demonstrated worse outcomes for a variety of infxns with even minor delays of appropriate antimicrobial treatment

However, low specificity of diagnostic tests (e.g., CXR for the dx of VAP) often leads to over-diagnosis of infectious syndromes

Overuse of abx leads to individual complications (e.g., colonization with resistant organisms & clostridium difficile colitis) & increased rates of antimicrobial resistance in the ICU

Must balance need to treat potential infxns early with harm of unnecessary abx

It is essential to ***de-escalate*** abx therapy as clinical situation evolves

Abx deescalation involves:

Stopping abx when it is clear that no infxn is present

Tailoring abx when sensitivity of infecting organism is known

Abx resistance in the ICU

Factors leading to high rates of antimicrobial resistance in the ICU: high rates of previous exposure to broad-spectrum abx; high use of invasive catheters; high rates of comorbid conditions

The most commonly encountered abx-resistant infxns in the ICU are:

MRSA

Vancomycin-resistant Enterococcus (VRE)

Resistant gram-negative organisms (Pseudomonas, ESBLs, KPC-producing Klebsiella, Acinetobacter)

Antifungal therapy in ICU

Candida species far & away are the most common fungal pathogen in the ICU

Other fungi causing infxn in the ICU include *Aspergillus* sp. & zygomycoses but these occur primarily in the severely immunosuppressed with either neutropenia or T-cell dysfunction (AIDS, transplantation, high-dose steroid therapy)

Some pt may be at high risk of invasive fungal infxn & may benefit from empiric antifungal therapy when presenting with sepsis

Risk factors for *Candida* bloodstream infxn:

TPN, GI surgery or bowel disruption, neutropenia/hematologic malignancy/bone marrow transplant/high-dose steroids, previous exposure to broad-spectrum abx, high APACHE score, colonization with *Candida* sp. at multiple sites

Typical Empiric Antibiotic Regimens			
Catheter-related bloodstream Infxn	*Gram-positive bacteria* Preferred: Vancomycin Alternative: Daptomycin	*Gram-negative bacteria (if high risk or sepsis)* 3rd- or 4th-generation cephalosporin (e.g., ceftriaxone or cefepime) **or** β-lactam/β-lactamase inhibitor (e.g., piperacillin-tazobactam) **or** carbapenem (e.g., imipenem) & aminoglycoside (e.g., gentamicin) *or* fluroquinolone (e.g., ciprofloxacin)	*Fungal (if high risk & sepsis)* Eichinocandin (e.g., micafungin)
Ventilator-associated pneumonia	*Gram-positive bacteria* Vancomycin or Linezolid	*Gram-negative bacteria* Antipseudomonal cephalosporin (e.g., cefepime or ceftazidime) **or** β-lactam/β-lactamase inhibitor (e.g., piperacillin-tazobactam) **or** carbapenem (e.g., imipenem) & aminoglycoside (e.g., gentamicin) or fluroquinolone (e.g., levofloxacin)	

Other Antibiotics	
Antibiotic	**Spectrum**
Vancomycin	Gram positive bacteria incl. MRSA, PCNase-producing pneumococci & enterococci (except VRE)
Linezolid **Daptomycin** **Quinopristin/ Dalfopristin**	GPC incl. MRSA & VRE (check susceptibility for VRE)
Quinolones	Enteric GNR & atypicals. 3rd & 4th generation ↑ activity vs. gram positive
Aminoglycosides	GNR. Synergy w/cell-wall active abx (β-lactam, vanco) vs. GPC. ↓ activity in low pH (e.g., abscess). No activity vs. anaerobes
Macrolides	GPC, some respiratory gram negative, atypicals
TMP/SMX	Some enteric GNR, Pneumocystis jiroveci pneumonia, *Nocardia, Toxoplasma,* most community-acquired MRSA
Clindamycin	Most gram positive (except enterococci) & anaerobes (*B. fragilis* resistance increasing)
Metronidazole	Almost all anaerobic gram negative, most anaerobic gram positive
Doxycycline	*Rickettsia, Ehrlichia, Chlamydia, Mycoplasma, Nocardia,* Lyme
Tigecycline	Many GPC incl. MRSA & VRE; some GNR incl. ESBL but not *Pseudomonas* or *Proteus*. Approved for abd or skin/soft tissue infxns. Check susceptibility if organism isolated

MRSA, methicillin-resistant *Staphylococcus aureus*; PCN, penicillin; TMP/SMX, trimetoprime + sulfonamide; GPC, gram-positive cocci; GNR, gram-negative rods; ESBL, extended spectrum β-lactamase.

The following tables for the spectrum of activity for different abx are generalizations. Sensitivity data at your own institution should be used to guide therapy.

Penicillins		
Generation	**Properties**	**Spectrum**
Natural (e.g., penicillin)	Some GPC, GPR, GNC, most anaerobes (except *Bacteroides*)	Group A streptococci Enterococci, *Listeria, Pasteurella Actinomyces,* Syphilis
Anti-Staph (e.g., nafcillin)	Active vs. PCNase-producing Staph Little activity vs. gram negative	Staphylococci (except MRSA) Streptococci
Amino (e.g., ampicillin)	Penetrate porin channel of gram negative Not stable against PCNases	*E. coli, Proteus, H. influenzae Salmonella, Shigella Enterococci, Listeria*
Extended (e.g., piperacillin)	Penetrate porin channel of gram negative More resistant to PCNases	Most GNR incl. *Enterobacter, Pseudomonas, Serratia*
Carbapenem (e.g., imipenem)	Resistant to most β-lactamases	Most Gram positive & negative bacteria including anaerobes, but *not* MRSA or VRE
Monobactams (aztreonam)	Active vs. gram negative but not gram positive	Gram negative bacterial infxn in pt w/PCN or Ceph allergy
β-Lactamase Inhibitors (e.g., sulbactam)	Inhibit plasma-mediated β-lactamases	Adds Staph, *B. fragilis* & some GNR (*H. influenzae, M. catarrhalis,* some *Klebsiella*); intrinsic activity against *Acinetobacter* (sulbactam only)

Cephalosporins		
Not active against ESBL producing GNRs or MRSA		
Generation	**Spectrum**	**Indications**
1st (e.g., cefazolin)	Most GPC (incl. Staph & Strep, not MRSA) Some GNR (incl. *E. coli, Proteus, Klebsiella*)	Used for surgical ppx & skin infxns
2nd (e.g., cefuroxime, cefotetan)	↓ activity vs. GPC, ↑ vs. GNR. 2 subgroups: Respiratory: *H. influenzae* & *M. catarrhalis* GI/GU: ↑ activity vs. *B. fragilis*	PNA/COPD flare Abd infxns
3rd (e.g., ceftriaxone)	Broad activity vs. GNR & some anaerobes Ceftazidime active vs. *Pseudomonas*	PNA, sepsis, meningitis
4th (e.g., cefepime)	↑ resistance to β-lactamases (incl. of Staph & *Enterobacter*)	Similar to 3rd-generation MonoRx for nonlocalizing febrile neutropenia
5th (e.g., ceftaroline)	Broad gram positive/gram negative coverage including MRSA	PNA & skin & soft tissue infxns

Sepsis and Septic Shock

Sepsis-3 (Singer M, et al. *JAMA.* 2016;315(8):801–810) and The Surviving Sepsis Guidelines 2012 (Dellinger RP, et al. *Crit Care Med.* 2013;41:580–637)

Sepsis: is a condition of life-threatening organ dysfunction (such as hypotension, altered mentation, oliguria, & others) due to a dysregulated host response to infxn (confirmed or suspected).

Organ dysfunction can be broadly defined as an acute change of ≥2 points of the SOFA score (see components of SOFA score & the scoring tables below). An increase of ≥2 points in the SOFA score is associated with a 10% expected mortality (Singer M, et al. *JAMA.* 2016;315(8):801–810). SOFA score is assumed to be 0 for pt who are known not to have organ dysfunction at the 1st encounter.

Septic Shock: is a severe form of sepsis in which underlying circulatory & cellular/metabolic abnormalities are profound enough to cause a substantial increase in mortality.

Septic shock is characterized by refractory hypotension & vasopressor requirement (hemodynamic instability) despite of sufficient IV fluid resuscitation (20 ml/kg of colloids or 40 ml/kg of crystalloids) to maintain a MAP ≥65 mm Hg & having a serum lactate level >2 mmol/l (18 mg/dl). Pt who meet these criteria have an expected mortality of 30–40% (variable by geography & level of organized sepsis care).

The new 2016 sepsis guidelines (Sepsis-3; Singer M, et al. *JAMA.* 2016;315(8):801–810) were intended to increase the precision & speed of sepsis dx. They shifted the diagnostic focus to infxn-triggered organ dysfunction (from systemic inflammation), & eliminated the categories of SIRS & severe sepsis, leaving sepsis & septic shock as the 2 entities of the sepsis spectrum.

Diagnostic guide for identifying pt with sepsis:
For **pt with a diagnosed or suspected infxn, the dx of sepsis should be established by the presence of organ dysfunction** as reflected by an increase from their baseline score of ≥2 points:

in their qSOFA score if they are outside of the ICU (or in the absence of lab data enabling the use of the more detailed SOFA score)
in their SOFA score if they are in the ICU or have data enabling the use of the more detailed SOFA score

See website for a calculator for SOFA & qSOFA: http://www.mdcalc.com/sequential-organ-failure-assessment-sofa-score.

qSOFA (quick Sequential [sepsis related] Organ Failure Assessment) **score** is calculated from (range 0–3 points; Singer M, et al. *JAMA.* 2016;315(8):801–810):
RR ≥22
Systolic BP ≥100
Any altered mental status (or Glasgow Coma Scale (GCS) ≤13 if established)

SOFA score is comprised (range 0–24 points; *Intensive Care Med.* 1996;22:707) of the following components & degrees of organ dysfunction:

Respiratory	
PaO_2/FiO_2 (mm Hg)	SOFA Score
<400	1
<300	2
<200 & mechanically ventilated	3
<100 & mechanically ventilated	4

Liver	
Bilirubin (mg/dl) [μmol/l]	SOFA Score
1.2–1.9 (>20–32)	1
2.0–5.9 (33–101)	2
6.0–11.9 (102–204)	3
>12.0 (>204)	4

If bilirubin is less than 1.2, the score is 0.

Nervous System	
Glasgow Coma Scale	SOFA Score
13–14	1
10–12	2
6–9	3
<6	4

Coagulation	
Platelets $\times 10^3/\mu l$	SOFA Score
<150	1
<100	2
<50	3
<20	4

If platelet is more than 150, then score is 0.

Cardiovascular System	
Mean Arterial Pressure OR Administration of Vasopressors Required	SOFA Score
MAP <70 mm Hg	1
dopamine ≤5 or dobutamine (any dose)	2
dopamine >5 OR epinephrine ≤0.1 OR norepinephrine ≤0.1	3
dopamine >15 OR epinephrine >0.1 OR norepinephrine >0.1	4

(vasopressor drug doses are in µg/kg/min)

Kidneys	
Creatinine (mg/dl) [µmol/l] (or Urine Output)	SOFA Score
1.2–1.9 (110–170)	1
2.0–3.4 (171–299)	2
3.5–4.9 (300–440) (or <500 ml/d)	3
>5.0 (>440) (or <200 ml/d)	4

Recommended strategies for the early dx of sepsis (Sepsis-3—Singer M, et al. *JAMA*. 2016;315(8):801–810)

Summary of Recommendations—Surviving Sepsis Campaign 2012

(Published in *Crit Care Med.* 2013;41:580–637)

Evidence-based classification for grading the quality of evidence & the strength of recommendations: Quality of evidence: A (highest), B, C, D (lowest); Strength of recommendation: 1 (recommended), 2 (suggested)

Hospital-wide focused care should be implemented (1C) for the management of sepsis, & performance should be measured against those (many hospitals deploy special sepsis-teams).

Initial Resuscitation

Early fluid resuscitation should begin immediately as shock is diagnosed for septic pt (persistent hypotension, or if blood lactate >4 mmol/l). While recent studies did not show benefits to a protocol-based fluid replacement strategy (ProCESS Investigators, Yealy DM, et al. *NEJM.* 2014;370(18):1683–1693) judicious, early fluid resuscitation has become the standard of care now & it has improved the outcomes of sepsis (as large observational studies have documented).

The goals of quantitative resuscitation during the 1st 6 hrs of management are (1C):

MAP ≥65 mm Hg

Urine output ≥0.5 ml/kg/hr

Central venous pressure (CVP) 8–12 mm Hg; 12–15 if mechanically ventilated

Central venous (superior vena cava) $ScvO_2$ ≥70% or mixed venous SvO_2 ≥65 mm Hg

Continue fluid resuscitation until lactate is normalized (2C)

If venous O_2 saturation target not achieved (despite of achieving CVP target)

Administer dobutamine (up to 20 mcg/kg/min) to help achieve central venous O_2 saturation target (2C)

Diagnosis

Obtain at least 2 blood cx (preferably before antimicrobial therapy is administered, however, abx administration should not be delayed more than 45 min in order to obtain these cx) (1C)

Blood cx should be obtained from peripheral veins/arteries; 1 may be obtained from indwelling catheters if the catheter has been in place longer than 48 hrs

Use 1,3 β-D-glucan assay (2B) & mannan & anti-mannan antibody assays for the early dx of invasive candidiasis (2C)

Additional diagnostic imaging studies after the pt is stabilized & is safe to move

Antibiotic Therapy

Begin broad-spectrum IV abx as soon as possible, but no later than within 1 hr of identifying septic shock (1B) or sepsis (1C)

Use broad-spectrum agents with good penetration into presumed source (double gram-negative & MRSA coverage)

Reassess antimicrobial regimen to optimize efficacy, prevent resistance, & reduce toxicity. Reevaluate daily & deescalate abx as soon as cx data is avail.

Stop abx if the cause of illness is noninfectious

Source Control

Specific anatomical dx (nidus) of infxn should be sought (e.g., necrotizing soft tissue infxn, peritonitis with intra-abd infxn, cholangitis, intestinal infarction, etc.) or ruled out, & emergent source control be sought as rapidly as possible (Dellinger RP, et al. *Crit Care Med.* 2008;36:296–327)

Surgical drainage (if required) should be undertaken within 12 hrs of the dx for source control for more stable pt (1C)

Fluid Therapy

Crystalloids should be the primary fluid used for initial resuscitation (1A)

Albumin can be added to initial fluid resuscitation (2B)

Do not recommend the use of hydroxyethyl starches (1B)

For pt with signs of tissue hypoperfusion due to sepsis & hypovolemia a minimum of >1,000 ml crystalloids (minimum of 30 ml/kg resuscitation) should be administered within the 1st 4–6 hrs. More fluid may be needed to achieve the goals of initial fluid resuscitation as described above (1B)

For fluid challenge, recommend the administration of incremental fluid boluses to the goals described above & until hemodynamic improvement occurs in the dynamic (delta pulse pressure, stroke volume variation) or static (arterial pressure, HR) variables (1C) measures

Vasopressor Therapy and Vasopressors

Vasopressor therapy should initially target a mean arterial BP (MAP) 65 mm Hg (1C)

Norepinephrine should be the 1st-line pressor used (1B)

Epinephrine should be added (or substituted) when BP is poorly responsive to norepinephrine (2B)

Vasopressin 0.03 U/min may be added to norepinephrine to improve MAP (2A)

The use of dopamine (as an alternative to norepinephrine) is only suggested for highly selected pt at very low risk of arrhythmias, with bradycardia (2C)

Phenylephrine is not recommended, unless norepinephrine causes severe arrhythmias, or as salvage when other vasopressors/inotropes fail to achieve MAP target (1C)

Inotropic Therapy

Dobutamine should be administered (or added to vasopressors) when the following are present (1C):

Myocardial dysfunction (elevated cardiac filling pressure with low CO)

Ongoing signs of tissue hypoperfusion (lactate elevation) despite of achieving adequate intravascular volume & MAP

Blood Product Administration

Transfuse RBCs to maintain Hgb >7.0 g/dl once hypoperfusion is resolved & there are no signs of myocardial ischemia or severe other heart dz, severe hypoxemia, acute hemorrhage or lactic acidosis (for those keep Hct >30, Hgb >10 g/dl) (1B)

Mechanical Ventilation, Sepsis-Induced ARDS

Use 6 ml/kg tidal volumes for pt with ARDS/ALI or at risk of ARDS (some exceptions are acceptable based on pt respiratory drive) (1A), & to maintain plateau pressure of <30 cm H_2O (in pt with normal extrapulmonary compliance) (1B)

Higher levels of positive end-expiratory pressure (PEEP) should be used when higher FiO_2 is required for pt with more severe ARDS (2C)

May use recruitment maneuvers for pt with severe refractory hypoxemia (2C)

Suggest prone positioning for pt with very severe ARDS PaO_2/FiO_2 <100 after recruitment maneuvers in facilities with experience with such practices (2C)

Sedation, Analgesia, and Neuromuscular Blockade in Sepsis

Neuromuscular blocking agents (NMBA) should be avoided for pt without ARDS, as there is a risk of a prolonged blockade

If NMBA are used, intermittent small boluses or low-dose infusion should be used, with monitoring of the depth of the blockade (train-of-4 nerve stimulator) (1C)

For pt with severe sepsis-induced ARDS a short course (<48 hrs) of NMBA can be used (2C) while monitoring blockade

Appropriate sedation & pain control must be maintained while receiving NMBA

Glucose Control

Begin insulin when 2 consecutive blood glucose measurements exceed 180 mg/dl

Protocolized glucose management should aim to keep blood glucose <180 mg/dl (1A)

Deep Venous Thrombosis (DVT) Prophylaxis

Recommend the use of daily subcutaneous low–molecular-wt heparin (LMWH) for the prevention of DVT (1B)

If LMWH is not avail. (or deemed too high risk for bleeding) low-dose sc unfractionated heparin should be used (1B)

Recommend the combination of heparin pharmacotherapy & pneumatic compression devices (unless contraindicated) for pt with severe sepsis (2C)

Nutrition

Early appropriate nutritional support should begin as soon as it is safe; the enteric route is preferred, unless contraindicated

Corticosteroids

Do NOT use corticosteroid treatment for adult septic shock pt if fluid resuscitation & vasopressor therapy are able to restore tissue perfusion & hemodynamic stability (no mortality benefit [Sprung CL, et al. *N Engl J Med.* 2008;358:111–124.])

When tissue perfusion is impaired & hemodynamics are unstable, 200 mg IV hydrocortisone (rather than other steroids (2B)) can be given in continuous infusion (2C); hydrocortisone ALONE should be used without fludrocortisones (1B)

Do NOT use ACTH stimulation test (2B)

Goals of Care, Communication of Prognosis

Discuss with pt & families:

Goals of care & the prognosis (1B), should be addressed no later than 72 hrs after admission depending on cultural considerations (2C)

Integrate those goals into 1 unified treatment plan, including palliative care plans & end-of-life planning (1B)

Summary of National Quality Forum/Surviving Sepsis Campaign Management Bundles/Milestones

To be completed within 3 hrs of presentation

1. Measure lactate level
2. Obtain blood cx prior to abx administration
3. Administer broad-spectrum abx (administer within 1 hr)
4. Administer 30 ml/kg crystalloid for hypotension or for lactate >4 mmol/l

To be completed within 6 hrs of presentation

1. Apply vasopressors if unresponsive to appropriate fluid resuscitation (goal MAP ≥65 mm Hg)
2. If hypotension is sustained after initial fluid resuscitation
   a. measure & follow CVP trend
   b. measure & follow $ScvO_2$
3. If lactate is elevated, remeasure & aim for normalizing lactate

Severe Acute Pancreatitis: Pancreatitis with Persistent Organ Failure >48 Hours

Most common causes: alcohol, biliary stones, drugs, hypertriglyceridemia, infxn

Dx: clinical & lab features

Constant epigastric pain radiating to the back

Nausea & vomiting

Fever & hypotension

Flank (Grey Turner sign) or umbilical (Cullen sign) ecchymoses

Elevated amylase & lipase (more specific), levels do not correlate with severity

Contrast CT: Enlarged interstitial edematous pancreas with heterogeneous enhancement

Abd US: Enlarged hypoechoic pancreas

Predictors of Disease Severity

Early detection of severe dz may be difficult.

Ranson criteria: Severe pancreatitis is likely if the score ≥3 (Ranson JH, Rifkind KM, Turner JW. *Surg Gynecol Obstet.* 1976;143:209–219).

At admission (1 point each):

Age >55 yrs

AST >250 IU/I

LDH >350 IU/l

WBC >16,000 cells/mm^3

Glucose >200 mg/dl

At 48 hrs (1 point each):

Ca <8 mg/dl

Hct ↓ >10%

PaO_2 <60 mm Hg

Base deficit >4 mEq/l

Fluid sequestration >6 l

BUN increase ≥5 mg/dl following fluid resuscitation

Organ failure, hypotension or Apache II ≥8

CT criteria:

Single or multiple fluid collections (Balthazar EJ, Robinson DL, Megibow AJ, et al. *Radiology*. 1990;174:331–336)

Necrosis, abscess, pseudocyst

EPIC (extrapancreatic inflammation on CT) score ≥4 (De Waele JJ, et al. *Pancreas.* 2007;34:185–190)

Treatment:

Vigorous fluid resuscitation: 200–350 ml/hr for 24–48 hrs if cardiac status permits

Supplemental oxygen, correction of metabolic abnormalities.

Abx

Only indicated for infected necrosis/abscess/or suspected sepsis.

No prophylactic abx indicated even for severe necrotizing pancreatitis.

Sterile vs. infected necrosis determined by percutaneous aspiration.

Nutrition:

Should begin immediately in mild pancreatitis & within 24–72 hrs in moderate to severe

Oral intake preferred if tolerated & not limited by significant nausea, vomiting or pain

If unable to tolerate diet mouth enteral feeding via feeding tube indicated

Nasojejunal feedings preferred but nasogastric acceptable

TPN for intolerant pt who remain NPO >7 days

Analgesia: frequently requires parenteral opioids

ERCP indicated for gallstone pancreatitis or cholangitis

Management of pancreatic necrosis: CT-guided needle aspiration vs. surgical debridement depending on response to therapy & stability of pt

Cholecystectomy for gallstone pancreatitis should be performed after recovery

ENDOCRINE DISORDERS AND RENAL ISSUES IN THE ICU AND RENAL ISSUES

ERNEST I. MANDEL, MD • KENNETH B. CHRISTOPHER, MD

Hyperglycemia—Diabetic Emergencies

Diabetic Ketoacidosis (DKA)

Precipitating factors—5 I's

Insulin—nonadherence

Infxn/inflammation

Ischemia/infarction

Intra-abd process—pancreatitis, cholecystitis, appendicitis, splenic injury, ischemic bowel

Iatrogenesis—steroids

Manifestations

Altered mental status

Nausea, vomiting, abd pain

Volume depletion

Kussmaul breathing

Acetone odor on breath

Polyuria/polydipsia

Volume depletion (& polyuria) less likely in ESRD

Test

Check serum & urine glucose, acetone, β-hydroxybutyrate

Management

Insulin infusion until AG (anion gap) closed

10 units IV push → 0.1 units/kg/hr

Once glucose <250 & AG closed, transition to SQ insulin with IV overlap of 2–3 hrs

If glucose <250 & AG still high, continue insulin infusion & add dextrose infusion

Volume resuscitation—patients (pt) are profoundly volume depleted from polyuria

Start NS 10–14 ml/kg/hr depending on degree of volume depletion & cardiac function

Need to monitor closely for resultant hypernatremia after volume resuscitation

Electrolytes

Sodium—pseudohyponatremia

Corrected Na = measured serum Na + 1.6 × (glucose/100)

May in fact be hypernatremic from osmotic diuresis

Potassium—total body K is depleted; serum K may be artificially high due to volume depletion & acidosis; with volume resuscitation & correction of acidosis true K depletion will become apparent

If K <4.5 add 20–40 mEq KCl to IVF

Bicarbonate

If pH <7.0, can use isotonic bicarbonate for initial fluid resuscitation

May need to increase threshold for K supplementation (e.g., <5.3) due to intracellular shift from correcting acidosis

Phosphate—often total body PO_4 depleted; like K depletion, may be masked by volume depletion & acidosis & revealed/magnified by volume resuscitation & correction of acidosis

Administer phosphate if <1.0

Hyperglycemic Hyperosmolar Nonketotic (HHNK) Coma

Precipitating factors

Same as DKA

Manifestations

Altered mental status

Volume depletion

Polyuria/polydipsia

Management

Insulin—use lower doses than in DKA, e.g., 0.05 units/kg/hr

Volume resuscitation—may also be profoundly free water depleted

Start NS or ½ NS 10–14 ml/kg/hr depending on degree of volume depletion, free water depletion, & cardiac function

Glycemic Control

Nondiabetics

No mortality benefit from intensive insulin therapy (generally glucose of 80–110 mg/dl) in several studies of both surgical & medical pt & in fact intensive control may increase mortality (Van den Berghe G, et al. *N Engl J Med.* 2001;345:1359–1367; Van den Berghe G, et al. *N Engl J Med.* 2006;354:449–461; NICE-SUGAR Study Investigators, Finfer S, Chittock DR. *N Engl J Med.* 2009;360:1283–1297)

Less intensive arm generally 140–180 mg/dl; therefore suggest goal of blood glucose <180 mg/dl

Diabetics

Subanalyses of diabetics or dedicated diabetic trials did not show a mortality benefit from intensive insulin therapy, including in setting of acute MI; therefore suggested goal of blood glucose <180 mg/dl (Moghissi ES, et al. *Diabetes Care.* 32:1119–1131)

Adrenal Insufficiency

Absolute adrenal insufficiency (AI)

Primary AI should receive usual dose & possibly increased dose of corticosteroid if critically ill or undergoing major surgery

100–150 mg IV hydrocortisone or 50–100 mg hydrocortisone q6–8h periprocedure or during critical illness may be reasonable (Coursin DB, Wood KE. *JAMA*. 287:236–240)

Relative adrenal insufficiency—in Sepsis (Annane D, et al. *JAMA*. 288:862–871; see Chapter 23 for sepsis)

Criteria

Severe hypotension refractory to volume resuscitation & at least 1 vasopressor

Treatment

Hydrocortisone 50–100 mg q6–8h or 200 mg infused over 24 Hr

Thyroid Disease

Hypothyroidism

Definition

Low free T4

TSH variable (primary—low; secondary [central]—variable)

Clinical manifestations

General

Metabolic slowing—weakness, fatigue, cold intolerance, wt gain, delayed relaxation of DTRs

Accumulation of matrix substances (glycosaminoglycans)—dry skin, nonpitting edema

Other—depression, dysmenorrhea

Subclinical hypothyroidism

Mildly elevated TSH with normal T4

Euthyroid sick syndrome

Abnormal TFTs in setting of nonthyroidal illness (critical illness, post-CABG)

Low T4, low T3, high TSH

Reverse T3 may be high

No benefit to thyroid hormone replacement

Myxedema coma

Myxedema with hypotension, hypothermia, hyponatremia

Etiology & precipitants

With goiter—Hashimoto's, postthyroiditis, iodine deficiency; general risk factors include age, female sex

Without goiter—surgical removal or destruction, neck radiation exposure, radioactive iodine, amiodarone

Management

General—levothyroxine replacement at 1.5–1.7 mcg/kg/d, may convert to IV if unable to take PO

Myxedema coma—5–8 mcg/kg of T4 IV, then 50–100 mcg IV daily; may also need glucocorticoid replacement for concomitant adrenal insufficiency

Hyperthyroidism

Definition

Elevated free T4 & free T3

TSH low unless TSH-secreting tumor

Clinical manifestations

General

Restlessness, tachycardia, Afib, wt loss, hyperreflexia, dysmenorrhea, fine hair

Thyroid storm

Tachycardia, delirium, hyperthermia, systolic HTN, GI sx

Etiology & precipitants

Graves' dz, thyroiditis, toxic adenomas, TSH-secreting pituitary tumors, iodine-induced

Acute illness, infxn, postpartum

Management—ICU focus

Thyroid storm

Beta blockers for tachycardia, esp. propranolol (decreases T4 to T3 conversion)

PTU

Iodide (for "Wolff–Chaikoff" effect—iodine administration temporarily inhibits iodine organification in the thyroid gland)

Steroids (decrease T4 to T3 conversion)

Hypopituitarism

Manifestations

Central adrenal insufficiency (ACTH deficiency) with mineralocorticoid axis intact

Central hypothyroidism (TSH deficiency)—need to follow T4 directly as TSH may be low (or inappropriately normal)

Central diabetes insipidus (ADH deficiency)—polyuria, mild hypernatremia

Other abnormalities—prolactin deficiency, growth hormone deficiency, FSH & LH deficiency

Etiologies

Posttransphenoidal surgery, trauma, tumor, infxn, infiltration (sarcoid, hemochromatosis), Sheehan syndrome (ischemia), cavernous sinus thrombosis, pituitary apoplexy (hemorrhage)

Management

See individual conditions

Renal Issues Encountered in the ICU

Acute Kidney Injury

The most commonly seen renal problem in the ICU

Definitions—largely for epidemiologic/research purposes—RIFLE (Bellomo R, et al. *Crit Care.* 2004;8:R204–R212) & AKIN (Mehta RL, et al. *Crit Care.* 2007;11:R31); from AKIN:

a. Serum creatinine rise—abrupt (within 48 hrs) absolute increase in SeCr of 0.3 mg/dl or ≥50%
b. Oliguria—<0.5 ml/kg for 6 hrs

Etiology

Prerenal—decreased perfusion

Causes:

Volume depletion—absolute or 3rd spacing (↓ ECV)
Hypotension (even relative) from ↓ CO or ↓ SVR
Renal vasoconstriction (NSAIDs, ACE/ARB, CNIs, hepatorenal syndrome, hypercalcemia)

Hepatorenal syndrome (HRS)

Definitions/dx

Type I (days to 2 wks) vs. Type II (wks to mo)
Usually bland sediment, UNa usually <10
No response to volume resuscitation
No other cause—volume depletion (recent paracentesis), infxn (esp. SBP), hypotension/shock, nephrotoxins

Management

Colloid to increase MAP
Midodrine/octreotide (Angeli P, et al. *Hepatology.* 1999;29:1690–1697)
Vasopressin (Kiser TH, et al. *Nephrol Dial Transplant.* 2005;20:1813–1820)
TIPS procedure (Brensing KA, et al. *Gut.* 2000;47:288–295)
Liver transplant
Renal replacement therapy (RRT)—supportive if TIPS or liver transplant possible

Acute Tubular Necrosis (ATN)

Causes

Ischemic—decreased perfusion, acute or as consequence of prolonged prerenal state

Nephrotoxic—drugs (AG, vancomycin, platins, amphotericin)

Radiocontrast nephropathy (RCN)

Causes prerenal/ischemic ATN (afferent vasoconstriction), nephrotoxic ATN (oxidative damage)

Cr rise 24–96 hrs postcontrast

Prevention includes pre/posthydration, NAC 600–1,200 mg BID day prior to, & day of contrast

Pigment nephropathy—myoglobin (rhabdomyolysis), Hb (intravascular hemolysis)

Rhabdomyolysis causes prerenal/ischemic ATN (volume loss, 3rd spacing to damaged tissue), nephrotoxic ATN (oxidative damage from myoglobin), & tubular obstruction from precipitation of myoglobin

Dx includes urine dip positive for blood but no RBC on microscopy, elevated CK (usually >1,000 IU/l)

Management includes volume resuscitation with NS, maintenance of high urine output with volume alone or with diuretic (lasix or mannitol) +/− alkalinization

Intravascular hemolysis—postthrombectomy (e.g., DVT treatment)

Management same as rhabdomyolysis

Acute Interstitial Nephritis (AIN)

Culprits

Abx (penicillins, sulfa, cephalosporins), NSAIDs, antacids (H2 blockers & PPIs), cancer biologics

Sarcoidosis, Sjogren syndrome

Hx/time course

With drug-related AIN it requires 5–7 days of previous exposure prior to manifestations (or past exposure leading to accelerated time course on rechallenge)

Dx based on hx; sediment with WBC or WBC casts suggestive but often bland; unclear utility of urine eosinophils

Management

Removal of offending agent

Steroids—limited evidence to support, balance with risk (esp. infectious when abx induced); suggested doses include prednisone 1 mg/kg (max 60 mg) for 3–14 days then taper or in severe cases pulse methylprednisolone (0.5–1 mg daily for 3 days) followed by taper

Rapidly Progressive Glomerulonephritis (RPGN)—ICU Focus

Etiology

Pulmonary-renal syndromes

ANCA

Anti-GBM

SLE-related

When to suspect/clinical manifestations

Hx suggestive (hemoptysis, SLE-related serositis)

Sediment with acanthocytes or RBC casts

Workup

Serology—ANCA, anti-GBM, C3, C4, CH50, ANA/dsDNA

Renal biopsy

Management—empirically while awaiting biopsy

Steroids 0.5–1.0 g methylprednisolone daily for 3 days, then taper

Induction—once confirmed by biopsy, cyclophosphamide or mycophenolate depending on etiology

Pheresis (TPE) to be considered esp. in anti-GBM if needed for RRT

RRT for usual indications (uremia, acidosis, volume overload)

Obstruction

Consider: elderly male, recent Foley catheter, hx of prostate dz (BPH or cancer), abd/pelvic tumor (extrinsic compression), significant ascites, or abd distension

Check post-void residual, renal US

Caution: esp. in setting of volume depletion, degree (or presence) of hydronephrosis may not reflect degree (or presence) of obstruction

Abd compartment syndrome

Ascites (liver failure, malignant), intra-abd hemorrhage (trauma, postoperative)

Transduce bladder pressure; 20–30 abnormally high, >30 very concerning

Other Dz Causing Renal Impairment

Thrombotic thrombocytopenic purpura & hemolytic-uremic syndrome (TTP-HUS)

Microangiopathic hemolytic anemia (MAHA) & acute kidney injury (AKI) may also include other signs/sx—fever, altered mental status

Associated with drugs (calcineurin inhibitor), SLE, cancers, infxn, ADAMTS13 deficiency

Consider pheresis/TPE in addition to usual AKI management

Tumor lysis—obstructive urate nephropathy in setting malignancy

Spontaneous or perichemotherapy

Usually leukemia or lymphoma, rarely solid tumors

Management

Volume expansion & maintenance of high urine output (150–300 ml/hr) +/− alkalinization

Allopurinol

Uricase administration

General Workup for Renal Problems Occurring in the ICU

Careful hx & physical exam

Review of vital signs/op reports for hypotensive episodes

Review of medications & lab data for precipitants (e.g., ACE/ARB, NSAIDs, drop in Hb/hematocrit)

Charting/graphing of Cr to narrow timing of insult

FENa <1% suggests prerenal; >2% suggests ATN; 1–2% indeterminate
(Steiner RW. *Am J Med.* 1984;77:699–702)

If on diuretics, FEUrea <35% suggests prerenal; >35% suggests ATN
(Carvounis CP, et al. *Kidney Int.* 2002;62:2223–2229)

Urine osm may suggest severity of ischemic ATN (the closer to isotonic, the less remaining concentrating ability & the more severe the ATN; also less likely volume sensitive/prerenal component)

Urine microscopy & sediment analysis

r/o obstruction via renal US or other modality

Further lab testing (serologies, etc.) as suggested by above evaluation

Treatment Approach/Strategies—EBM

Failed therapeutic interventions

Diuretics (Ho KM, Sheridan DJ. *BMJ.* 2006;333:420)

Dopamine (Bellomo R, et al. *Lancet.* 2000;356:2139–2143)

ANP (atrial natriuretic peptide) (Robin LA, et al. *N Engl J Med.* 1997;336:828–834)

Fenoldopam (AJKD. 46;26)

IGF-1 (Kidney International. 55;2423)

Thyroxine (Kidney International. 57;293)

Hemodynamic support

Maintain MAP >65; 70–80 for optimal renal perfusion

Volume management

Judicious IVF to achieve/maintain euvolemia

Central venous monitoring may be helpful

Withdrawal of offending agents

Avoidance of nephrotoxins

ACE-I/ARB

NSAIDs

Contrast dye

Aminoglycosides, cisplatin

Drug dosing/changes

Assume CrCl <10 if creatinine rising or anuric for purpose of med dosing

Abx dosing by levels when appropriate

Nutrition & electrolyte considerations

Minimize potassium intake

Minimize phosphate intake, may consider phosphate binders such as calcium acetate, sevelamer, lanthanum if taking PO; use limited (6–8 doses) aluminum hydroxide if not taking PO (will still bind salivary PO_4)

Reduce dietary protein (d/c supplements) to minimize catabolism & high urea

Consider sodium bicarbonate PO or IV

Renal Replacement Therapy

Indications AEIOU

A—acidosis

E—electrolyte abnormalities (K, Ca)

I—ingestions

O—overload (volume management)

U—uremia (mental status changes, pericarditis; intractable uremic bleeding)

Modalities

Continuous vs. intermittent: no benefit to continuous over intermittent therapy in pt with MODS (Vinsonneau C, et al. *Lancet.* 368:379–385)

Standard vs. intensive: no benefit to intensive therapy when defined as hemodialysis 3 vs. 6 times per week or more intensive CVVH (The VA/NIH Acute Renal Failure Trial Network. *N Engl J Med.* 359:7–20)

Continuous Renal Replacement

Indications: the modality of choice for hypotensive, hemodynamically unstable pt needing RRT, effective for fluid removal. CVVH (& CVVHD/CVVHDF):

Driving force: convection/ultrafiltration—water ultrafiltered across semipermeable membrane; solute dragged across & removed as well

Replacement solution: solute concentrations (Na, Cl, buffer—bicarbonate or citrate, Mg) similar to normal plasma; can include K & Ca at various concentrations

Anticoagulation

Heparin—regional or systemic

Citrate—regional or systemic (citrate used as buffer)

Access: central venous catheter

Clinical considerations

Hyperkalemia: control of potassium is slow with continuous modalities; favor hemodialysis when hyperkalemia is of concern

Calcium/phosphate: may require repletion of Ca continuously & phosphate intermittently

Intravascular volume control—better, can change removal goals on minute-to-minute basis

Hemodynamics—already hypotensive pt better tolerate continuous therapy, may have less risk of hypotension

Intermittent Renal Replacement

Intermittent hemodialysis (IHD)

Driving force: diffusion—diffusion of water (osmosis) & solute down concentration gradient across semipermeable membrane

Replacement solution (dialysate): sodium, chloride, bicarbonate near normal plasma levels, K & Ca depending on clinical scenario

Anticoagulation: none, heparin, or other (e.g., argatroban in HIT)

Access: central venous catheter; arteriovenous fistula or graft

Clinical cnsiderations: preferred for hyperkalemia as removal is faster; volume management harder given intermittent nature; hemodynamics can be limiting if baseline hypotension, both for volume removal & successful treatment in general

IHD is the modality of choice for stable pt needing RRT who can better tolerate fluid shifts.

SLED (slow low-efficiency dialysis) & SCUF (slow continuous ultrafiltration)

Dialysis or ultrafiltration at low blood flow to minimize hypotension; not avail. at all centers

Peritoneal dialysis

Driving force: diffusion—diffusion of water (by osmosis) & solute down concentration gradient across semipermeable membrane—the peritoneum

Replacement solution (dialysate): Na, Cl, bicarbonate near normal plasma levels; glucose is solute determining gradient for osmosis, concentration can be varied to remove more or less volume

Access: peritoneal catheter; temporary catheter can also be placed acutely at some centers

Clinical considerations: acute PD possible though not avail. at all centers due to inability to place catheters acutely, or other staffing limitations

Special Considerations

Control of intra-vascular volume

ALI/ARDS—in pt without need for RRT, conservative fluid management may decrease time on ventilator & time in ICU though no significant effect on mortality (National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome [ARDS] Clinical Trials Network, Wiedemann HP, et al. *N Engl J Med.* 354:2564–2575); unclear how this applies to pt requiring RRT

Acidemia

Lactic acidosis—RRT will remove small amount of lactate & provide added buffer; however underlying cause of lactic acidosis must be addressed

Toxins & ingestions—consult nephrology early

Lithium

Altered mental status, tremor, level >2

Toxic alcohols

Calcium oxalate crystals may be present with ethylene glycol

EtOH or fomepizole antagonize metabolism & may prevent toxicity while awaiting dialytic therapy

Salicylates

Additional issues

Increased ICP (with liver failure, intracerebral hemorrhage, or CVA)—when requiring RRT, may favor slower removal/equilibration characteristic of continuous modality to avoid worsened cerebral edema

Electrolyte Abnormalities Most Commonly Associated with Renal Dysfunction

Hyperkalemia (see Chapters 1 & 22)

Hyponatremia (Figure 24-1)

Definition: represents total body water overload

Sx—altered mental status, gait instability, seizure, coma

Etiology & forms of hyponatremia

Appropriate ADH: decreased EAV (hypovolemia, hemorrhage, 3rd spacing, CHF, cirrhosis, nephrosis, myxedema, cortisol deficiency)

Inappropriate ADH

Central

Intracranial process—CVA, ICH, tumor, infxn

Medications—antidepressants, antipsychotics

Other—pain, postop (esp. orthopedic procedures)

Peripheral

Pulmonary process—SCLC, PNA, ILD, PPV, PTX, asthma/COPD

Exogenous

Oxytocin

DDAVP (iatrogenic for panhypopituitarism)

ADH-independent—polydipsia, decreased solute intake ("tea & toast," beer potomania), altered renal function, exercise-induced

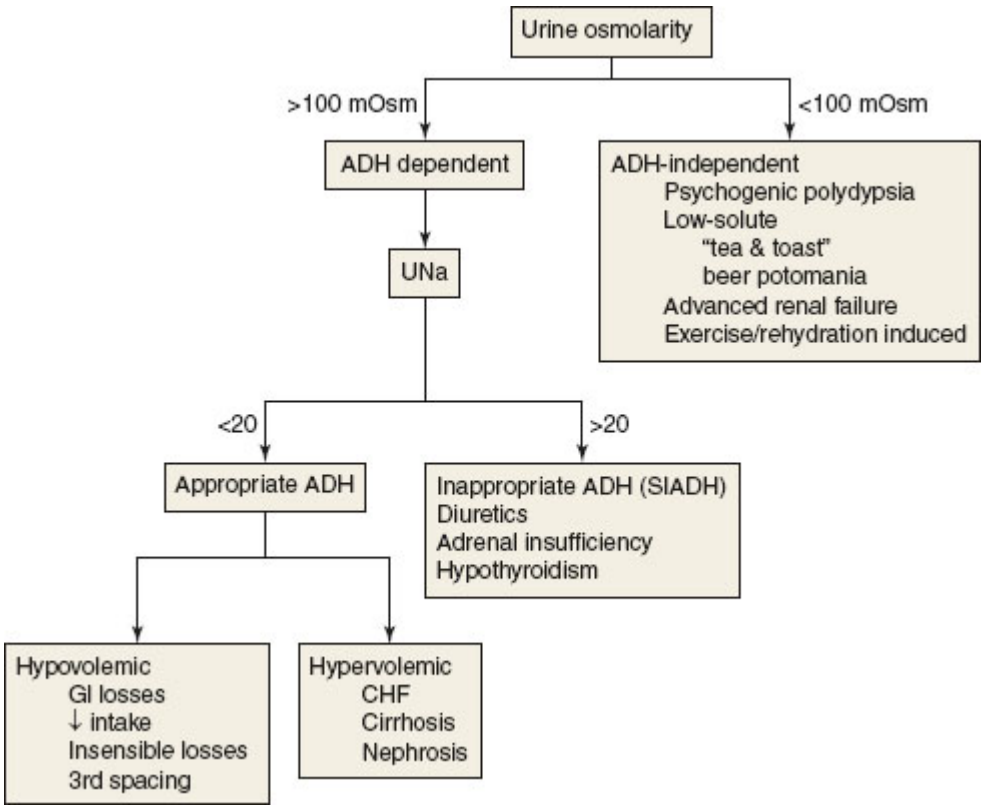
Other—pseudohyponatremia, generally lab artifact in setting hyperglycemia, hyperlipidemia, hyperproteinemia (e.g., paraprotein dz)

Workup

Urine osm, Urine Na

Hx & physical exam for volume status

Figure 24-1. Differential Diagnosis of Hyponatremia


Urine osmolarity
>100 mOsm
<100 mOsm
ADH dependent
ADH-independent
Psychogenic polydypsia
Low-solute
"tea & toast"
beer potomania
Advanced renal failure
Exercise/rehydration induced
UNa
<20
>20
Appropriate ADH
Inappropriate ADH (SIADH)
Diuretics
Adrenal insufficiency
Hypothyroidism
Hypovolemic
GI losses
↓ intake
Insensible losses
3rd spacing
Hypervolemic
CHF
Cirrhosis
Nephrosis

Management (caution: maximum rate of correction should not exceed 3 mEq/hr or 12 mEq/24 hr to avoid central pontine myelinolysis)

Remove ADH stimulus

Treat underlying cause (ICH, PNA)

Volume repletion

Recompensate heart failure

d/c causative meds

Free water restriction

Increase osmol intake (salt tabs, urea infusion)

NS +/− loop diuretic

NS only helpful if Uosmol < osmolarity of normal saline (NS: 308 mOsmol/L); caution in SIADH unless administering diuretic concomitantly to lower urine osm

Loop diuretic destroys medullary concentrating gradient, decreasing the osmotic gradient for H_2O reabsorption, thereby decreasing ADH responsiveness

Hypertonic saline

Use if symptomatic or if free water restriction fails to correct

Estimate initial hourly rate as sodium required to increase SeNa by 8–12 mEq/l in 1st 24 hrs

[Na deficit/513] × [1,000 ml/24 hr] where Na deficit = 8 × TBW (for goal 8 mEq/l in 24 hrs) where TBW = (0.60 × Wt in kg) × 0.85 if female × 0.85 if elderly

Value should always be <60 ml/hr (use online calculator to confirm rate)

Recheck SeNa very frequently as adjustment will be needed

Demeclocycline

Aquaporin channel blockers (“aquaretics”—tolvaptan, conivaptan)

Special considerations

In adrenal insufficiency

Administration of steroids in this setting can lead to rapid diuresis & result in overly rapid correction of Na; requires frequent monitoring & possible need for free water or ADH administration to slow rate of correction

Hypokalemia

Caution when repleting potassium in setting of hyponatremia as rapid repletion can lead to cellular shift of Na out of cells, exaggerating/accelerating Na rise

Hypernatremia

Definition: total body free water deficit

Etiology

Insensible losses/GI losses in setting of inadequate access to free water

Osmotic diuresis (e.g., DKA)

Diabetes insipidus (DI) as the cause of hypernatremia

Central

Nephrogenic

Drugs—Li, amphotericin, ifosfamide

Metabolic—hypercalcemia, severe hypokalemia

TI dz—sarcoid, SCD, Sjogren's

Workup

Hx & physical for volume status, source of loss

Urine osm & urine Na

UOsm >600 & UNa <20 suggests extrarenal loss, UNa >20 suggests renal loss

If DI suspected: Uosm <300 suggests complete, 300–600 suggests partial

Management

Correct underlying cause (restore euvolemia, manage DKA)

Replenish free water deficit

Target decreasing Na no more than 0.5 mEq/l/hr to avoid cerebral edema

Calculate free water deficit to replete in 1st 24 hrs as:

Free water deficit = desired change in SeNa × TBW = 8–12 × TBW where TBW = 0.60 × Wt in kg, 0.50 × Wt in kg if female; if elderly use 0.50 for men & 0.45 for women

Divide by 24 & replace hourly via IV infusion of D5W or enterally via diluted TF or intermittently as free water boluses

Also need to take into account & match ongoing losses to ensure net repletion of free water deficit

Diabetes Insipidus (DI)

Central DI

Treat with DDAVP

Nephrogenic DI

Treat underlying cause if feasible

Salt & protein restrict (decreased osmolar intake obligates less free water loss)

Distal diuretics (induces mild volume depletion which leads to greater proximal reabsorption of filtrate & less delivery distally preventing free water loss)

NSAIDs—prostaglandin inhibition eliminates prostaglandin-induced antagonism of ADH

Special Considerations

For increased ICP—mild hypernatremia may be desirable to decrease cerebral edema

Issues Related to Osmolality and Osmoregulation

Serum osm is calculated with the following formula: 2 × Na + (blood glucose/18) + (BUN/2.8)

In EtOH intoxication, add EtOH/4.6

Normal plasma range is 275–295 mOsmol/kg

It is an important factor to consider in clinical conditions where access to water is limited, as can be seen in critical illness.

Thirst & normal kidneys will compensate for changes in serum osm in healthy individuals with the influence of volume receptors & osmoreceptors. Physiologically, maintenance of plasma volume generally takes precedence over osm

Plasma hyperosm with urine hypoosm is a marker of DI (central or nephrogenic)

Plasma hypoosm with concentrated urines is a marker of either appropriate (prioritizing maintenance of circulating volume) or inappropriate ADH secretion

The abnormalities of calcium, magnesium, & phosphate homeostasis & their etiology, workup, & management are discussed in detail in Chapter 22.

CARDIAC SURGICAL CRITICAL CARE

MATTHEW T. DUDLEY, MD • MICHAEL A. GROPPER, MD, PhD

Cardiac Surgery Operating Room to ICU Handoff

OR to ICU Handoff Standardization (Agarwal HS, et al. *Crit Care Med*. 2012;40(7):2109–2115)

Standardized handoff from OR providers to ICU results in more complete exchange of critical information, does not prolong handoff & may decrease postoperative complications

Elements of Standardized Handoff	
Patient name	Date of birth
Medical record number	Age
Surgical team	Anesthesia team
Past medical history	Allergies
Procedures performed	
Surgical indications	
Intraoperative findings	
Intraoperative course	
Airway management	Cardiopulmonary Bypass time
Induction/Muscle relaxation/Reversal	Aortic cross Clamp time
Maintenance anesthetic	Circulatory arrest Time
Events on CPB	Fluids
Weaning from CPB	Crystalloid
TEE findings	Colloid
Recent lab values	Blood products
CBC	RBC
Chemistry	Cell saver
Coagulation	FFP
	Platelets
Ventilator settings	Cryoprecipitate
Current infusions	Antifibrinolytics
Peripheral venous access	Coagulation factors
Central venous access	
Arterial access	
Pacing modality & settings	
Chest tubes, drains, & location	
Plans for postoperative management	
Hemodynamic goals	
Anticipated problems	
Suitability for fast-track extubation	

Postcardiac Surgery Fast-Track Care

Fast-Track Intensive Care Following Adult Cardiac Surgery (Zhu F, et al. *Cochrane Database Syst Rev.* 2012;10:CD003587)

Foundation of low-dose opioid anesthesia & a time-directed extubation protocol with the goal of early extubation (within 6 hrs) after surgery to reduce the length of stay in the ICU. May also be extended to limitation of fluids & keeping patient (pt) warm

Risk of mortality, complications after surgery (such as myocardial infarction, stroke, major bleeding), & duration of hospital stay were similar between fast-track care group & the conventional (non–fast-track) groups

Extubation occurred earlier (3–11 hrs earlier) in fast-track pt

Time in ICU was shorter (0.4–8.7 hrs fewer) in fast-track pt

May have cost savings

Used for low-risk cases/pt (e.g., off-pump coronary artery bypass, short bypass runs)

Anesthetic plan should be tailored to include judicious dosages of hypnotics, analgesics, & muscle relaxants

Fast-Track Extubation Protocol Example

Place end-tidal CO_2 ($ETCO_2$) monitor in-line with ventilator circuit

Draw an ABG approx. 15 min after initiation of mechanical ventilation

Adjust ventilator parameters based on results of the ABG, as follows:

If PaO_2 >300 mm Hg, decrease FiO_2 to 0.5

If PaO_2 <200 mm Hg, notify intensivist or surgeon

If PaO_2 is between 200 & 300 mm Hg, decrease FiO_2 to 0.7 & titrate FiO_2 to 0.5 to keep SpO_2 >93%

Adjust VT and/or RR to keep $PaCO_2$ 35–45 mm Hg based on an end-tidal to arterial gradient at the time of the ABG above

When FiO_2 is <0.5, SpO_2 >93%, estimated $PaCO_2$ (from end-tidal monitor) is <50 mm Hg, & hemodynamics are stable, reduce ventilator rate by 50%

If pt remains stable (as defined above) after 20 min, initiate PSV trial using PEEP of 5 cm H_2O & PS 15–20 cm H_2O to keep V_T approx. equal to Volume Control V_T & RR <25 bpm

Wean PS to a minimum of 5 cm H_2O to keep RR <25 bpm when the following additional criteria below are met:

Pt is easily arousable, able to lift head off pillow, & in no apparent distress

VE (Minute Ventilation) >3 l/min & <12 l/min

Hemodynamics & body temp remain stable

RR is between 8 & 25 breaths per minute

If SpO_2 & $ETCO_2$ are within the parameters above, no pre-extubation ABG is necessary, unless there are metabolic or other values desired from ABG analysis

If pt continues to meet criteria above after 20 min, notify intensivist or surgeon of your intention to extubate

Extubate & administer O_2 to maintain SpO_2 >93% when extubated

Cardiopulmonary Bypass (CPB) and Extra Corporeal Life Support (ECLS) Sequelae

Coagulopathy

Interaction of blood with CPB/ECLS circuit yields multifactorial coagulopathies

Dilution from priming solution volume, thrombin formation in the pt & circuit, consumption of coagulation factors results in decrease of all coagulation factors

Platelet activation & consumption results qualitative & quantitative dysfunction

Anticoagulation, most commonly with unfractionated heparin, is required to prevent thrombus propagation in the circuit & requires reversal with protamine after weaning from support

Inflammation

Inflammatory reaction resulting in complement activation, SIRS, & endothelial damage & leaking

Hypothermia

Impairs activity of coagulation factor & impacts platelet function

Resultant vasoconstriction increases SVR & afterload

Shivering increases O_2 consumption

Decreased temp alters Hb-O_2 affinity & impairs O_2 delivery

Promotes arrhythmias including bradycardia & ventricular arrhythmias

Central Nervous System Injury

Stroke or spinal cord ischemia as a result of atheroembolism or vascular injury from aortic clamping; gas embolism; decreased perfusion during periods of relative or frank hypotension

Cardiovascular

Myocardial ischemia, infarction as a result of increased demand or inadequate cardioprotection

Cardiac arrhythmia due to ischemia, electrolyte perturbation, physical myocardial trauma

Vascular injury from invasive monitoring, vascular access, & bypass cannulation resulting in cold extremity, tissue ischemia, or compartment syndrome

Nonpulsatile flow may impair microcirculation

Acute Renal Injury

Acute renal injury due to relative hypotension & reperfusion injury

Deep Hypothermic Circulatory Arrest

Acceptable duration is around 30–40 min considering the increasing risk of cerebral injury with increasing time

Coagulopathy, bleeding, hemodynamic instability & organ dysfunction also increase with duration of DHCA

Common Postcardiac Surgery Management Issues

Bleeding

Differential dx: surgical bleeding; thrombocytopathia & thrombocytopenia; inadequate heparin reversal; DIC vs. primary fibrinolysis; coagulopathy secondary to hypothermia

Diagnostic techniques: monitor drain output; examine for localized vs. diffuse bleeding; serial CBC; PT/aPTT/INR; thromboelastography (TEG) or thromboelastometry (TEM); activated clotting time (ACT); fibrinogen & D-dimers, measure & normalize core temp

Surgical bleeding should be suspected & surgical reexploration of chest should be considered if there is:

>400 ml/h of blood loss during 1st postoperative hour

>200 ml/h in each of the 1st 2 postoperative hrs

>100 ml/h in each of the 1st 4 postoperative hrs

Hypotension

Differential dx: cardiac tamponade; hemothorax; tension pneumothorax (PTX); arrhythmias; myocardial ischemia (inadequate cardioplegia & cardioprotection, incomplete revascularization, reperfusion injury, etc.); acute coronary graft closure; electrolyte abnormalities; hypovolemia; bleeding; hypoxemia; acidosis (metabolic or respiratory); vasoplegia (associated with preoperative ACE-inhibitors/ARB use & extended CPB time); vasodilation on warming

Diagnostic techniques & interventions: CXR; 12-lead EKG; CBC; chem 10; ABG; transthoracic echocardiography; cardiac immediate bedside sternotomy if caused by cardiac tamponade; immediate needle decompression or chest tubes to suction if caused by PTX (have absent breath sounds; tracheal deviation); vasoplegia & vasodilation treatment may include norepinephrine & vasopressin

Hypertension

Differential dx: emergence from anesthesia; inadequate sedation; inadequate analgesia; volume overload; electrolyte abnormalities (low glucose); hypothermia; hypoxemia/hypercarbia (sympathetic stimulants)

Diagnostic techniques: postoperative pain management & sedation; ABG; FSBG; core temp

Arrhythmias

Differential dx: myocardial ischemia (incomplete revascularization, incomplete cardiac protection, new thrombosis, etc.); electrolyte abnormalities (esp. K, Mg); new AV conduction abnormalities due to valve suture placement; hypothermia; ectopy due to CVC/PA placement or malposition; hypoxemia/hypoventilation; acidosis

Diagnostic techniques: 12 lead EKG (atrial fibrillation is the most common dysrhythmia); chem 10; check pt's core temp; CXR for verification of central venous catheter position as cause of ectopy; ABG; check temporary (epicardial, transvenous) pacer settings

Alteration of Mental Status

Differential dx: CNS emboli/new CVA; neurocognitive dysfunction; residual anesthetic; delirium; electrolyte abnormalities & hypoglycemia; infxn; hypoxemia/hypercarbia

Diagnostic techniques: head CT; delirium screen; chem 10; ABG

Treatment: avoid hyperglycemia, hyperthermia, & anemia

Delirium Following Cardiac Surgery

Acute brain dysfunction characterized by inattention, fluctuating mental status, altered level of consciousness, & disorganized thinking

Postcardiotomy delirium was 1st reported in the 1960s

Incidence of delirium after cardiovascular surgery ranges from 30% to 73%

Predisposing factors: atrial fibrillation, cognitive impairment, depression, hx of stroke, older age, & peripheral vascular dz, medications (esp. benzodiazepines), sleep deprivation, hypoxia & anoxia, metabolic abnormalities, & a hx of alcohol or drug abuse

Delirium ABCDEF Bundle

Analgesia: assess, prevent & manage pain. Use appropriate pain scales (e.g., Critical-Care Pain Observation Tool [CPOT], Behavior Pain Scale)

Both: perform & pair Spontaneous Awakening Trials (SAT) & Spontaneous Breathing Tirals (SBT)
(http://www.iculiberation.org/Bundles/Pages/default.aspx
http://icudelirium.org/medicalprofessionals.html)

Choice of Analgesia & Sedation: set & monitor a target RASS & pain level decrease; avoid benzodiazepines when possible

Delirium: Assess, Prevent, & Manage

Early mobility & exercise: optimize mobility & exercise for every pt & advancing that daily as clinically indicated

Family engagement & empowerment: Encourage visits, interaction, & incorporation of familiar objects from home

Respiratory Failure (Hypoxemia, Hypoventilation)

Differential dx: reperfusion injury for (lung transplant); atelectasis; mucus plugging; pneumothorax; pulmonary edema from mobilization of fluids; respiratory insufficiency secondary to injury to phrenic and/or recurrent laryngeal nerve; residual neuromuscular blockade; pulmonary embolus

Diagnostic techniques/treatment: ABG; CXR; aggressive pulmonary toilet & bronchodilators; diuresis as needed; pain management; chest tube placement

Renal Failure

Differential dx: prerenal (perioperative hypotension; inadequate cardiac output; hypovolemia); CPB (nonpulsatile flow); hemolysis-associated tubular injury; ATN; Aortic cross-clamp placement (higher incidence with suprarenal clamps); contrast nephropathy; immunosuppressant (e.g., cyclosporine) nephrotoxicity

Diagnostic techniques: monitor UOP; UA with micro; FeNa or FeUrea; BUN/Cr

Treatment: remove nephrotoxic medications (e.g., NSAIDs, abx), hemodynamic support

Paraplegia: (Following Repair of Thoracoabdominal Aneurysm or Dissection)

Differential dx: anterior cord syndrome due to inadequate perfusion; epidural hematoma; accidental intrathecal placement of epidural catheter

Postoperative Atrial Fibrillation (POAF)

(Echahidi N, et al. *J Am Coll Cardiol.* 2008;51:793–801)

POAF

May significantly decrease CO as atrial kick provides approx. 40% of preload

Associated with thrombolic risk including stroke, tachycardia, hypotension, cardiac ischemia, & mortality

More common with open valve replacement & repair over coronary artery bypass grafting; most common in multiple valve surgeries & combined valve & CABG surgeries

Often transient, most common on postoperative day 2

Risk Factors for POAF

Advanced age (esp. age >70 yo), previous hx of AF, male gender, decreased left-ventricular ejection fraction, left atrial enlargement, valvular heart surgery, chronic obstructive pulmonary dz, chronic renal failure, metabolic syndrome, diabetes mellitus, & rheumatic heart dz

Prevention/Treatment POAF

Preoperative & postoperative β-blocker is 1st line for prevention & treatment

Biatrial pacing is likely less effective than β-blockers for prevention & requires placement of epicardial pacing leads intraoperatively

Medication	Adult Dosage	
Digoxin	0.25–1 mg IV then 0.125–0.5 mg daily IV/PO	May be used in heart failure. Not effective for prevention; may cause nausea, narrow therapeutic window
β-blocker (Class II)		
Esmolol	500 mcg/kg over 1 min then 0.05–0.2 mg/kg/min	Short-acting effect & short duration. Might worsen CHF; may cause bronchospasm, hypotension; AVB
Atenolol	1–5 mg IV over 5 min repeat after 10 min then 50–100 mg twice daily PO	Rapid onset of rate control when given IV
Metoprolol	1–5 mg IV over 2 min then 50–100 mg twice daily PO	Rapid onset of rate control when given IV
Potassium Channel Blocker (Class III)		
Amiodarone	IV: 150 mg over 10 min; then 1 mg/min for 6 hrs; Then 0.5 mg/min for 18 hrs or change to oral dosing; after 24 hrs, consider decreasing dose to 0.25 mg/min Oral: 400–600 mg daily in divided doses for 2–4 wks; Maintenance typically 100–200 mg QD	Also has α- & β-adrenergic blocking properties. May cause hypotension
Calcium Channel Blocker (Class IV)		
Verapamil	2.5 mg IV over 2 min then 80–120 mg twice daily PO	Short-acting effect
Diltiazem	0.25 mg/kg IV over 2 min then 5–15 mg/h IV	

Cardiac Surgical Procedures

Coronary Artery Bypass Grafting (CABG)

Preoperative β-blockers should be continued & restarted as postoperatively as they are associated with mortality benefit & prevention of postoperative atrial fibrillation

Aspirin & HMG-CoA reductase inhibitors should be routinely continued pre- & postoperatively

Complications

Postoperative MI as a result of inadequate myocardial protection during cardiopulmonary bypass, coronary air embolism, embolization of plaque, graft spasm, or early graft failure (within 30 days for 5–10% of saphenous vein grafts)

Approx. 4% of pt experience electrocardiographic or enzyme evidence of a heart attack after surgery. It is most common in high-risk pt including repeat CABG & combined CABG & valve surgery

Postoperative Q-wave MI is associated with higher in-hospital mortality

Aortic Surgery for Aneurysm or Dissection

Neurologic complications due to ischemia, air or atheroma embolization & bleeding as a result of long suture lines, extended CBP times or necessitation of deep hypothermic circulatory arrest are common complications

Aortic root surgeries commonly require replantation of coronary artery ostia into the graft which may result in impaired coronary blood flow & myocardial ischemia

Aortic arch surgeries may require deep hypothermic circulatory arrest with periods of interrupted cerebral perfusion

Aortic Valve Replacement (AVR)

Surgical AVR is recommended in pt who meet an indication for AVR with low or intermediate surgical risk

Current surgical AVR options include mechanical, bioprosthetic, & in specific situations homograft & autograft techniques

Immediate complications: HTN may risk aortic suture line integrity, coronary injury, obstruction or occlusion may result from valve malposition, proximity of AV note & left bundle branch risk conduction system injury & may necessitate temporary or permanent pacing, embolism from valve calcification/or vegetation

Mitral Valve Repair/Replacement

Immediate complications: coronary injury (left circumflex commonly at risk due to proximity); leaflet injury, atrial & ventricular rupture

Early complications: heart failure, stroke

Late complications: recurrent regurgitation

Pulmonary Valve Replacement

Rare in adults in absence of congenital heart dz or endocarditis

May be replaced percutaneously

Tricuspid Valve Repair/Replacement

Most commonly performed concurrently with other cardiac surgery

Immediate complications: coronary injury (right coronary artery is commonly at risk), conduction system injury, & RV failure are more common with replacement over repair

Hybrid and Percutaneous Cardiac Procedures

Vascular Access Site Considerations

Common access sites include radial, femoral, brachial

Access site bleeding/hematoma are the most common complication: immediate treatment starts with direct pressure over arteriotomy regardless of use of vascular closure device; resuscitation with IV fluids or blood products. Be aware of significant vagal reactions with direct pressure

Must be vigilant in the setting of procedural anticoagulation, dual platelet inhibitors, & IIb/IIIa inhibitors

Retroperitoneal bleeding/hematoma from femoral artery or vein access

Must be considered/ruled out with CT angiography

Pseudoaneurysm

Femoral pseudoaneurysm are more common with arterial punctures below the femoral head. Commonly treated with US guided manual pressure & collagen or thrombin. Previously, vascular surgical repair was required

Thromboembolism to distal access site

Infxn

More common with repeated vessel punctures & prolonged sheath presence (>24 hrs)

Contrast Induced Nephropathy (Shabbir A, et al. *Br J Cardiol.* 2015;22:34)

Avoiding dehydration & minimizing contrast exposure is the most reliable prevention of acute kidney injury due to radiologic contrast

Radiation Exposure

Prolonged exposure to fluoroscopy or cine angiography may result in soft tissue injury most common on skin closest to x-ray source/collimator (posterior torso/buttocks)

If such an injury is suspected, avoid wound bx & further mechanical injury

Transcatheter Aortic Valve Replacement (TAVR) or Transcatheter Aortic Valve Implantation (TAVI)

TAVR is a reasonable alternative to surgical AVR in pt who meet an indication for AVR & who have high surgical risk for surgical AVR

Delivery approach

Retrograde: Via femoral artery, retroperitoneal iliac artery with or without conduit, transaortic via partial J sternotomy, or right mini thoracotomy

Antegrade: Transapical, transvenous–transeptal

Post-TAVR Complications

Vascular complications after transfemoral TAVR are frequent & may be associated with unfavorable clinical outcomes

Aortic, iliac, or femoral artery dissection; coronary artery obstruction by the device, native valve apparatus, or calcium; left ventricular outflow tract obstruction; dislodgement of the aortic valve prosthesis; perivalvular leak; mitral valve injury resulting in acute MR; RV perforation PA catheter or pacemaker lead; pericardial tamponade; air embolism; stroke; acute kidney injury; aortic root injury

Conduction system injury including left bundle branch block & AV dissociation may be temporary or permanent

Postpercutaneous Coronary Intervention Considerations

Percutaneous Coronary Intervention (PCI) Includes

Percutaneous transluminal coronary angioplasty (PTCA) or plain old balloon angioplasty (POBA)

Coronary artery stent placement

Drug eluting stent (DES)

Bare metal stent (BMS)

Rotational atherectomy (e.g., Rotablator)

Medication Regimens

Dual antiplatelet therapy (aspirin plus clopidogrel, prasugrel, or ticagrelor) should be continued postprocedurally. Premature discontinuation of regimen may lead to stent thrombosis.

Glycoprotein IIb/IIIa inhibitors (abciximab, eptifibatide, tirofiban) are commonly used in PCI to prevent platelet aggregation & interfere with thrombus formation.

PCI Complications

Coronary artery injury

Coronary artery perforation may present as cardiac tamponade peri- or postprocedurally; often discovered during procedural angiography & may require procedural intervention with covered stent or surgical intervention

Coronary artery dissection may with diagnostic angiography & interventional procedures

Acute coronary artery thrombosis

Stent thrombosis: may occur intraprocedural, acute (within 24 hrs), subacute (within 30 days), late (31 days–1 yr), very late (greater than 1 yr)

More common with incomplete stent apposition immediately, cessation of antiplatelet therapy & use of drug-eluting stents later

Side branch occlusion

Myocardial ischemia or infarction: may be secondary to distal embolization of luminal & wall material into distal vascular beds (no reflow)

Ventricular arrhythmias

Stroke

Rate of stroke after diagnostic left heart catheterization or PCI ranges from 0.2% to 0.4%

Pulmonary Hypertension in Cardiac Surgery Patient

(Minai OA, et al. *Chest*. 2013;144:329–340)

Definition of Pulmonary Hypertension

Mean PA pressure of greater than 25 mm Hg at rest & pulmonary capillary wedge pressure of 15 mm Hg or less with a PVR greater than 3 Wood Units (WU)

Perioperative Risk of Pulmonary Hypertension

Pt with pulmonary HTN (PH) have increased risk of perioperative mortality in cardiac surgery & likely noncardiac surgery

Risk Factors for Perioperative Complications in Patients with Preoperative PH Undergoing Cardiac Surgery

Presence of preoperative PH

Systemic mean arterial pressure/mean pulmonary artery pressure <4 after anesthesia induction

Mean pulmonary artery pressure >50 mm Hg & PVR = 8.6 WU

Cardiac transplant

Pulmonary vascular resistance >4 WU

Pulmonary vascular resistance ≥5 WU despite acute vasodilator testing

Systolic PA pressure >60 mm Hg, pulmonary vascular resistance >6 WU, mean transpulmonary gradient (mPAP–mPCWP) >15 mm Hg despite maximal vasodilator therapy

Factors Contributing to Pulmonary Hypertension in the Perioperative Period

Preoperative pulmonary HTN
Increased sympathetic tone (e.g., pain, airway instrumentation, surgical manipulation)
Hypoxia
Hypercarbia
Acidosis
Ischemia–reperfusion injury
Fluid overload
Positive pressure ventilation
Left ventricular systolic or diastolic failure
Embolism: thromboembolism, CO_2 embolism, air embolism, amniotic fluid embolism
Acute lung injury/ARDS
Loss of vasculature (e.g., pneumonectomy)
Pharmacologic agents: protamine

General Guidelines for Management of Pulmonary Hypertension

Nonpharmacologic
Maintain normothermia
Maintain preload, right ventricular volume, contractility
Maintain SVR for adequate coronary blood flow. Systemic hypotension may contribute to RV ischemia & precipitate acute RV failure
Avoid hypothermia, hypoxia, hypercapnia, acidosis, atelectasis, & increased sympathetic tone as these states may increase pulmonary vascular resistance & precipitate acute RV failure
Pharmacologic:
Prostanoids: epoprostenol (Flolan) IV & commonly inhaled; treprostinil (Remodulin & Tyvaso); iloprost (Ventavis)
Phosphodiesterase inhibitors: sildenafil (Revatio); tadalafil (Adcirca); milrinone
Inhaled nitric oxide (iNO)
Endothelin antagonists: ambrisentan (Letairis); bosentan (Tracleer)
Calcium channel blockers
Abrupt cessation of pharmacologic treatment may result in acute pulmonary HTN/crisis & right ventricular failure

THORACIC SURGICAL CRITICAL CARE

SHANNON S. MCKENNA, MD

Introduction

Postoperative thoracic surgery patients (pt) may require ICU admission based on either the type of surgery or underlying medical dz

Surgery: esophagectomy, pneumonectomy, extra-pleural pneumonectomy, radical pleurectomy, decortication, sleeve lobectomy, lung transplantation

Comorbidity: severe COPD, pulmonary HTN, significant CAD, aortic stenosis, empyema, severe restrictive lung dz

Certain problems are commonly seen in the thoracic ICU. Atelectasis, pneumonia, & respiratory failure are the most common complications after thoracic surgery

Prevention/Treatment of Atelectasis and Secretion Retention

Contributing factors: splinting from pain, chest wall instability, diaphragmatic dysfunction, airway anastomoses, respiratory depression from opiates, COPD, pneumonia

Consequences: hypoxia, hypercarbia, limited exercise tolerance, pneumonia, mediastinal shift

Treatment:

Recruitment of lung volume: cough & deep breathing, ambulation, chest physiotherapy, incentive spirometry, effective pain control, IPPV

Cough assistance: chest physiotherapy, in-exsufflator, vibratory vest, acapella device or flutter device

Secretion management: humidified oxygen, nebulized saline, inhaled *N*-acetylcysteine, inhaled dornase, abx for pneumonia or bronchitis, fiberoptic bronchoscopy

Postoperative Hypotension

Etiology can be broken down into: pump dysfunction vs. inadequate venous return; universal vs. pt population-specific causes

Causes of Hypotension in Thoracic Surgical Patients		
Nonspecific Causes	**Medical Causes Associated with Thoracic Surgery**	**Mechanical Causes Associated with Thoracic Surgery**
Dehydration	Pulmonary HTN with right heart failure	Dynamic hyperinflation
Hemorrhage	Sympathectomy (epidural induced or mechanical)	Tension hemothorax or hydrothorax (chyle leak; infxn)
Myocardial ischemia/ dysfunction	Atrial fibrillation	Mediastinal shift
Sepsis		Cardiac herniation
PE		
Tension PTX		
Cardiac tamponade		

Management: find the specific etiology! EKG, CXR, & ECHO can be very helpful

Postoperative Acute Respiratory Distress Syndrome

Epidemiology

Incidence 4–5% for pneumonectomy (right > left); 2% for lobectomy
Mortality >50%

Pathophysiology

Diffuse inflammatory process involving neutrophils, macrophages, endothelial injury, & platelet aggregation

Proposed Triggers for Lung Injury
Ventilator-associated lung injury
Oxygen toxicity
Tissue injury with cytokine release
Loss of lymphatic drainage
Pulmonary HTN
Endothelial damage from increased blood flow

Management

Mirrors standard ARDS management (see Chapter 19)
May be complicated by chronic air leaks or bronchial suture lines that limit achievable/desirable airway pressure; bronchial stump may break down in the setting of critical illness leading to proximal bronchopleural fistula (BPF) (see below)

Massive Hemoptysis

Defined as >600 ml of blood (hemoptysis) in 24 hrs
Death is by asphyxia not exsanguination

Causes of Massive Hemoptysis
Pulmonary infxn
Bronchiectasis
Tumor eroding into a bronchial artery or PA
PA rupture from Swan–Ganz catheter
Trauma to chest
Pulmonary HTN
Primary vascular abnormality (arterio-venous malformation (AVM), aneurysm, vasculitis)

Management: Protect the Good Lung & Stop the Bleeding

Turn bleeding side down
Isolate nonbleeding lung: mainstem intubation of good lung, bronchial blocker placed in bleeding lung, double lumen ET tube placement
Bronchoscopy, CT, or angiography to determine site of bleeding
Treatment: bronchoscopy-based therapies, embolization, radiation, surgical resection

Bronchopleural Fistula (BPF)

Proximal (large airway open) or distal (lung surface injury)

Causes of BPF	
Proximal	**Distal**
Breakdown of bronchial stump	Alveolar rupture
Breakdown of airway anastomosis	Persistent air leak after resection
Traumatic injury to conducting airway	Traumatic injury of lung parenchyma
Tumor erosion or necrosis	Infxn with necrosis

Risk factors for stump breakdown: technical error, empyema or pneumonia, irradiation, recurrent tumor, malnutrition, poor wound healing

Consequences of proximal BPF: soilage of good lung, airflow preferentially via BPF, development of empyema

Mechanical ventilation with proximal BPF: may need to exclude the BPF (endobronchial intubation); if not excluded, pressure modes of ventilation may not work properly

Mechanical ventilation with distal BPF: gas lost through chest tube participates in gas exchange; reported (expiratory) tidal volumes & minute ventilation underestimate alveolar ventilation; target inspiratory volumes instead

Pulmonary Hypertension Leading to Right Heart Failure

(Zamanian RT, et al. *Crit Care Med.* 2007;35:2037–2050)

Risk factors: COPD, interstitial lung dz, s/p pneumonectomy, ALI with severe hypoxemia, PE

Signs/sx: hypotension, oliguria, acidosis, increased CVP, peripheral edema, hepatic engorgement/dysfunction

Assessment: EKG for ischemia, ECHO, CXR, right heart catheterization

Treatment: initially aimed at minimizing PVR & supporting RV

Treat reversible causes of increased PA pressure: hypoxia, hypercarbia, acidosis, fever, pain, hypervolemia, pulmonary hyperinflation

Pharmacologic support of RV: inodilators (dobutamine & milrinone) provide inotropic support while decreasing PVR; inotropes (epinephrine, dopamine, norepinephrine) provide inotropic support but may increase PVR

Acute pharmacologic therapies to decrease PVR: systemic nitrates (cause hypotension), systemic prostacyclin (cause hypotension), inhaled prostacyclin, inhaled nitric oxide, sildenafil

Involve pulmonary vascular medicine service early if pulmonary HTN persistent

Atrial Fibrillation

Incidence: 13–44%; highest for pneumonectomy

Purposed etiologies: atrial stretch, myocardial ischemia, pulmonary HTN, electrolyte imbalance, vagus nerve irritation, high catecholamine levels

Ppx: β-blockers & calcium channel blockers reduce incidence

Treatment: (Frendl G, et al. *J Thorac Cardiovasc Surg.* 2014;148:e153–e193)

Rate control

Rhythm control typically not successful acutely

By 6 wks most pt back in sinus rhythm

Afib-induced hypotension usually improves when rate slowed

β-Blockers & calcium channel blockers mainstays; amiodarone, digoxin, & sotalol have a role in some pt

Control of precipitating factors: pain, agitation, hypervolemia, hypokalemia, hypomagnesemia, hypoxia, & hypercarbia leading to pulmonary HTN or myocardial ischemia, respiratory distress

Anticoagulation: if in atrial fibrillation for more than 48 hrs & not contraindicated

Pain Management

Critical to prevent atelectasis, pneumonia, & alveolar hypoventilation

Pain sources: skin/soft tissue, ribs, intercostal n., pleura, pulmonary parenchyma

Afferent pathways: intercostal nerves, phrenic, & vagus

Treatment modalities for thoracic surgical pain: thoracic epidural, intercostal nerve block, paravertebral block, incisional catheters, systemic opiates, NSAIDs, acetaminophen, lidocaine patches

Thoracotomy pain typically requires multimodality approach; care must be taken to evaluate potential side effects in each pt before prescribing any given treatment

VASCULAR SURGICAL CRITICAL CARE

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Perioperative Risk

(Ford MK, et al. *Ann Intern Med*. 2010;152:26–35)

Revised Cardiac Risk Index

1. Hx of ischemic heart dz
2. Hx of CHF
3. Hx of cerebrovascular dz (stroke or transient ischemic attack)
4. Hx of diabetes requiring insulin
5. Chronic kidney dz (creatinine >2 mg/dl)
6. Undergoing suprainguinal vascular, intraperitoneal, or intrathoracic surgery

Risk for cardiac death, nonfatal MI, nonfatal cardiac arrest: 0 predictors = 0.4%, 1 = 0.9%, 2 = 6.6%, ≥3 = >11%

Most patients with vascular dz are at high risk for perioperative complications

Preoperative cardiac testing & medical optimization often necessary

Focus on smoking cessation, blood sugar control, BP control, β-blocker, statin, antiplatelet agent

Carotid Artery Stenosis

Accounts for up to 12% of stroke, the 3rd leading cause of death in industrialized nations

Surgery indicated: symptomatic >50% stenosis, asymptomatic >60% stenosis

Carotid stenting with lower cardiac complication but higher stroke rate than open surgery

Stenting may be indicated in symptomatic pt with difficult anatomy (prior neck surgery/radiation) or severe uncorrectable comorbidities

Complications of Carotid Endarterectomy (Litsky J, et al. *Curr Cardol Rep.* 2014;16:462; Ricotta JJ, et al. *J Vasc Surg.* 2011;54(3):832–836; Howell SJ. *Br J Anaesth.* 2007;99(1):119–131)

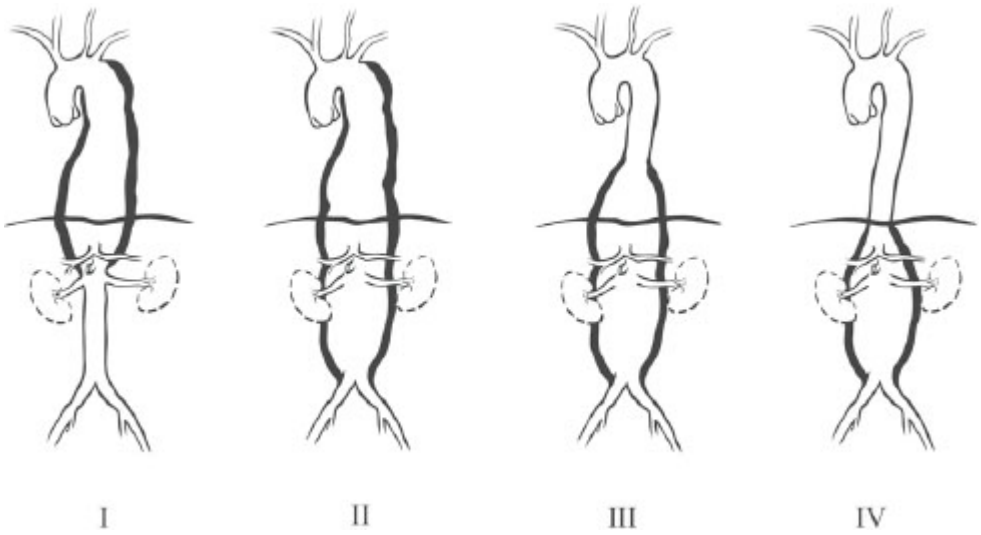
Neurologic	Cardiac	Airway/Pulmonary
Stroke: 3.4% (due to clamping, thromboembolic events, or hemorrhage) **Cerebral hyperperfusion syndrome:** 0–3% (↑ in ipsilateral perfusion after flow through the carotid artery is reestablished. Can lead to cerebral edema & death) **CN injury** (majority transient)	**MI:** 2.2% **Bradydysrhythmias & hypotension** (from manipulation of the carotid sinus) **HTN**	**Obstruction/tracheal compression** (results from an expanding neck hematoma & can be fatal if not immediately recognized) **Hypoxia & hypercarbia** (due to dysfunction of the carotid body chemoreceptors) **Hoarse or weak voice** (due to vagus nerve injury)

Aortic Aneurysms (Figure 27-1 and Figure 27-2)

(Isselbacher EM. *Circulation.* 2005;111(6):816–828)

Types of Aortic Aneurysm			
	Ascending (ATAA)	**Descending (DTAA) Thoracic/ Thoracoabdominal**	**Abdominal (AAA)**
Etiology	Cystic medial degeneration	Atherosclerotic deposits	Atherosclerotic deposits
Risks	HTN, connective tissue dz, syphilis	Smoking, HTN, age, hyperlipidemia	Smoking, HTN, age, hyperlipidemia

Figure 27-1. Crawford Classification of Thoracoabdominal Aortic Aneurysms



Surgical Approach to Aortic Aneurysm Repair

(Cao CQ, et al. *Ann Thorac Cardiovasc Surg.* 2011;17:1–6; Nicolaou G, et al. *Anesthesiol Clin.* 2013;31(2):451–478; De Bruin JL, et al. *N Engl J Med.* 2010;362(20):1881–1889; IMPROVE Trial Investigators, Powell JT, et al. *BMJ.* 2014;348:f7661)

Mortality for elective open DTAA & AAA repair 4.6–10%. Increasing to 30–50%, if emergent

Decreased early mortality & perioperative complications for endovascular repair

However similar 5 yrs all-cause mortality for endovascular and open repair

2010 AHA guidelines suggest consideration of endovascular repair for DTAAs, if technically feasible

2011 AHA guidelines suggest endovascular or open repair for AAAs

Hybrid procedures expand the scope for endovascular repair using extra-anatomic bypass techniques

Endovascular repairs require regular follow up. Higher rate of reintervention

No ICU requirement after endovascular repair unless high risk of spinal cord ischemia (SCI)

Complications of Aortic Repair (Crimi E, et al. *Anesthesiol Clin.* 2014;32(3):735–757; Bavaria JE, et al. *J Thorac Cardiovasc Surg.* 2007;133:369–377; Cheng D, et al. *J Am Coll Cardiol.* 2010; 55:986–1001)

Complication (Open vs. Endovascular)	Pathophysiology	Risk Factors	Management
CV: **(Open 10–20%)** MI **(6.3 vs. 2.3%)** CHF Dysrhythmias (Afib)	Plaque rupture (early MI) Myocardial VO_2/DO_2 mismatch (late MI) Perioperative fluid shifts	CAD CKD HTN Tachycardia Hypotension Massive resuscitation	Target SBP within 20% baseline TEE/TTE/Invasive hemodynamic monitors Maintain euvolemia Continue β-blocker, statin, antiplatelet
Pulmonary: **(20 vs. 4%)** Ventilator >48 hrs Reintubation Tracheostomy	ALI Edema/Effusion Atelectasis Pneumonia Diaphragmatic dysfunction	Smoking hx COPD Phrenic nerve ligation Diaphragmatic division Massive resuscitation 1-lung ventilation	Lung-protective ventilation Conservative transfusion strategy. Aim Hg >7 g/dl Early extubation Early mobilization VAP bundle Maintain euvolemia Aggressive pulmonary toilet Early use of NIPPV

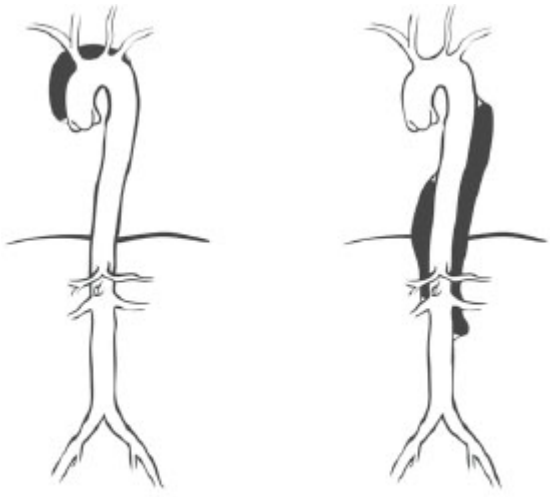
Renal: **(15 vs. 5%)** Acute kidney injury Dialysis Requirement	Acute tubular necrosis Contrast nephropathy Cholesterol embolization Rhabdomyolysis	CKD X-clamp time X-clamp position Hemodynamic instability Hypovolemia Transfusion Nephrotoxins	Maintain euvolemia Maintain renal perfusion Minimize aortic X-clamp time Limit exposure to toxins Iso-osmolar contrast Minimize contrast volume Prompt institution RRT
CVA **(6 vs. 5%)**	Ischemia Embolization Hemorrhagic	Prior CVA Age Extensive atheroma Emergent repair Long segment	Neurologic exams Prompt CT/CTA/MRI Maintain CPP (if confirmed nonhemorrhagic) Avoid hyperglycemia Avoid hyperthermia
Spinal Cord Ischemia **(14 vs. 3%)** Paraparesis Paralysis	Anterior spinal artery syndrome Coverage artery of Adamkiewicz T9–T12	Aneurysm extent Aortic dissection Emergent surgery Hypotension X-clamp time	Reduce ischemic time Distal aortic perfusion Support MAP Monitor spinal cord function CSF drainage (7–8 mm Hg)
Postoperative Hemorrhage **Requiring reoperation (6.5 vs. 0.01%)** **Pt requiring transfusion (83.7 vs. 3.9%)**	Coagulopathy (dilution/consumptive) DIC Platelet sequestration	Extensive surgery Major intraop blood loss Hypothermia/ hypoCa/acidemia	Replace blood & components Monitor INR/PTT/ fibrinogen/TEG Maintain normothermia Replace calcium Avoid hyperkalemia
Mesenteric Ischemia/ Ischemic colitis **(open 0.6–2%) but 45–65% mortality**	Splanchnic hypoperfusion Embolic/thrombotic/ mechanical obstruction	Extent atheroma Extent aneurysm Sacrifice of IMA	Monitor for abd pain Monitor for persistent lactic acidosis Early radiologic evaluation Early surgical consult

Acute Aortic Syndrome (80–90% aortic dissection)

Etiology is a tear in the intima of the vessel wall which allows blood to flow between the layers of the aorta, creating a "false" lumen (Kamalakannan D, et al. *Crit Care Clin.* 2007;23(4):779–800.)

Risks are HTN, connective tissue disorder (Marfan, Ehlers–Danlos), bicuspid aortic valve, massive blunt chest trauma, preeclampsia, cocaine abuse

Figure 27-2. Stanford Classification of Aortic Dissection



Diagnosis

Diagnostic Modalities	
CXR	Widened mediastinum; aortic "knob"
Contrast CT scan	Contrast delineates 2 lumens, initiation point, & extent of dissection
MRI	Gold standard; 3D reconstruction
TEE	Real-time viewing; color Doppler allows for visualization of flow & dynamic components of flow in true/false lumens

Treatment (Debakey ME, et al. *J Thorac Cardiovasc Surg.* 1965;49:130–149; Setacci F, et al. *J Cardiovasc Surg (Torino).* 2010;51(5): 641–646; Bombien R, et al. *Rev Cardiovasc Med.*

2013;14:e99–e106)

Treatment Options for Dissected Aortic Aneurysms		
Stanford A	**Stanford B**	**Complicated Stanford B**
1–2% mortality per hour after sx onset Requires surgical/ definitive treatment	Medical management Control pain Control HR to 60 Control spontaneous bacterial peritonitis 100–120 mm Hg 1st-line IV β-blocker (caution if aortic regurgitation) 2nd-line calcium channel blocker	Presence of malperfusion, rapid aortic expansion, or rupture Surgical intervention Endovascular procedures increasingly considered

Peripheral Vascular Disease

Etiology is atherosclerosis, similar to that occurring in the heart & aorta
Claudication is usually the presenting sx
Treatments include angioplasty, stenting, or open surgery to improve or divert flow to affected areas
ICU care generally reserved for open procedures (femoral–popliteal or femoral–tibial bypass graft) with need generally correlating to duration of surgery & underlying comorbidities

Complications: (Ghansah JN, et al. *Semin Cardiothorac Vasc Anesth.* 2004;8:335–361)

Typical Complications of Peripheral Vascular Disease	
Sepsis	"Septic limb" should be treated by emergent surgery for source control
Rhabdomyolysis	Compartment syndrome can develop if a graft is occluded or kinked, or if there is ongoing ischemia to the limb
Death	Most commonly due to CV morbidity

NEUROLOGIC CRITICAL CARE

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Coma and Disorders of Consciousness

Coma: a state of unarousable unresponsiveness
Stupor: severely diminished arousal & responsiveness
Delirium: high (hyperactive) or low (hypoactive) arousal with confusion & inattention
Vegetative State: awake (eyes open) but unaware of self or environment, with preservation of sleep/wake cycles & complete or partial preservation of hypothalamic & brain stem autonomic functions
Persistent Vegetative State (PVS): >1 mo in vegetative state
"Permanent" Vegetative State: 3 mo after nontraumatic brain injury, 1 yr after traumatic brain injury (TBI), but reports of late recovery of awareness in pt with TBI & nontraumatic brain injuries have undermined concept of permanence (Estraneo A, et al. *Neurology.* 2010;75:239–245)
Minimally Conscious State (MCS): severely impaired consciousness in which minimal but definite behavioral evidence of self-awareness or environmental awareness is demonstrated
NOTE: neurologic examination associated with ~40% misdiagnosis rate of VS when compared to neurobehavioral assessment with Coma Recovery Scale-Revised, which is more sensitive for diagnosing MCS (Schnakers C, et al. *BMC Neurology.* 2009;9:35)
Locked-in Syndrome: state of de-efferentation with quadriplegia & loss of lower CN function but preservation of sensation, cognition, & eye movements
Catatonia: a state of unresponsiveness predicated on a psychiatric disorder with disturbance of motor behavior but maintenance of consciousness. Stuporous & hyperexcitable forms of catatonia exist, with stuporous form potentially being mistaken for coma. Behavioral disturbances include mutism, posturing, waxy flexibility, & catalepsy
Coma Scales: multiple coma scales exist; see Chapter 43 for **Glasgow Coma Scale (GCS)**
Pathophysiology, Ddx, and Clinical Manifestations:
Neuroanatomic localization: dysfunction of brain stem reticular activating system, thalamic relay nuclei, and/or bilateral diffuse dysfunction of cerebral hemispheres. In coma of unknown etiology, subsequently determined causes: diffuse and/or metabolic brain dysfunction >

supratentorial lesion > infratentorial lesion > psychiatric "coma" (conversion reaction, depression, catatonic stupor)

Etiologies of Coma (Plum and Posner's Diagnosis of Stupor and Coma, 4th ed. Oxford University Press. Oxford; 2007)

Structural causes (compressive/destructive): *hemispheres* (EDH, SDH, SAH, ICH, stroke, hypoxic ischemic encephalopathy, tumor, abscess, meningitis, encephalitis, vasculitis, leukoencephalopathy, prion dz, progressive multifocal leukoencephalopathy); *diencephalon* (basal ganglia ICH, stroke, tumor, abscess, pituitary tumor, pineal tumor, encephalitis, fatal familial insomnia, paraneoplastic syndrome); *Brain stem* (cerebellar stroke, ICH, tumor, abscess; brain stem stroke, ICH, tumor, or infxn)

Diffuse, multifocal, or metabolic causes: hypoxia, ischemia, hypoglycemia, vitamin cofactor deficiency: thiamine, niacin, pyridoxine, $B1_2$, folate; endogenous metabolic products (hepatic coma, uremic coma, CO_2 narcosis, exocrine pancreatic encephalopathy, myxedema–thyrotoxicosis, hypo- or hyperparathyroidism, adrenal dz); meds/poisons (sedatives, acidic agents, psychotropic drugs, medication overdose); sepsis, hypo- or hypernatremia, acidosis or alkalosis, hypo- or hyper-Mg, hypo- or hyper-Ca, hypo-phos, temp dysregulation (hypothermia or heat stroke), seizure or postictal state, concussion, psychogenic

Clinical Features of Coma, PVS, MCS, and Locked-in Syndrome				
	Coma	PVS	MCS	Locked-in Syndrome
Consciousness	None	None	Partial	Full
Sleep/wake	Absent	Present	Present	Present
Motor function	Reflex & postural	Postures or withdraws to noxious stimulus; occasional nonpurposeful movement	Localizes; reaches for & holds objects; automatic movements, e.g., scratching	Quadriplegic
Auditory function	None	Startle; briefly orients to sound	Localizes to sound location; inconsistent following of verbal commands	Preserved
Visual function	None	Startle; brief visual fixation	Sustained visual fixation & visual pursuit	Preserved
Communication	None	None	Contingent vocalization; inconsistent but intelligible verbalization or gesture	Aphonic & anarthric; blinking & vertical eye movements usually intact
Emotion	None	May have reflexive crying or smiling	Contingent crying or smiling	Preserved

PVS, persistent vegetative state; MCS, minimally conscious state.
Source: Giacino JT, et al. *Neurology.* 2002;58:349.

Initial Management and Evaluation of Coma and Impaired Consciousness:

ABCs, 1 mg/kg IV thiamine, 1 gm/kg IV dextrose, 0.01 mg/kg IV naloxone
Comprehensive metabolic panel, CBC with diff, coags, ABG/VBG, serum & urine tox screen, serum osms, EKG; consider thyroid function tests, adrenal function tests, UA/Ucx, blood cx
Head CT and/or brain MRI. Consider LP, EEG
Additional lab & imaging investigations based on clinical suspicion for specific etiology.

Prognosis of Coma, PVS and MCS: coma prognosis varies widely depending on underlying cause. Traumatic coma has better outcomes than hypoxic–ischemic coma.

Prolonged coma rare; most progress to PVS within 1 mo. Both PVS & MCS can exist as permanent or transitional states. Likelihood of significant functional improvement decreases over time for both PVS & MCS.

Brain Death

Definition of Brain Death: irreversible cessation of all spontaneous & reflexive brain functions. Brain death is clinically determined by coma, absence of brain stem reflexes, & apnea. Ancillary testing not necessary in adults but may be used for determination of brain death when clinical testing is limited or questionable (Wijdicks EF. *N Engl J Med.* 2001;344:1215)

Preparation for Brain Death Assessment: (1) Notify local organ bank. (2) Involve pt's nurse & if appropriate, religious officials and/or medical ethics services before discussing plans for brain death assessment with family. (3) Discontinue sedatives or hypnotics. (4) Confirm that the following clinical criteria are met: known & irreversible cause of neurologic injury; clinical or radiologic evidence of CNS catastrophe consistent with brain death; if cardiac arrest is the etiology, consider observing >6 hrs then reexamining; no severe acid/base, electrolyte, endocrinologic disturbances or hyperammonemia; no drug/EtOH intoxication (if barbiturates levels present, must be <10 μg/ml or "absent" on tox screen); if significant doses of CNS depressants have been administered recently, use ancillary testing; no neuromuscular blockade (if pt recently received neuromuscular blocking agents, must confirm reversal with train-of-4 stimulation); if severe facial trauma, prior pupillary abnormalities, toxic levels of sedative drugs, or severe chronic CO_2 retention limit the clinical assessment of brain death, use ancillary testing

Clinical Findings Consistent with Brain Death: facial myokymias; spontaneous spinal movements of limbs (Ropper AH. *Neurology.* 1984;34:1089); respiratory-like movements: shoulder elevation/adduction, back arching, intercostal expansion without significant tidal volume; sweating, blushing, tachycardia; normal osmolar control mechanisms (absence of diabetes insipidus); presence of DTR's.

Clinical Findings Not Consistent with Brain Death: decerebrate or decorticate posturing of the limbs; pinpoint pupils → must r/o narcotic overdose; spontaneous breathing movements.

Clinical Criteria for Brain Death

Coma: no eye opening, verbal response, or purposeful movement. No purposeful response to noxious stim with supraorbital pressure & nail-bed pressure in all 4 extremities.

Absence of brain stem reflexes: Pupils: fixed pupils, even with bright light & magnifying glass; ocular movements: no oculocephalic reflex → only test if C-spine integrity has been ensured; no oculovestibular reflex (absent caloric stimulation response) → confirm integrity or tympanic membrane & absence of significant blood/cerumen in external auditory canal, elevate head-of-bed to 30° & irrigate external auditory canal with 30–50 ml of ice water; observe for ocular response (1 min); repeat on contralateral side after >5-min delay.

Facial motor responses: no corneal reflex to touch with cotton swab. No facial grimace to deep pressure on nail beds, supraorbital ridge, or TMJ.

Pharyngeal and tracheal reflexes: no gag with stimulation of posterior pharynx. No cough to bronchial suctioning.

Apnea testing: prerequisites & prep: core temp ≥36.5°C (96.8°F). Spontaneous bacterial peritonitis >90 → if pt requiring pressors or experiencing arrhythmias, consider ancillary testing instead of proceeding with apnea test. Euvolemia → if diabetes insipidus present, need + fluid balance over prior 6 hrs. Adjust ventilator settings to achieve arterial pH 7.35–7.45 & $PaCO_2$ 35–45 mm Hg ≥20 min prior to apnea testing (or to pt's baseline, if known CO_2 retainer). Preoxygenate with 100% FiO_2 for 5 min to PaO_2 >200 mm Hg. Procedure: disconnect pt from ventilator. Administer 100% O_2 at 8–10 l/min via ETT or tracheostomy to the level of carina immediately after disconnecting vent. Observe for respiratory movements for approx. ~8 min → abd or chest excursions. After 8-min period elapses, check ABG to measure PaO_2, $PaCO_2$, & pH. Reconnect pt to ventilator after ABG is drawn. If during 8-min period off ventilator, pt develops cyanosis, spontaneous bacterial peritonitis <90 mm Hg, significant O_2 desaturation, or cardiac arrhythmia → draw STAT ABG, discontinue apnea testing, & reconnect ventilator. Positive Apnea Test (consistent with brain death): no respiratory movements. ABG Criteria: $PaCO_2$ ≥60 mm Hg or $PaCO_2$ increase ≥20 mm Hg from baseline. Apnea test considered positive if stopped early as long as no respiratory movements are observed & ABG criteria are met. Negative Apnea Test: respiratory movements observed OR ABG criteria not met after sufficient time elapsed. Indeterminate Apnea

Test: apnea test performed, with no respiratory movements observed but ABG criteria not met → may repeat test for longer time period if clinically stable, or proceed to ancillary testing.

Ancillary Testing to Confirm Brain Death	
Diagnostic Test	**Findings Consistent with Brain Death**
EEG	Core temp must be ≥36.5°C (96.8°F) No change in EEG record with auditory, visual, or noxious stimulation EEG interpretation must be confirmed by attending neurologist
4-Vessel Angiogram	No contrast filling of cerebral vasculature in anterior or posterior circulation Contrast filling of ICAs should stop abruptly at petrous segment where ICA becomes intracranial Delayed filling of superior sagittal sinus may be seen due to patency of external carotid circulation
SPECT with Tech 99	No uptake of isotope in brain parenchyma → study must be interpreted by attending nuclear medicine physician Isotope uptake within meninges & skull vessels may be seen due to perfusion from external carotids
Transcranial Doppler (TCD)	Perform TCD cerebral blood flow velocity measurements in b/l intracranial cerebral vasculature & extracranial vasculature (CCAs, ICAs, cervical portions of vertebral arteries) Must observe small systolic peaks in early systole without diastolic flow or with reverberating flow → suggests high vascular resistance from ↑ ICP & absence of tissue blood flow TCDs must be performed 2 times 30 min apart

Documentation of Brain Death in Medical Record: date & time of death (for ancillary testing, use time of interpretation), name the physician declaring brain death, etiology & irreversibility of neurologic injury, absence of eye opening or verbal response, absence of brain stem reflexes, absence of motor response to noxious stimuli, details of apnea test → time of test initiation, preapnea & postapnea pH & $PaCO_2$, use of ancillary testing, indication, & interpreting physician's name, results of repeat neurologic examinations, if performed, time & reason for contacting medical examiner, if appropriate.

Hypoxic–Ischemic Injury after Cardiac Arrest

<10% survival for out-of-hospital cardiac arrest after CPR (Callans DJ. *N Engl J Med.* 2004;351:632–634).
<20% survival to d/c for in-hospital cardiac arrest after CPR (Peberdy MA, et al. *Resuscitation.* 2003;58:297).
Increased duration of anoxia prior to CPR & increased duration CPR → decreased outcome (Rogove HJ, et al. *Crit Care Med.* 1995;23:18–25)
NOTE: prognostication, as detailed below, has been studied primarily in pt NOT treated with hypothermia

Prognosis after Cardiac Arrest in patients NOT tx with Hypothermia

Neurologic Examination: absence of pupillary & corneal responses has strong predictive value within 1–3 d postarrest. Eye opening & spontaneous eye movements may occur early without indicating good outcome; best predictive value after 3 d. Motor response is stronger predictor than overall GCS score & is most specific for poor outcome after 3 d. Single seizure & intermittent focal myoclonus do NOT predict poor outcome, but in pt not treated with hypothermia, diffuse myoclonus strongly a/w in-hospital death & poor outcome even if brain stem reflexes intact (Zandbergen EG, et al. *Neurology.* 2006;66:62–68). Good outcome may occur rarely in pt with diffuse myoclonus who have been treated with hypothermia (Rossetti AO, et al. *Neurology.* 2009;72:744–749).

Prognosis after Cardiac Arrest Using Neurologic Examination Patients *NOT* Treated with Hypothermia (*Neurol.* 2006;67: 203–210)

Time after Arrest	Virtually No Chance of Regaining Independence	Best Chance of Regaining Independence
Initial exam	Absent brain stem reflexes	Pupillary light reflex present Decorticate or decerebrate posturing Conjugate roving or orienting eye movements
Day 1	Myoclonus or status epilepticus	Motor response withdrawal or better Eye opening spontaneously or to noise
Days 1–3	Absent SSEP N20 response Serum NSE >33 µg/l	Motor response withdrawal or better
Day 3	Absent pupillary or corneal reflexes; extensor/absent motor responses	Motor response withdrawal or better NL spontaneous eye movements
> Day 3	Unknown	Motor response obeying commands

MRI: absence of diffusion restriction on DWI/ADC associated with better neurologic outcome (Barrett KM, et al. *Mayo Clin Proc.* 2007;82:828). Reduction in whole-brain median ADC may predict poor outcome (Wu O, et al. *Radiology.* 2009;252:173). Qualitative evaluation of imaging abnormalities by stroke physicians' highly sensitive method with limited specificity for predicting poor outcome (Greer D, et al. *Neurocrit Care.* 2012;17:240). Common DWI/ADC abnormalities include cortical ribbon, watershed infarct, thalamus, basal ganglia. Findings on MRI follow characteristic temporal & spatial patterns involving the basal ganglia & cerebellum initially, followed by cortical & white matter changes in early & late subacute periods (Greer D, et al. *Neurocrit Care.* 2011;14:61–67).

EEG: Rhythmic delta activity associated with better prognosis, while suppressed voltage & burst-suppression patterns with generalized epileptiform activity associated with poor prognosis (Søholm H, et al. *Resuscitation.* 2014;85:1580–1585). Alpha coma pattern is NOT invariably associated with poor outcome (Austin EJ, et al. *Neurology.* 1988;38:773). Postanoxic status epilepticus is NOT invariably a/w poor outcome after therapeutic hypothermia (Rossetti AO, et al. *Neurology.* 2009;72:744–749). Absence of background reactivity is associated with poor outcome (Rossetti AO, et al. *Lancet Neurol.* 2016;15:597)

SSEPs: more accurate prognostic tool than EEG b/c less confounding by medications & metabolic encephalopathy. B/l absence of N20 with median nerve stim strongly predicts poor outcome. Insufficient data for prognostic value of BAERs & VEPs.

Biochemical Markers: neuron-specific enolase >33 μg/l at days 1–3 a/w poor outcome. Serum astroglial S100 does not have prognostic value.

ICP and Brain Oxygen Monitoring: insufficient evidence for prognostic value.

Therapeutic Hypothermia for Coma after Cardiac Arrest

Inclusion criteria: Not following commands within 6 hrs of cardiac arrest.
Relative exclusion criteria: Hemodynamic instability requiring high-dose pressors. Major head trauma → r/o ICH by head CT prior to cooling if clinical suspicion for head trauma at the time of arrest. Recent major surgery (within 14 d). Systemic infxn/sepsis → hypothermia interferes with immune function. Other etiology for low level of consciousness → drug/EtOH, preexisting coma prior to arrest. Active bleeding → hypothermia impairs clotting factor activity. Admin of thrombolytic, antiplatelet, or anticoagulation meds for cardiac condition is NOT a contraindication to hypothermia.
Mechanisms of Action: reduces cerebral metabolic rate & oxygen demand. Reduces cerebral edema & ICP by preserving blood–brain barrier integrity. Reduces excitotoxic neuronal injury. Minimizes free radical release. Suppresses inflammation.
Supporting Data: mortality & neurologic recovery benefits demonstrated by multiple randomized trials (Hypothermia after Cardiac Arrest Study Group. *N Engl J Med.* 2002;346:549–556; Bernard SA, et al. *N Engl J Med.* 2002;346:557–563). More recent literature on out-of-hospital cardiac arrest pt who present in coma—hypothermia below target temp of 36°C showed no additional benefit (Nielsen N, et al. *N Engl J Med*. 2014;369:2197). Therapeutic cooling NOT proven to be beneficial for coma after primary respiratory arrest without concomitant cardiac arrest. *Hyperthermia is detrimental:* odds ratio for unfavorable outcome is >2 for each 1°C increase in temp after arrest (Zeiner A, et al. *Arch Int Med.* 2001;161:2007–2012).
Basic Principles and Approach to Therapeutic Hypothermia: avoid hyperthermia & rapidly initiate cooling. Multiple cooling methods may be required to meet temp goal 33°–36°C.
Total cooling period 24 hrs, begins when cooling is initiated, NOT when target temp is reached. Shivering may have to be managed to avoid hyperthermia.

Therapeutic Hypothermia Protocol (May Vary by Institution)

1. *External cooling with cooling blankets & ice:* obtain 2 cooling blankets & cables (1 machine) to "sandwich" the pt → place sheets b/n blankets & pt to protect skin. Cold saline via peripheral lines may be helpful.
2. *External cooling with cooling vest devices:* set target temp goal on device. Consider secondary temp monitor → record pt's temp on cooling vest device, secondary temp source, & follow water temp of the cooling device → water temp indicates work device must perform to keep pt at target body temp.
3. *Monitoring & supportive therapy during hypothermia:* monitor vitals closely. No indication for BIS or train-of-4 monitoring during hypothermia; Consider EEG monitoring to diagnose subclinical status epilepticus masked by neuromuscular blockade (Legriel S, et al. *Neurocrit Care.* 2009;11:338–344). MAP >90 mm Hg. Check electrolytes, CBC, & glucose at 12 & 24 hrs → hypothermia may cause hypokalemia, esp. during concurrent insulin administration; rewarming may cause hyperkalemia due to K+ efflux from intracellular compartment. Hyperglycemia & increases in serum amylase & lipase may occur during cooling. Goal $PaCO_2$ 35–45 mm Hg → analyze all ABGs at pt's body temp. Examine skin for burns q2h if using cold blankets.
4. *Approach to Shivering:* Start with extremity counter warming & escalate to acetaminophen, buspirone 30 mg q8h, Mg infusion with serum goal level of 3–4, dantrolene 2.5 mg/kg q6h, meperidine 25–75 mg q4h, dexmedetomidine 0.2–0.7 μg/kg/h, propofol and/or paralysis (Badjatia, et al. *Crit Care Med.* 2009;37:1893–1897).
5. *Rewarming: Basic Principles:* Do NOT rewarm faster than 0.25°C or 0.5°F per hour → passive or controlled rewarming should take at least 8–12 hrs. Shunting of CO to reopening peripheral vascular beds may cause hypotension. Aim for normothermia once rewarming phase is completed.

Prognosis after Cardiac Arrest for Patients Treated with Hypothermia (*Ann Neurol.* 2010;67:301–307)		
Prognostic value of a combination of at least 2 of the following negative findings (measured after rewarming after therapeutic hypothermia, between 36 & 72 hrs postcardiac arrest) Bilaterally absent SSEP — Unreactive EEG Background, Early myoclonus — Incomplete recovery of brain stem reflexes		
Prediction	**In-Hospital Mortality**	**Poor 3–6 month Outcome**
Sensitivity (95% CI)	79 (67–88)%	62 (51–72)%
False-positive rate (95% CI)	0 (0–8)%	0 (0–14)%
PPV (95% CI)	100 (93–100)%	100 (93–100)%
NPV (95% CI)	76 (63–86)%	44 (31–58)%
Based on outcomes in 111 comatose survivors of cardiac arrest treated with TH.		

Decompressive Craniectomy (see more details in Chapter 43)

Indications: reverse mass effect & brain tissue shifts, decrease ICP, & improve cerebral perfusion pressure. Craniectomy lowers ICP by 15%, opening dura lowers ICP by 70%. Considered for: cerebral mass lesions, intracerebral hemorrhage, subarachnoid hemorrhage, malignant cerebral edema from stroke, hemispheric encephalitis

Malignant Edema after MCA Infarct

Epidemiology: 10% of strokes develop malignant cerebral edema (Moulin DE, et al. *Stroke.* 1985;16(2):282–284)

Clinical Presentation: NIHSS score >15 for right, >20 for left hemispheric infarctions

Forced gaze deviation, visual field cut, hemiplegia, aphasia, or neglect. 78% mortality rate due to temporal lobe herniation with brain stem compression/torque (Hacke W, et al. *Arch Neurol.* 1996;53:309–315)

Imaging Predictors: head CT: large hypodensity >50% MCA territory most important predictor of malignant edema, herniation, & death (von Kummer R, et al. *AJNR Am J Neuroradiol.* 1994;15:9–15); septum pellucidum midline shift >5 mm. Brain MRI: volume of infarct >80 cm^3 on DWI (Thomalla GJ, et al. *Stroke.* 2003;34:1892–1899). CTA/MRA: large vessel occlusions (ICA, proximal MCA)

Clinical Predictors: age: <50 yrs. Early-onset decreased consciousness. N/V <24 hrs; spontaneous bacterial peritonitis > 180 mm Hg <12 hrs. Elevated white blood cell count. Heart failure (Kasner SE, et al. *Stroke.* 2001;32:2117)

Evidence: RCTs: HAMLET, DESTINY, DECIMAL 93 pt, <55 yo Rx <48 hrs for large MCA infarct with decompressive hemicraniectomy. 1-yr favorable outcome (mRS 0–4): 75% craniectomy pt, 24% control group; mRS 3 or less: 43% craniectomy, 21% control group. 1-yr survival: 78% hemicraniectomy, 29% control group. Benefit offset if there was delay to surgery >3 days. DESTINY II: hemicraniectomy also increases survival without severe disability in pt >60 yo.

Edema in Posterior Fossa

Neurologic Emergency: swelling can cause hydrocephalus due to compression of 4th ventricle, brain stem compression by upward transtentorial or tonsillar herniation

Clinical Presentation: unsteady gait, N/V, HA, dizziness, diplopia, dysarthria, anisocoria.

Rx: (1) Medical: mannitol, hypertonic saline, hyperventilation (for acute herniation syndromes); (2) surgery: suboccipital craniectomy with possible resection of infarcted brain & ventriculostomy. Maintain ventriculostomy postop until clear evidence of no sig hematoma or continued mass effect/edema. Suboccipital craniectomy: life-saving if medical Rx unable to prevent progression of swelling or clinical deterioration. Should be performed prior to clinical decompensation; do not wait for medical therapy to fail in a pt with a large stroke & clear progression of 4th ventricular compression; hydrocephalus can occur acutely & lead to rapid, fatal deterioration. *Considerations:* time from sx onset, size of infarct, pt's age, potential for neurologic recovery. Most pt recover with relatively good quality of life.

Intracerebral Hemorrhage

Indications: cerebellar hemorrhages >3 cm with clinical deterioration, brain stem compression, or hydrocephalus (Broderick J, et al. *Stroke.* 2007;38:2001–2003). Cerebral hematoma evacuation controversial: considered for supratentorial lobar clots within 1 cm of cortical surface.

Relative contraindications: advanced age, serious medical comorbidities, stable clinical condition, remote onset of hemorrhage, bleed in dominant hemisphere

STICH 1 & 2 trials: these trials failed to demonstrate the benefit of early surgical hematoma evacuation in pt with intracranial hemorrhage. The role of surgery is being explored in subset of pt with novel techniques, including minimally invasive approaches, advanced imaging guidance, & endoscopic techniques (Mendelow AD, et al. *Lancet.* 2013;382:397–408).

Pt with moderately sized hematomas & decreased arousal may be appropriate surgical candidates for hematoma evacuation

Anticoagulation Reversal		
Anticoagulant	**Agent**	**Dose**
Warfarin	4 factor PCC Kcentra	INR >6 → 50 IU/kg INR 4–6 → 35 IU/kg INR <4 → 25 IU/kg
	+ Vitamin K	10 mg IV over 10 min
	or Profilnine SD	INR >4 → 50 IU/kg INR <4 → 25 IU/kg
	or FFP	2–6 units
TPA	RiaSTAP	Fibrinogen >150 → 2 vials Fibrinogen <150 → 2 + 2 vials
	or Cryoprecipitate	Fibrinogen >150 → 20 Fibrinogen <150 → 20 units + 20 units
Heparin	Protamine	1 mg/100 heparin units over the last 4 hrs
Enoxaparin	Protamine	If <8 hrs → 1 mg/mg of enoxaparin If > 8 hrs → 0.5 mg/mg of enoxaparin
	Andexanet	Investigational
Aspirin	Platelets	6 packs
Plavix	ddAVP	0.3 μg/kg over 30 min
	Platelets	6 packs
Dabigatran (thrombin) Check TT	Idarucizumab	5 g IV × 1
	FEIBA	100 units/kg
Rivaroxaban, Apixaban, Edoxaban, (factor Xa) Check Xa & PT	Kcentra	35 IU/kg
	Andexanet	Investigational
Uremia	ddAVP	0.3 μg/kg over 30 min
Fondaparinux	Factor VIIa	90 μg/kg
Argatroban	ddAVP	0.3 μg/kg over 30 min
	Cryoprecipitate	10 units

Postoperative Care: (1) Swallowing precautions, incentive spirometry, crystalloid fluids. (2) Prevention of ICP elevation. (3) Airway management: risk of airway collapse due to prolonged recovery of consciousness, esp. in cases of brain retraction during surgery. (4) Refractory N/V after posterior fossa surgery more common in women: ondansetron 1–4 mg IV or promethazine 12.5–25 mg IV. (5) Unrest, anxiety, discomfort due to ETT: dexmedetomidine, an α-2-adrenergic agonist, decreases anxiety without causing respiratory depression; approved for use only for 1st 2 postoperative days. (6) Chemical DVT ppx may be considered 24–48 hrs after craniotomy

Complications: meningitis, abscess, hemorrhage, stroke, cerebral edema, seizure, air embolism

Mechanical Ventilation of Neurologic Patients

Depressed level of consciousness: prevent aspiration, promote optimal gas exchange, start with controlled modes, & as drive recovers transition to support modes

Elevated ICP: for short duration (as a bridge to definitive intervention) can use hyperventilation to lower $PaCO_2$ to 30–35 mm Hg, decrease 1–2 ml/min CBF/decrease 1 mm Hg $PaCO_2$; avoid worsening ICP elevation during intubation; avoid succinylcholine; propofol, lidocaine, or thiopental may lower ICP, but watch for hypotension; use etomidate if low BP; caution ischemia; rebound elevation in ICP if hyperventilating for extended duration.

Spinal cord injury: phrenic nerve paralysis, intercostals & abd weakness; caution with jaw lift, ET intubation; may need tracheostomy in severe injuries; increased aspiration risk from ileus; watch for delayed apnea in high cervical injuries. Hypersensitivity to depolarizing blockade agents, seen esp. with denervating dz, extreme muscle disuse; avoid usage >48 hrs, else severe hyperkalemia → cardiac arrest. Alternatives—nondepolarizing agents.

Neuromuscular ventilatory failure: (1) *Acute polyneuropathy:* autonomic instability → decreased BP with sedation (barbiturates, benzodiazepines, opioids), increased K+ with succinylcholine (use nondepolarizing blockade); topical anesthetics (short-acting benzodiazepines, atropine), blind nasal ET intubation; SIMV & PS; bedside cardiac meds for resuscitation prn. (2) *NMJ dz:* exaggerated response to nondepolarizing agents, e.g., vecuronium; unpredictable response to succinylcholine. (3) *Myopathies:* AVOID succinylcholine; risk of hyperkalemia/rhabdomyolysis.

Recovery from neurogenic respiratory failure: ventilatory drive & chemosensitivity recover 1st → wean from controlled to assist mode, can be hypercapnic at night when have decreased LOC, so controlled mode at night. Respiratory muscle strength recovery next → PS mode, ensure adequate inspiratory pressure.

NEUROVASCULAR CRITICAL CARE

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Transient Ischemic Attacks

General: Transient Ischemic Attack (TIA): brief, reversible episode of focal neuro sx (by definition <24 hrs, most <1 hr). Newer definition: brief, reversible episode of focal neuro sx due to ischemia with a negative magnetic resonance imaging (MRI). Often hard to diagnose, given multiple mimics. Longer TIAs more likely from an embolus; repeated TIAs with similar sx suggest impending vessel occlusion. *TIAs should be worked up urgently.* Early work up & treatment of TIA/minor stroke reduces risk of stroke by up to 80% (Rothwell PM, et al. *Lancet Neurol.* 2007;370:1432).

Approach to Transient Neurologic Symptoms

Top 3: TIA, seizure (seizure), migraine. Others: syncope, compressive neuropathy, anxiety, conversion, malingering, prior stroke sx remanifested by metabolic derangement/infxn, amyloid spell.

TIA: *Pt:* older, M > F, stroke risk factors (HTN, DM). *Sx:* negative (e.g., aphasia). If multiple modalities (i.e., sensory, motor) usually occur all at once. HA: occasional. *Duration:* brief (usually <15 min). Scoring system: ABCD2.

Seizures: *pt:* younger. *Sx:* Begins with positive (tingling) → Negative (e.g., paresis, aphasia) postictally. *Duration:* very brief (sec–min). Negative can sometimes last hours.

Migraines: *pt:* younger, F > M, +FHx. *Sx:* HA after attack, N/V, photo-/phonophobia. Begins positive sx (bright lights), followed by negative sx. Slowly evolving (e.g., tingling spreads up arm). Modalities affected sequentially (e.g., vision → sensory/motor). *Duration:* longer (30 min–hrs).

Ischemic Strokes

Etiologies: *embolic:* sudden onset sx, maximal at onset. Occasionally patient (pt) reports getting up to go to bathroom & developing sx. *Hemodynamic/thrombotic:* full main deficit sometimes preceded by warning signs (either TIAs or minor sx) or stuttering course (progressive neurologic worsening over several hours).

Main Subtypes	
Large artery atherosclerosis (~18%)	• Most common sites: carotid bifurcation, vertebrals at origin or at vertebrobasilar junction, MCA at stem/bifurcation • Rare for plaque to develop beyond 1st branching point • Risk factors: HTN, DM, dyslipidemia, smoking
Cardioembolic (~21%)	• Afib, MI, CHF, prosthetic valves, rheumatic heart dz • Most often lodge in MCA (esp. superior division) or PCA territory • Small embolus → cortical/penetrating arteries; large → main branches
Small vessel (lacunar) (24%)	• Due to lipohyalinosis → concentric narrowing of small penetrating vessels • Infarcts up to 2 cm in size • Often associated with HTN

Other Causes

Vasculitis: Due to autoimmune dz, arteritis (temporal, Takayasu), infectious (Tb, syphilis, VZV), or primary CNS vasculitis

Dissections: Strokes typically in younger pt (35–50 yo) but can happen in older pt. Anticoag vs. antiplatelets

Fibromuscular Dysplasia: Uncommon, affects women (30–50 yo). Imaging: string of beads (segmental narrowing & dilations of arteries), usually B/L. Arteries affected: renal, ICA > vertebral > intracranial. Can cause dissection. Rx: antiplatelet therapy

Moyamoya: Mostly in Asians but occurs worldwide. Occlusion of large arteries (usually distal ICA or main stem MCA/ACA) → lenticulostriate develops collaterals. *Angio:* collaterals = "puff of smoke" = moyamoya in Japanese. Stroke 2/2 large artery occl, intracerebral hemorrhage (ICH) 2/2 breakdown/fragility of collaterals. *Rx:* surgical (decreased ischemic stroke): encephalo-duro-arterio-synangiosis (if bypass not feasible, involves laying branch of superficial temporal artery (STA) onto affected brain hoping it will grow into brain) or bypass of STA to MCA

Drugs: Amphetamines, cocaine, heroin, cause either acute HTN, drug-induced vasculopathy, or emboli/endocarditis

Subcortical Vascular Dementia: Elderly with longstanding HTN; multiple subcortical infarctions → dementia. MR: extensive white matter Δ's. Rx: Alzheimer meds not found to be helpful (Dichgans M, et al. *Lancet Neurol.* 2008;7:310). Treat underlying cause of infarcts with antithrombotics & risk factor modification

Cadasil (cerebral autosomal dominant arteriopathy with subcortical infarcts & leukoencephalopathy): 30–50 yo, inherited (incomplete penetrance), Notch 3 mutation. Presents with: lacunar strokes, progressive dementia, h/o migraine with aura. MR: extensive white matter Δ's.

Hypercoagulable States: see below

Unknown Causes: "Paradoxical embolism": technically "cryptogenic" (not lacunar, no clear cardioembolic [e.g., Afib]/large artery source. 2/2 patent foramen ovale (PFO)), see later for Rx.

Ischemic Stroke Workup

Urgent ED studies: CBC, BMP, PT, PTT, troponins; noncontrast head CT: r/o ICH (only required imaging for IV rt-PA decision); CT angiography head & neck for large vessel syndrome, consideration of IA therapy

Studies for secondary risk prevention:
Labs: Fasting lipid panel, including lipoprotein (a); Hb $A1_c$ (looking for underlying DM, glucose may be elevated s/p stroke); homocysteine; TSH: looking for hyperthyroidism (increases risk of Afib); ESR & CRP if suspecting vasculitis or endocarditis; in younger pt (<60), hypercoagulable panel (before starting heparin): antiphospholipid antibodies, lupus anticoagulant, prothrombin G20210A gene mutation, factor V Leiden, protein C/protein S/antithrombin III deficiencies, β-2 microglobulin
Imaging: *CTA:* for endovascular intervention/medical therapy (e.g., dissection, atherosclerosis, vasculitis), comparable to US for ICA stenosis. *MRI/MRA:* may quantify extent of stroke, Se 95% with in 1st few hours of stroke. *Carotid U/S* if CTA or MRA not done
Other tests: *Hazard ratio:* 24-hr Holter, looking for atrial fibrillation, in pt with high suspicion of Afib can do extended cardiac monitoring for 30 days (or longer) as outpatient. *Echocardiogram:* ruling out PFO or atrial septal aneurysm (ASA) (in cryptogenic stroke), CHF, thrombus, left atrial dilatation (increases risk for Afib), LV hypokinesis, valvular abn. *Consider TEE* for younger pt without clear cause, better for looking at valves. May be less sensitive for PFO detection than TTE as pt unable to Valsalva due to sedation. *LE US* to evaluate for DVT if PFO present, *CT Venogram* of pelvis: *LE US* does not evaluate iliac veins

Early Management of Acute Ischemic Strokes

Thrombolysis: IV rt-PA in 1st 3 hrs of sx onset (dose: 0.9 mg/kg, 10% as bolus): Can also be given for select pt at 3–4.5 hrs of sx onset (Del Zoppo GJ, et al *Stroke.* 2009;40:2945–2948). Number needed to treat for improvement: 3; number needed to harm: 30. Use caution in minor/mild sx, rapidly resolving sx; contraindications: hemorrhage, AVM, endocarditis, abscess. Sooner Rx → better outcome (<2 million neurons lost every minute) (Saver JL. *Stroke.* 2006;37:263). *BP prior to & during rt-PA:* BP ≤185/110 (If BP increases, give labetalol or nicardipine IV; if BP remains stable at target, can give rt-PA). *Post rt-PA precautions for 24 hrs:* No NG tube, NPO. No arterial sticks in noncompressible sites. No antiplatelets or anticoagulation (including DVT dosing of heparin/LMWH). Use TEDs/pneumoboots for DVT prevention. CT scan at 24 hrs to determine whether hemorrhage present, earlier with any clinical worsening. *Hemorrhagic transformation:* important complication of rt-PA: increased risk with increased NIHSS:

score ≥20 → 17% risk, <10 → 3% risk. Sx: Increased somnolence, HA, neurologic deterioration. If suspected: stop rt-PA, STAT noncontrast CT, coagulation panel, type & cross-match 6–8 units of platelets & cryoprecipitate, PCCs. Negative CT: resume rt-PA (if still within 3-hr window); Positive CT: transfuse, neurosurgery consult. *Angioedema* (orolingual) in 5% receiving rt-PA, usu mild (Rx: steroids & antihistamine)

Heparin: Guidelines do not recommend heparin; some centers consider it for large artery etiology (including actively embolizing carotid, some evidence) or for Afib (little evidence); others: LV thrombus, mechanical heart valve, dissection, cerebral VT. Do not give heparin if coma, large infarction, mass effect or ICH on CT, MAP >130, NIHSS >15.

Endovascular treatments: Major breakthroughs in 2015, with 5 NEJM trials showing benefit of thrombectomy with stent retrievers for large vessel occlusion, compared with IV thrombolysis alone. Treat within 8 hrs. Number needed to treat ~4 in most trials. Improvement in both survival & functional outcome. Decision based on imaging characteristics, either CT/CTP APSECTS score or automated software using CT/MRI. (MR CLEAN; Berkhemer OA, et al. *N Engl J Med.* 2015;372:11. EXTEND IA; Campbell BC, et al. *N Engl J Med.* 2015;373:1009. ESCAPE; Goyal M, et al. *N Engl J Med.* 2015;372:1019).

ASA: ASA 81 mg qd (full dose not proven more effective). No other antiplt tested acutely (e.g., clopidogrel, ticlopidine, dipyridamole). 2 large trials showed (nonsignificant) decrease in death or disability with ASA within 48 hrs (CAST& IST; *Lancet.* 1997;349:1641; *Lancet.* 1997;349:1569). Meta-analysis of both trials → modest/significant benefit: 7 strokes prevented/1000 pt treated, 4 deaths/1000; likely no effect on severity of current stroke but decreased recurrent ones.

Statins: For secondary prevention. Some rec high-dose statin (as in ACS) acutely (for atherosclerotic stroke—see AHA/ASA guidelines 2014). A small study testing acute statin use, safety & efficacy trial, statin started <12 hrs, not powered to detect clinical benefit, showed no difference in mortality/outcome. *Recent statin withdrawal study* (*Neurology.* 2009;69:904): Stopping outpatient statin → worse outcome (<5 × increase in death/dependence) & worse infarct volume; statin withdrawal may trigger prothrombotic/inflammatory response.

Induced HTN: Small clinical trials, useful in select group of pt, use with caution. Possibly increased BP restores perfusion to penumbra. *How to do trial of HTN:* consider in pt with fluctuating exam with BP changes (i.e.,

worse when decrease in BP). Exclude pt with h/o CAD, PVD, CHF, ischemic, ICH/midline shift, rt-PA, spontaneous bacterial peritonitis >200, heparin drip. Increased admission of spontaneous bacterial peritonitis by 20% (max spontaneous bacterial peritonitis 200) with phenylephrine drip, titrate to neurologic improvement. If NIHSS decreased by 2 points after 30 min, continue drip. Daily attempt to titrate drip off, only if neurologic sx do not worsen during titration. Should be seen as bridge to more definitive therapy (surgery)

General Medical Care

HTN: >60% of stroke pt have spontaneous bacterial peritonitis >160. Rx BP >220/120, in pt *not* receiving rt-PA, or if end-organ damage (kidney, heart, eye). Rx BP >185/110 in pt receiving rt-PA. Do not decrease BP by >15%. Can initiate HTN meds within 24 hrs of stroke.
Hypotension: worse outcomes, esp. <100/70. Rx underlying cause of hypotension (volume depletion, arrhythmia, blood loss, sepsis). Rx: fluids, pressors

Glucose: hyperglycemia: goal BG 80–180, Rx with ISS or insulin drip. $^{1}/_{3}$ stroke pt affected, associated with poor outcomes, few studies in stroke pt, studies extrapolated from other scenarios (medical/surgical ICU).
Hypoglycemia: promptly correct (may mimic strokes)
Temp: fever: increase mortality, seek cause of fever & Rx with antipyretic.
Hypothermia: insufficient data for use of cooling in stroke; consider in pt with malignant edema, elevated ICP
Oxygenation: keep O_2 saturation ≥92%. Pt needing intubation have 50% mortality at 30 days. Aspiration pneumonia (PNA) important complication & leading cause of death

Acute Stroke Treatment Evidence

rt-PA

NINDS rtPA (*N Engl J Med.* 1995;333:1581–1587): 624 pt, placebo vs. rt-PA within 3 hrs, 2 parts: part 1: no diff in neuroimprovement at 24 hrs vs. placebo. Part 2: favorable outcome vs. placebo at 3 mo (OR for favorable outcome 1.7). Increased benefit for pt treated within 90 min, no difference in mortality.
ECASS (Hacke W, et al. *JAMA.* 1995;274:1017–1025): European trial, multicenter, 620 pt, placebo vs. rt-PA within 6 hrs, slightly larger rt-PA dose. Overall no

difference at 3 mo in rt-PA vs. placebo, increased mortality with rt-PA. Posthoc analysis: (nonsignificant) trend → better outcome with pt Rx'd within 3 hrs
ECASS II (Hacke W, et al. *Lancet.* 1998;352:1245–1251): 800 pt, same dose as NINDS (0.9 mg/kg), within 6 hrs. No benefit with rt-PA, not enough pt to see whether Rx within 3 hrs makes a difference.
ATLANTIS (Clark WM, et al. *JAMA.* 1999;282:2019): Rt-PA 3–5 hrs, 613 pt. No difference in functional outcome & mortality, Extending window >3 hrs not beneficial.
ECASS III (Hacke W, et al. *N Engl J Med.* 2008;359:1317): 821 pt, Rt-PA 3–4.5 hrs. Rt-PA → better outcome at 90 days. Select for the age of 80 yrs, no h/o stroke with diabetes, NIHSS >25, any anticoagulant

Complications of ischemic stroke:
Ischemic brain swelling: see Chapters 28 & 43. *Hemorrhagic transformation:* <5% of infractions → symptomatic ICH, Rx: depends on extent. *Seizure:* risk <2%, increased with cortical strokes, no need for prophylactic antiseizure medication, commonly partial seizures (+/− secondary generalization)

Secondary Stroke Prevention

Antiplatelet Agents

ASA: High- & low-dose equal efficacy. Increased ASA dose does not decrease stroke risk but increases risk of bleeding
Dipyridamole & ASA: French Toulouse Study/AICLA: no benefit of adding dipyridamole to ASA. ESPS-2 trial: ASA decreases relative stroke risk by 18%, ASA/ext.-release dipyridamole by 37%; neither affected mortality (Diener HC, et al. *J Neuro Sci.* 1996;143(1–2):1–13). HA most common SE of dipyridamole (decrease this by giving med everyday with baby ASA × 1 wk then dropping ASA & switching med to b.i.d.)
Clopidogrel: Used if pt allergic to ASA, conflicting evidence. *CAPRIE:* (CAPRIE Steering Committee. *Lancet.* 1996;348:1329): Clopidogrel more effective than ASA in a *composite* risk of ischemic stroke, MI, or vascular death. But in pt with prior strokes, the benefit was *not* statistically significant, nor was stroke as an outcome reduced for the total population. *CHARISMA:* ASA vs. ASA + Clopidogrel in vascular pt & those with vascular risk factors, no difference in composite risk stroke, MI, or vascular death, but sig increase in bleeding events (Bhatt DL, et al. *N Engl J Med.* 2006;354:1706). *MATCH:*

clopidogrel vs. ASA + Clopidogrel in stroke pt, no difference for stroke or other end points, combination caused increased bleeding (Diener HC, et al. *Lancet.* 2004;364:331). *PROFESS:* clopidogrel equivalent to combination ASA + Dipyridamole in >22,000 stroke pt (Diener HC, et al. *Lancet.* 2008;7:875–884)

Extracranial Atherosclerosis

Carotid Endarterectomy (CEA): Indications: *symptomatic stenosis:* stenosis 70–99% & life expectancy >5 yrs. 50–69% stenosis: men with at least 5-yr life expectancy; Women → no CEA, medically manage. *Asymptomatic stenosis:* controversial; medically stable men with stenosis 60–99% with life expectancy of at least 5 yrs. Women → no CEA, medically manage

Carotid Artery Stenting (CAS): shown to be equivalent to CEA in CREST trial (Brott TG, et al. *N Engl J Med.* 2010;363:11–23); 2502 pt randomized; lower stroke risk with CEA, but lower MI risk with CAS; younger pt (<70) better outcomes with CAS, older had better outcomes with CEA

Extracranial/Intracranial Bypass: Used in carotid occlusion: STA anastomosed to MCA. 1985 International EC/IC bypass: no benefit (*Stroke.* 1985;16:397–406). (Criticism: pt with completed infarctions included, no perfusion studies). COSS Trial showed EC/IC bypass + medical therapy not superior to medical therapy alone (Powers WJ, et al. *JAMA.* 2011;306:1983).

Complete Carotid Occlusion (CAO): (Powers WJ, et al. *Neurology.* 2000;54:878): asymptomatic CAO stroke risk: 0% at 2 yrs, 4.4% at 3 yrs (i.e., benign prognosis). Symptomatic CAO stroke risk: 19% at 2 yrs, 21% at 3 yrs. Once occluded, no benefit from CEA/CAS

Intracranial Atherosclerosis

Medical Rx: Antiplatelets or warfarin. ASA usually given, but if severe flow-limiting → consider anticoagulant to decrease progression. <10% strokes & TIAs 2/2 intracranial stenosis (50–99% stenotic).

WASID Trial (Chimowitz MI, et al. *N Engl J Med.* 2005;352:1305): ASA vs. warfarin for intracranial stenosis: no difference in outcome. Pt on warfarin: therapeutic 63.1% of the time (little better than real-life PCP monitoring). When INR in range, rate of ischemic stroke reduced from 25/100 to 5/100

Angioplasty/Stenting: SAMPPRIS trial showed no benefit to stenting vs. medical therapy (Chimowitz MI, et al. *N Engl J Med.* 2011;365:993–1003)

Cardioembolism

Atrial Fibrillation: 75,000 strokes/yr. Anticoagulate with warfarin INR (2–3) within 2 wks of stroke/TIA. Warfarin superior to ASA in pt with Afib & recent stroke/TIA.

ACTIVE A Trial (ACTIVE Investigators, Connolly SJ, et al. *N Engl J Med.* 2009;360:2066–2078): ASA vs. ASA/Clopidogrel. Latter had decreased composite risk of stroke, MI, death from vascular event, embolism but increased risk of major bleeding (including ICH). Stroke risk: ASA 3.3% vs. ASA/Clopidogrel 2.4%. Major hemorrhage: ASA 1.3% vs. ASA/Clopidogrel 2%. Number needed to treat to avoid 1 stroke was 111 pt. Cost decreased 202,464 to prevent a single stroke/yr (*N Engl J Med.* 2009;361:13). All pt received ASA at dose of 75–100 mg/day, but only ASA 325 mg shown to decrease risk of stroke in Afib (*Circulation.* 1991;84:527)

NOACs recently shown to decrease risk of stroke with Afib as effectively as warfarin, do not require monitoring. Caution with renal insufficiency. Only dabigatran showed *decrease* in stroke rates. Rivaraoxaban currently being studied in cryptogenic embolic stroke (NAVIGATE ESUS).

CHF: Causes stasis & increased risk for thromboembolism. Use of warfarin in CHF controversial, warfarin sometimes used in pt with very low EF (<20%), most guidelines do not routinely recommend it unless pt has DVT/PE, mobile LV thrombus, or Afib. Main trials (no RCT with conclusive evidence yet): *WASH:* no difference between ASA & warfarin (Cleland JG, et al. *AHJ.* 2004;148:157). *WATCH:* no difference, ended early due to poor recruitment, underpowered (Massie BM, et al. *J Card Fail.* 2004;10:101). *WARCEF:* no benefit of warfarin over aspirin (decreased embolic events offset by increased hemorrhages) (Homma S, et al. *N Engl J Med.* 2012;366,1859). For pt with CHF & recent TIA/stroke, either warfarin (goal INR 2–3) or antiplatelets

LV Thrombus: Warfarin (goal INR 2–3) for 3–12 mo if acute stroke/TIA, +ASA if CAD

Atrial Septal Abnormalities: *PFO:* fetal anomaly, allows communication b/n atria.

ASA: redundant tissue in the region of the fossa ovalis, acts as a nidus for thrombus formation. Association between cryptogenic strokes in pt ≥55 yo & PFO ± ASA in 1 study. In pt <55 yo, PFO + ASA > ASA > PFO

significantly a/w stroke. 1 study showed association with PFO/cryptogenic strokes & older pt (Handke M, et al. *N Engl J Med.* 2007;357:2262–2268).

Rx: 4 main modalities: antiplatelet, anticoag, surgical closure, percutaneous closure. *PICSS* found no difference between aspirin & warfarin (Homma S, et al. *Circulation.* 2002;105:2625–2631) but was a very limited substudy; probably did not study the proper population

Guidelines: atrial anomalies with ischemic stroke: antiplatelets (use warfarin if pt is at high risk or has concomitant DVT or PE). PFO closure: considered in pt who fail medical therapy (i.e., get recurrent cryptogenic strokes), although all closure trials negative.

Valvular Heart Dz: *Rheumatic Mitral Valve Dz:* Warfarin (INR 2–3) recommended. If pt has recurrent embolism despite adequate warfarin, may add ASA. *Prosthetic heart valve:* modern mechanical valve & ischemic stroke/TIA: Warfarin (INR 2.5–3.5); consider adding ASA if pt has another stroke despite adequate warfarin treatment. Bioprosthetic heart valve with ischemic stroke, consider warfarin with INR goal 2–3. *All other valvular dz:* antiplatelet agents.

Hypercoagulable States

Possible association with ischemic stroke/cerebral VT in pt <50 yo. Strongest association with antiphospholipid antibody syndrome. If testing abnl, repeat at f/u (as can be abnormal acutely). Most guidelines recommend testing in pt <50 yo with VT, no recs for acute ischemic stroke. *Rx:* controversial, usually for *venous* thromboembolism: warfarin; for arterial thrombus (ischemic stroke) ASA vs. warfarin (except for antiphospholipid Ab syndrome → warfarin).

Antiphospholipid Antibody Syndrome: Acquired, can be a/w autoimmune dz (e.g., lupus), sx are recurrent pregnancy loss/thrombotic events.

Dx: Clinical event + 1 Lab abnl: (1) Antibodies against: cardiolipin & β-2 glycoprotein I, or (2) Lupus anticoagulant (misnomer, not a test just for lupus pt, not an anticoagulant!). If lab test abnormal, recheck in 12 wks. *Rx:* anticoagulation for life (goal INR 2–3).

Prothrombin G20210A Gene Mutation: Increased prothrombin synth by liver.

Factor V Leiden: Factor V mutation → resistant to degradation (by activated protein C). Screen with activated protein C resistance.
Protein C, Protein S, or Antithrombin III Deficiencies: Very uncommon. Dx difficult due to false +'s, esp. acutely after stroke. All 3 decreased in acute thrombosis/surgery, or hepatic dysfn (i.e., decreased production), heparin decreases antithrombin, warfarin/OCPs decrease protein C/S.

Dissections

35–50 yo; ICA dissection 3× more common than vertebral, extracranial > intracranial. Unlike atherosclerosis, dissections usually occur past the bifurcation of ICA. *Carotid dissection:* 2–3 cm distal to bulb, irregular stenosis, does not usually extend intracranially (passes through tight foramina often preventing extension). *Vertebral dissection:* most often in freely moveable areas: at C1/C2 (as the artery wraps around the cervical vertebrae) & b/n origin & entrance into intervertebral foramina (can extend intracranially).

Etiologies: *Trauma:* almost any form of trauma can cause it, e.g., MVA, vigorous coughing, & chiropractic manipulation (estimation of 1 stroke per 20,000 spinal manipulation). *Genetic:* Ehlers–Danlos syndrome, Marfan's syndrome, fibromuscular dysplasia, polycystic kidney dz, homocystinemia, α-1 antitrypsin. *Other:* Smoking, HTN, OCPs, possibly infxns (esp. URI).

Clinical Features: *ICA dissection:* triad: neck/face/head pain. Partial Horner's in <50% (symp fibers run along ICA, ptosis/miosis but no anhidrosis—those fibers run along external carotid artery). Cerebral/retinal ischemia. Lower CN palsy (esp. XII & VI, which run near ICA) in <12%. *Vertebral Dissection:* HA/pain back of neck, then posterior circulation ischemia (e.g., dizziness, dysarthria).

Dx: Imaging: "flame-like" appearance, tapered vessel, crescent shape around lumen. Doppler (See >90%): high-resistance flow in distal artery. T1 MRI with fat suppression, or CTA.

Rx: *Asymptomatic Dissections:* ASA. *Intradural dissections:* anticoag risks pseudoaneurysm formation, SAH. *Symptomatic Dissection (extradural):* Anticoagulant vs. antiplatelet, no difference. (CADISS trial investigators, et al. *Lancet Neurol.* 2015;14:361–367). Consider warfarin INR 2–3 for 3–6 mo, then switch to antiplatelet. F/U monitoring at 3–6 mo with MRA or CTA. Surgery/endovascular intervention if pt with sx despite adequate anticoagulant: angioplasty & stenting, vessel occlusion by embolization, vessel coiling or ligations, & bypass procedures.

Prognosis: worse for intracranial dissections (a/w more severe sx & bleeds). 72–100% dissections recanalize. Recurrence rate: 1%/yr (risk lasts up to a decade), higher in 1st mo (2%). No evidence that ASA or anticoag prevents dissections.

Intracerebral Hemorrhage

10–15% of 1st ever strokes are ICH (35% mortality at 30 days → half occur in 1st 2 days). Only 20% of pt with ICH are expected to be functionally independent at 6 mo. Classically, sudden focal neuro deficit that progresses, ± HA/vomiting. Volume of ICH & GCS on admission best predictors of 30 days mortality (ICH score).

Etiologies: *HTN:* deep hemorrhage. In basal ganglia, pons, cerebellum, or deep hemispheric white matter. *Other:* vascular malformation, aneurysm, trauma, coagulopathy, cocaine, vasculitis, neoplasm, sinus thrombosis, cerebral amyloid angiopathy.

ICH Score: (1) GCS: 3–4 = 2 points, 5–12 = 1 point, 13–15 = 0 points. (2) ICH volume (ml): ≥30 = 1, <30 = 0. (3) intraventricular hemorrhage: Yes = 1, No = 0. (4) Age: ≥80 = 1, <80 = 0 (5) Infratentorial: Yes = 1, No = 0. Predicted *30 days mortality:* (5+,4,3,2,1,0) points → (100,97,72,26,13,0)% mortality.

Volume Estimation: ICH volume: measured (ABC)/2 → A = longest diameter, B = diameter perpendicular to A, C = Increases of slices × thickness of 5-mm slices.

Clinical features and dx of ICH: 50% basal ganglia, 33% hemisphere, 16% brain stem/cerebellum. Peak deterioration/swelling on days 3–7 but delayed edema can occur. Autonomic instability can occur (increased RR, increased or decreased HR, increased glucose).

Neuroimaging: *CT:* CTA r/o underlying vascular lesion. Subarachnoid blood = aneurysm. Temporal hemorrhage = trauma or cerebral VT. Fluid–fluid levels in hematoma = coagulopathy (e.g., warfarin). Rescan for changes in exam & on day 2.

MRI: consider imaging to r/o underlying mass, if suspect amyloid angiopathy. Hyperacute bleed: center → iso to hypointense on T2; rim → hypointense T1. Subacute: hyper on T2/T1. Chronic: hypo on T2/T1.

Rx: *BP:* over-aggressively decreasing BP may drop cerebral perfusion pressure. Unclear what BP goal should be (guidelines spontaneous bacterial peritonitis <180; in practice, many rec spontaneous bacterial peritonitis <160) (Broderick J, et al. *Stroke.* 2007;38:2001–2023). BP meds to use: labetalol, nicardipine, esmolol.

Seizures: Occur early in 4.2% of pt & 8.1% within 30 days (De Santis A, et al. *Epilepsia.* 2002;43:175). Lobar ICH significantly increased risk (esp. if extends to cortical ribbon). Prophylactic Rx: unproven benefit, no proof that it effects mortality/morbidity, consider in large cortical ICH.

Glucose: elevated glucose associated with increased mortality; goal 100–180 mg/dl

Temp: Fever worsens outcome, seek out sources, treat with acetaminophen, cooling blankets, surface/endovascular devices. Persistent fever (>24 hrs) a/w poor prognosis & ventricular extension

DVT/PE ppx: at admit, intermittent pneumatic compressions. 1 study showed no increased risk for bleed on day 2 of ICH onset (with 5,000 units of heparin t.i.d.); likely LMWH is just as safe. Pt with DVT/PE, probably should get IVC filter.

Surgery: supratentorial ICH: STICH I & II trials → surgical clot evacuation no effect on mortality (1 subgroup showed a trend to better outcome but not statistically significant: lobar clots within 1 cm of surface & GCS ≥ 9). *Cerebellar hemorrhage* (not included in STICH): >3 cm with deterioration or brain stem/4th ventricle compression fair better with surgery. *Minimally invasive surgery* (e.g., endoscopic aspiration): info limited, need more trials.

Warfarin: Rate ICH on warfarin = 0.3–0.6%/yr. Risk doubles for every 0.5 above INR 4.5. Warfarin-related ICH Rx: Goal INR < 1.4 (PT/INR q4h × 24 hrs). Vit K 10 mg IV (takes 6 hrs to normalize INR), FFP (10–20 ml/kg, <4–6 U, risk of volume overload, give furosemide in CHF pt), PCCs

Restarting warfarin: Risk of stroke in Afib 5% per year, in pt with previous stroke, it increases to 12%. Survivors of prior lobar ICH should not be restarted on warfarin (even if high-risk pt for thromboembolic stroke; Eckman MH, et al. *Stroke.* 2003;34:1710). May consider in hypertensive ICH if BP well controlled.

Other drug-induced coagulopathies:

Heparin induced: Rx: protamine → 1 mg per 100 units of heparin over last 3 hrs; q1h PTT × 4 then q4h. If heparin stopped 30–60 min ago, give 0.5–0.75, if 60–120 min, give 0.375–0.5 mg, if >120 min, then give 0.25–0.375.

Enoxaparin induced: Rx: protamine → 1 mg per 1 mg of enoxaparin; recheck PTT in 2–4 hrs; if still elevated, consider giving an additional 0.5 mg of protamine.

ASA/Clopidogrel: No evidence for platelet transfusion, restart ASA <1 wk after ICH, Rx: Transfuse platelets if count <100,000.

SEIZURES

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Differential Diagnosis of Seizures

DDx: Transient ischemic attack (TIA); transient global amnesia; panic attacks & other anxiety manifestations, migraine; narcolepsy/other sleep disorders; tremor, nonepileptic myoclonus, dystonia/other movement disorders; pseudoseizures, malingering, breath-holding spells; stereotypies in cognitively impaired individuals.
TIA: signs/symptomssx usually (−), but can be (+) (e.g., jerking, rigidity, hallucinations, visual illusions). *Limb shaking TIAs:* a/w preocclusive dz in internal carotid artery (ICA) or middle cerebral artery (MCA), usually orthostatic. *Todd's paralysis* (transient weakness after seizures) can mimic TIA/stroke.
Migraine aura (e.g., visual illusions/hallucinations, acute mental status change with basilar migraine) can mimic complex partial seizure (CPS); aura onset usually more gradual & duration less. Headache (HA) after CPS can mimic migraine.
Syncope: Including "convulsive syncope": see later.

Provoked Seizures: Etiologies

Etiology of Provoked Seizures	
Primary Neurologic Disorders Acute/subacute neurologic insult: head trauma, meningitis/encephalitis, brain abscess, stroke, subarachnoid arachnoid hemorrhage (SAH), HIV encephalopathy, cerebral anoxia, hypertensive encephalopathy/posterior reversible encephalopathy syndrome (PRES), eclampsia, neurosurgery Structural abnormalities: mass lesions, vascular malformations Hyperthermia High fever: in children	**Systemic Disorders** Metabolic: hypoglycemia, hyperglycemia, hyperosmolar state, hyponatremia, hypoCa, hypomagnesemia, uremia, hepatic encephalopathy, porphyria, hyperthyroidism Drugs: overdose, withdrawal (EtOH, sedatives); others (see below) Sleep deprivation
Drugs That Commonly Cause Seizures or Decrease Seizure Threshold	
• Anticholinesterases (organophosphates, physostigmine) • Antidepressants (e.g., wellbutrin) • Analgesics (e.g., meperidine, tramadol) • Abx (e.g., fluoroquinolones, trimethoprim/sulfamethoxazole (TMP/SMX)) • Antihistamines • Antipsychotics (phenothiazines, butyrophenones, clozapine) • Chemotherapy drugs (etoposide, ifosfamide, cisplatinum) • Beta-blockers (propranolol, oxprenolol) • Local anesthetics (bupivacaine, lidocaine, procaine, etidocaine)	• Cyclosporine, FK506 • Hypoglycemic medications • Isoniazid • General anesthetics (e.g., enflurane) • Methylxanthines (theophylline, aminophylline) • Narcotics (fentanyl, meperidine, pentazocine, propoxyphene, tramadol) • Penicillins (esp. with renal failure) • Phencyclidine, stimulants (amphetamines, cocaine, ephedrine, 3,4-methylenedioxymethamphetamine (MDMA) [ecstasy], phenylpropanolamine, terbutaline)

Workup of First Seizure

NOTE: for status epilepticus (SE) or impending status (seizures >5 min or multiple seizures without return to baseline) → proceed to the SE algorithm.
CLINICAL EVAL: HPI: preceding illness/fever, trauma; aura, ictal, & postictal phenomena (e.g., confusion, depression, aphasia, embarrassment, exhaustion, sleep, fear, HA, amnesia, nausea, pain, perceptual distortions, psychosis, thirst, weakness)
PMH/ROS: early hx (prenatal, birth, perinatal), febrile seizures, milestones (motor, language), birthmarks/other congenital anomalies, myoclonic jerks, photosensitivity, prior seizures, FHx of seizures, stroke, head trauma, CNS infxns, diurnal variation, relation to menses, triggers (e.g., emotion, exercise, loud music, flashing lights, television, fever, menses, sleep deprivation, coughing), injuries during seizure, number of seizures ED visits past year, prior AEDs & why d/c'd, prior studies (EEG, CT, MRI, PET, SPECT). **GEN EXAM:** skin exam for neuroectodermal disorders (e.g., neurofibromatosis, tuberous sclerosis). **NEURO EXAM:** focal abnormalities (suggestive of underlying cause)
TESTS: (1) *Labs:* chem7, LFTs, serum & urine tox screen, antiepileptic drug (AED) levels, urinary analysis (UA), erythrocyte sedimentation rate (ESR), & C-reactive protein (CRP), CXR, (2) *Imaging:* CT before LP **if** focal deficits, r/o space occupying lesion or acute hemorrhage. MRI preferable if nonemergency. (3) **LP** if: suspect meningitis/encephalitis; all HIV + pt; elderly; focal deficits. (4) MRI ± gado (r/o structural causes, e.g., tumor, stroke, infxn, AVM); (5) EEG within 24–48 hrs, or emergently if persistent MSΔ.

Antiepileptic Drugs

Antiepileptic Drug (AED) Trade Names and Abbreviations		
Generic Name	**Trade Name**	**Abbreviation**
First Generation ("Old") AEDs		
Phenytoin	Dilantin	PHT
Carbamazepine	Tegretol, Tegretol XR, Carbatrol	CBZ
Primidone	Mysoline	PRM
Valproic acid	Depakote, Depakote ER, Depakene	VPA
Phenobarbital	Luminal, Solfoton	PHB
Ethosuximide	Zarontin	ESX
Benzodizepines: lorazepam, diazepam, midazolam, clonazepam, clorazepate	Klonopin, Tranxene	LZ, DZ, MZ, CZP, CLZ
2nd Generation ("New") AEDs		
Felbamate	Felbatol	FBM
Lamotrigine	Lamictal	LTG
Gabapentin	Neurontin	GBP
Topiramate	Topamax	TOP
Oxcarbazepine	Trileptal	OXC
Tiagabine	Gabitril	TGB
Levetiracetam	Keppra	LEV
Zonisamide	Zonegran	ZNS
Pregabalin	Lyrica	PGB
Lacosamide	Vimpat	LCS
Rufinamide	Banzel	RUF

Choice of AED in the ICU: General Principles

Special Considerations When Choosing an AED

Seizure type: *Narrow spectrum* (focal or tonic–clonic seizures): CBZ, OXC, PHT, PHB, PRM, GBP, PGB, TGB. *Broad spectrum* (focal + generalized, including myoclonic & absence): LEV, VPA, TOP, ZNS, LTG (less effective for myoclonic), FBM.

Adding Medications: When adding extra AEDs, consider interactions with other AEDs.

Some combinations to monitor closely b/c pharmacokinetic or pharmacodynamic interactions (there are many more): PHB + VPA, PHT + CBZ, CBZ + LTG, VPA + LTG (increased SE & efficacy).

Other meds: Consider interactions with other non-AED medications.

Elderly: Lower threshold for side effects, esp. cognitive dysfunction, tremor, gait problems. CrCl, hepatic clearance decreases after the age of 65 y; albumin levels decrease with age – need to decrease doses of protein-bound drugs; generally use lower doses titrated more slowly.
IV formulations (when rapid titration is necessary): avail. for: PHT, VPA, LEV, PHB, LCS.

Side Effects, Interactions, Comorbidities, and Monitoring

Influence of Comorbid Conditions on AED Choice	
AEDs to Use Cautiously or Avoid	
Liver dz	VPA, PHT, PHB, CBZ, LTG, ZNS, FBM
Renal impairment	LEV, GBP, PHB, PGB, TOP, ZNS
h/o renal stones	ZNS, TOP
Arrhythmias	CBZ, PHT
Pancreatic dz	VPA, CBZ
Hypothyroidism	CBZ, OXC, PHT
Hyponatremia (or risk for)	CBZ, OXC,
Osteopenia	PHT > CBZ, PHB
Obesity	VPA, PGB (↑ 10–50 lb), ?CBZ, ?GBP (increased 5–10 lb)
Anorexia/malnourished	FBT, TOP, ZNS
Polycyctic ovarian syndrome (PCOS)	VPA
Taking oral contraceptive pills (OCPs)	CBZ, OXC, PHT, PHB, TOP (at dose >200)
Bleeding diathesis	VPA
Blood dyscrasias	CBZ
Peripheral edema	PGB
h/o hypersensitivity rxns	AEDs with risk of rash (esp. PHT, CBZ, LTG)
Absence seizure's	CBZ, OXC, TGB
Myoclonic seizure's	GBP, LTG, OXC, CBZ, TGB, PGB,
Generalized seizure's	GBP, CBZ, OXC, (may exacerbate)
Psychiatric d/o	LEV, PHB
AEDs That May Help the Condition	
Mood instability	OXC, VPA, LTG, CBZ
Headache (HA)	TOP, VPA, CBZ in children
Neuropathic pain	GBP, OXC, CBZ, TOP
Obesity	TOP, ZNS
Periodic leg movement syndrome (PLMS)	CZP, GBP, TOP, ZNS
Tremor	CZP, PBT, PRI, ELV, TOP
Insomnia	TGB

Commonly Used Antiepileptic Agents in ICU		
Drug Class	**Dose**	**Adverse Effects**
Benzodiazepines Lorazepam Midazolam	0.1 mg/kg at 2 mg/min, up to 8 mg 0.2 mg/kg bolus, 0.75–10 μg/kg/min infusion	Sedation, paradoxical excitation, hypotension, respiratory depression
Phenytoin	20 mg/kg IV bolus, then 5–7 mg/kg/d	Rapid infusion–hypotension, arrhythmias Nystagmus, diplopia, ataxia, sedation, lethargy Idiosyncratic: rash, fever, bone marrow suppression, hepatitis, Steven–Johnson syndrome
Fosphenytoin	20-mg phenytoin equivalent (PE)/kg IV bolus	Hypotension, bradycardia, phlebitis
Phenobarbital	20 mg/kg IV bolus	Sedation, nystagmus, ataxia, N/V
Propofol	30–200 mcg/kg/min	Hypotension, bradycardia, hypertriglyceridemia
Levetiracetam	500–1,000 mg IV/PO q12h	Sedation, N/V
Sodium valproate	1,000–2,500 mg/d IV/PO in 2–4 divided doses	Sedation, diplopia, N/V, diarrhea, hepatotoxicity, pancreatitis, rash
Lacosamide	100 mg/d, up to 200–400 mg/d PO/IV	Dizziness, N/V, diplopia, blurred vision, fatigue, ataxia

Status Epilepticus

SE: over 30-min interval: continuous seizure, or >1 seizure without full return of consciousness/return to baseline between seizure's. Can be: focal vs. gen, convulsive vs. nonconvulsive.
"Prolonged seizure": >5 min: signifies failure of seizure termination and risk of SE.
"Impending status": >10 min (treated as SE)
Clusters of seizures: considered transitional state toward SE.
Generalized convulsive SE (GCSE: G between CSE): convulsions are evident clinically. (Includes tonic-clonic SE [most common], tonic-SE, clonic-SE, myoclonic-SE).
Nonconvulsive SE (NCSE): electrographic SE without clinically evident "convulsions" (but other signs are present, e.g., altered consciousness).
Refractory SE (RSE): Ongoing seizure following 1st- & 2nd-line drug Rx.
Epidemiology: GCSE: most common neurologic emergency. In US 50–200 K/yr. ~⅓ known epilepsy, ~⅓ new epilepsy, ~⅓ acute neurologic disturbance (proportions vary by age). 15% of pt with epilepsy will have at least 1 episode of status. Most common precipitant: withdrawal of AEDs or noncompliance with AEDs. **NCSE:** accounts for 25–50% of all SE. In comatose ICU pt, incidence ~30%. Incidence in medical ICU: ~0.5%; in neuro ICU: ~10%.
Refractory SE: ~30% of SE cases (varies greatly with cause: e.g., more likely with encephalitis, generalize tonic-clonic seizures (GTC); less with low AED levels, drug withdrawal).
Etiology of SE: Main risk factor: prior SE (25%), but most SE occurs without prior seizure. In 1st time SE, cause in order of increasing frequency (but varies by age): tumor, trauma, infxn, unknown, metabolic, anoxia, EtOH/drugs, medication change, stroke. Most common type: GCSE, from evolution of primary or secondarily generalized GTCs.
Pathophysiology: Disruption of nl seizure-terminating mechanisms. Includes intxns between neuronal injury & systemic disturbances (cause & caused by SE): *neuronal injury:* excitotoxicity, increased met. demand, increased blood flow, increased edema/mass effect. *Systemic disturbances:* pulmonary edema, high output cardiac failure, contraction band necrosis, cardiac arrhythmias, aspiration pneumonia (PNA), fever, metabolic

disturbances (glucose, K, Na, Phos, pH), hypoxia, acute tubular necrosis (ATN), rhabdomyolysis → acute renal failure (ARF).
Prognosis: GCSE: M&M vary with age, etiology, duration. Mortality: children ~3%; adults ~20%. Highest mortality: anoxic injury; lowest mortality: AED, EtOH, or benzodiazepine withdrawal. Mortality increased 20% for SE lasting >1–2 hrs; no obvious reln at longer durations.
NCSE: Prognosis less well understood. M&M generally < than GCSE, though cause is critical.

Mortality Prediction Score for Status Epilepticus (*Neurology*. 2006;66:1736)

	Features	Score
Level of consciousness	Alert, somnolent, or confused Stuporous or comatose	0 1
Seizure type	Simple or complex partial Generalized NCSE + Coma	0 1 2
Age	<65 >65	0 2
Previous seizures	Yes No	0 1
Total		0–6

Using cutoff ≥3 to predict death results in the following test statistics:
Sensitivity 81%, Specificity 65%, PPV 25%, NPV 96%, accuracy 73%.

Diagnosis

GCSE: suspect after witnessed seizure without arousal after 5 min, or if subsequent seizure. Distinguish from "seizure cluster" (pt awakes between seizure's)—less urgent, but risk of → SE. Motor activity may decrease after multiple seizure's. Pseudoseizures/nonepileptic seizure's: sometimes hard to distinguish from GCSE. Clues favoring GCSE: hypoxemia, increased CPK, acidosis; clues against GCSE: avoidance behavior.
NCSE: Clinical picture + EEG evidence of nonconvulsive seizures >30 min. If routine EEG unavailable, interim hairline EEG is useful (but less sensitive). Routine continuous EEG in ICU pt & required duration is controversial. 95% noncomatose pt have 1st seizure in 24 hrs. In comatose pt who get seizures: 80% in 24 hrs, ~95% in 48 hrs (Jirsch J, Hirsch LJ. *Clin Neurophysiol.* 2007;118(8):1660–1670). Specific interictal patterns predict increased risk of delayed NCSE, e.g., periodic lateralized epileptiform discharges (PLEDS). Benzodiazepine trial is useful when dx in doubt about NCSE, but must have clinical + EEG improvement to be diagnostic.

Criteria for Nonconvulsive Seizure

***EEG pattern = Nonconvulsive* seizure if:**

Duration >10 s and satisfies at least 1 of 3 primary criteria

Primary criteria

1. Repetitive generalized or focal spikes, sharp waves, spike-&-wave, or sharp-&-slow wave complexes at ≥**3 Hz.**
2. Same as above but frequency <**3/s** + satisfies the secondary criterion (later)
3. Sequential rhythmic, periodic, or quasi-periodic waves at ≥1 **Hz** & unequivocal **evolution** in frequency (gradually increased or decreased by at least 1 Hz), 1/s, e.g., 2–3/s, morphology, or location (gradual spread into or out of a region involving at least 2 electrodes). Evolution in amplitude alone or in sharpness without other change in morphology is not enough to satisfy evolution in morphology.

Secondary criterion

- Significant improvement in clinical state or appearance of previously absent normal EEG patterns (such as posterior-dominant "alpha" rhythm) following admin of rapidly acting AED (see next table: benzodiazepine trial).

[a]Resolution of the "epileptiform" discharges leaving diffuse slowing without clinical improvement & without appearance of previously absent normal EEG patterns would not satisfy the secondary criterion.

[a]From Chong & Hirsch, 2005, who modified the criteria of Young et al, 1996.

Benzodiazepine Trial for Diagnosis of NCSE
(*Clin Neurophys*. 2007;118:1660–1670)

Monitoring: EEG, pulse ox, BP, ECG, RR with dedicated nurse
Benzodiazepine trial: Sequential doses of rapidly acting short-duration benzodiazepine, e.g., midazolam at 1 mg/dose. Between doses, repeated clinical & EEG assessment. Trial is stopped after any of the following: (1) persistent resolution of the EEG pattern (& exam repeated); (2) definite clinical improvement; (3) respiratory depression, hypotension, or other adverse effect; (4) maximum allowed dose is reached (e.g., 0.2 mg/kg midazolam)

Test is (+) if: Resolution of ictal EEG pattern resolves & **EITHER:** improvement in the clinical state **OR:** appearance of previously absent nl EEG patterns (e.g., posterior-dominant "alpha" rhythm). *Test is equivocal if:* EEG improves but pt does not.

Treatment of Adult Convulsive SE

Significant morbidity & mortality with delayed Rx. Best to use preestablished time-based algorithm.
Pediatric status epilepticus: see Chapter 33.
NCSE: optimal mgt less well defined than for NCSE, b/c morbidity & mortality is generally less; risks/benefits of aggressive seizure termination are similar. *General principles:* (1) Promptly establish high therapeutic AED doses. (2) Tailor to clinical course, esp. level of consciousness. (3) Avoid intubation & drug-induced coma if possible. (4) Otherwise follow algorithm for GCSE.
GCSE: See later for in-hospital/ED protocol. **If at home with seizure clusters, prolonged seizure, impending status:** Rectal diazepam gel (diastat) 0.2 mg/kg, OR SL lorazepam 1 mg, OR nasal midazolam 0.1–0.2 mg/kg; Call EMS.

Treatment Algorithm for ADULT Status Epilepticus (In ED or Hospital Rx)	
Time	**Interventions/Actions**
0–5 min	• Initial rapid assessment: airway, breathing, circulation • VS • Monitor: O_2 saturation, ECG • IV access (at least 2 IVs), send labs: CBC, chem7, Ca, Mg, PO_4, LFTs, AED levels, tox screen, ABG • Thiamine 100 mg IV then D50 50 ml IV bolus (after thiamine) • Consider abxs & LP, esp. if febrile or not known epileptic
5–20 min	***Initial therapy*** *Benzodiazepine is the initial therapy of choice* • Lorazepam 0.1 mg/kg IV, max 4 mg/dose, may repeat dose once, OR • Midazolam 10 mg IM for >40 kg, 5 mg for 13–40 kg, single dose, OR • Diazepam (0.15–0.2 mg/kg/dose, max 10 mg/dose), may repeat dose once If none of the 3 options are avail., choose 1 of the following: • Phenobarbital IV (15 mg/kg/dose, single dose) OR • Diazepam, rectal (0.2–0.5 mg/kg, max 20 mg/dose, single dose) OR • Midazolam intranasal or buccal midazolam
20–40 min	***If seizures persist*** *There is no evidence preferred 2nd therapy of choice* • Phenytoin (50 mg/min) or FOS-PHT (150 mg/min): 20 mg/kg IV OR • Levetiracetam IV (60 mg/kg, max 4,500 mg/dose, single dose) OR • Valproic acid (40 mg/kg, max 3,000 mg/dose, single dose) If none of the aforementioned options are avail., choose 1 of the following (if not given already)
40–60 min	***If seizures persist*** There is no clear evidence to guide therapy in this 3rd phase of therapy Intubate (if not already done) & initiate continuous EEG monitoring & treatment goal is burst suppression on the EEG • Phenobarbital IV (75 mg/min) 20 mg/kg over 5–10 min) OR • Midazolam 0.2 mg/kg IV (loading dose), titrate dose (0.1–0.4 mg/kg/hr) OR • Pentobarbital, 5 mg/kg IV (loading dose) titrate (0.3–9 mg/kg/hr, avg = 4 mg/kg/hr) for burst suppression, maintain at 0.5–5 mg/kg/hr OR • Propofol, IV, 1–2 mg/kg load, 2–10 mg/kg/hr maintenance
3–24 hrs	• Correct underlying cause of SE • Adjust AED doses to therapeutic effect (with continuous EEG guidance). • Taper midazolam, pentobarbital, or propofol after above is complete, while maintaining high therapeutic levels of PHT (18–30 mg/l) and/or PHB (25–50 mg/l) and/or VPA (70–120 mg/l) to avoid recurrent seizure's.

WEAKNESS IN THE INTENSIVE CARE UNIT

GALEN V. HENDERSON, MD

Patients (pt) in the ICUs may be weak or have difficulty weaning from ventilatory support as a complication of their underlying disorder or treatments given during the ICU stay. These pts are usually difficult to assess because of limited or absent communication ability of the pt & participation with the examination.

Assessment in the ICU

The assessment of the ICU pt can be difficult & it is important to establish means of communication with the pt. We must utilize a range of minimal movements that may be utilized to facilitate communication. This may include forehead winking, eye blinks, mouth movements, & head or limb twitches. Communication aids may be needed & must be remembered that many pt may find it easier to communicate their native language. Achieving adequate communication is crucial in relieving the extreme frustration experienced by the pt, relatives, & health care providers.

History prior to ICU

Pt who are referred following a prolonged ICU admission, a detailed evaluation of the preceding hx, ICU care must be performed. Some of this information may be obtained from family and/or friends

Helpful examples of history before the ICU

If the prodrome may include progressive headaches, breathlessness, & orthopnea suggesting hypoventilation. This may give clues to myasthenia gravis

If here was a preceding upper resp diarrheal illness, there may a concern for Guillain–Barre syndrome (GBS)

The rate & pattern of onset may be helpful to guide the dx & prognosis. Progressive limb & trunk weakness developing over days or wks suggest a progressive neuromuscular disorder, & a h/o fatigue–ability may indicate a neuromuscular junction abnormality

The presence of systemic abnormalities such as abd pain may point to porphyria or diabetes

Dietary factors such as tainted food may have precipitated botulism

History while in the ICU

Take note of any h/o hypoxic–ischemic brain damage, sepsis, organ failure, metabolic or endocrine abnormalities

Medications used in the ICU such as anesthesia, sedation, abxs, neuromuscular blocking agents, & steroids are important. In addition, events that may have occurred in the ICU include stroke or central pontine myelinolysis

The presence of systemic illness may obscure a neurologic cause for the primary presentation

Persistent weakness or failure to wean from the ventilator following a routine anesthetic may suggest either an intercurrent event that has occurred, e.g., stroke or that a previously unsuspected neuromuscular condition has become symptomatic

In pt who fail to wean following cardiac surgery, impaired diaphragm function manifests as orthopnea, or failure to wean when supine may suggest phrenic nerve damage, while focal sensor loss may indicate a border zone (middle cerebral artery (MCA)–posterior cerebral artery (PCA) stroke

Clinical Examination

The examination provides important clues to the dx but is very difficult to fully interpret due to the pt's altered mental status. There are key clues within the neurologic examination that will give the examiner insight into the clinical dx. For example:

When performing the CN examination, if there is ophthalmoplegia and/or bilateral facial weakness, there should be raised concerns about the dx of GBS.

If there is associated ptosis, this may indicate myasthenia

If the pupils are poorly responsive or nonresponsive, there should be a concern regarding Lambert–Eaton syndrome.

Bulbar function is extremely difficult to characterize because many of these pt will have an ETT in place. Despite the ETT, we do try to get a sense of tongue movement & pharyngeal reflex.

In regard to patterns of weakness, neck flexion & shoulder abduction often give a helpful guide to weakness of the respiratory muscles & in particular the diaphragm.

If there is the presence of fasciculation & weakness in the extremities, there may be a concern for motor neuron dz whereas fatigable weakness indicates a neuromuscular junction abnormality

Weakness of the extremities with sensory loss suggests critical illness neuropathy, & if there is no sensory loss, there is more of a concern for critical illness myopathy

Breathing

The pattern of breathing on attempted weaning may also be an important guide

In central brain stem lesions, interfering with the generation of the resp rhythm will be no volitional respiratory movement; however, with respiratory muscle weakness, there may be partial ventilatory response, which is inadequate to maintain ventilation without support

With selective involvement of the phrenic nerve or diaphragm weakness, there may be prominent orthopnea & paradoxical movement of the diaphragm. Inward movement of the abdomen on inspiration of the pt is supine, because the paralyzed diaphragm is unable to contract on inspiration &, therefore, passively ascends with the chest wall (the paralyzed diaphragm descends on inspiration when the pt is erect because of gravity &, therefore, diaphragm excursion appears normal)

Investigations/Tests

It is important to remember that weakness is often multifactorial & combination of factors may be relevant in an individual pt. The typical types of investigations may include these tests based on the clinical suspicion:

Hematology, electrolytes, thyroid function, creatine–kinase

Cerebral or spinal imaging may show stroke or demyelination

EEG may be helpful in showing partial epilepsy or subclinical szs

Cerebrospinal fluid examination may show malignant infiltration or inflammatory process

Neurophysiology to evaluate for GBS, myasthenia, or some other neuromuscular process

Considerations for Weakness in the Intensive Care Unit
• Primary neurologic dx (stroke, cerebral hemorrhage, GBS, myasthenia gravis, myotonic dystrophy, etc)
• Progression or exacerbation of preexisting neuromuscular disorder
• Complications of treatment (prolonged neuromuscular blockade, critical illness myopathy)
• Unrelated event (sz, stroke)

Factors Associated with Weakness after Critical Illness
• Sepsis
• Drugs
• Multiple organ failure
• Metabolic: hypermagnesemia, hypophosphatemia
• Status epilepticus
• Neuromuscular—critical illness polyneuropathy, critical illness myopathy
• Primary CNS inflammation—acute disseminated encephalomyelitis, multiple sclerosis
• Stroke or cerebral hemorrhage
• Hypoxic—ischemic encephalopathy

Drugs That Affect the Neuromuscular Junction	
Neuromuscular blocking agents (nondepolarizing)	Pancuronium, vecuronium pipecuronium, rocuronium
Abxs	Aminoglycosides, clindamycin, tetracycline, quinolones, polymyxin, erythromycin
Local anesthetics	Lidocaine
Antiarrhythmics	Quinidine, procainamide
β-blocking agents	Propranolol, atenolol, acebutolol, bisoprolol, labetalol, metoprolol, oxprenolol, pindolol, sotalol, timolol
Immunosuppressants	Cyclophosphamide, cyclosporin
Calcium channel blockers	Verapamil, diltiazem
Diuretics	
Corticosteroids	
Statins	
Antiretrovirals	Zidovudine, lamivudine
Others	Lithium carbonate, interferon-α, phenytoin, dantrolene, d-penicillamine

Causes of Weakness in the ICU

Disorders of cortex & brain stem

Epilepsy—status epilepticus
Vascular—stroke, hemorrhage, or cerebral hemorrhage
Infxn
Metabolic
Hypoxic–ischemic encephalopathy
White matter dz—toxic encephalopathy, posterior reversible leukoencephalopathy
Autoimmune encephalitis—Hashimoto, paraneoplastic

Disorders of the spinal cord

Trauma including surgery
Acute epidural compression due to neoplasm, infxn, hematoma
Acute transverse myelitis
Cord infarction

Anterior horn cell

Motor neuron dz
Poliomyelitis & postpolio syndrome
Paraneoplastic syndrome

Multiple radiculopathies
Leptomeningeal dz
AIDS polyradiculitis

Acute polyneuropathy
Acute inflammatory demyelinating polyneuropathy (AIDP)
Acute motor & sensory axonal neuropathy (AMSAN)
Acute motor axonal neuropathy (AMAN)
Phrenic neuropathies
Critical illness polyneuropathy
Others—toxic neuropathies, vasculitis, diphtheria, porphyria, HIV, etc

Chronic polyneuropathies
Chronic inflammatory demyelinating polyneuropathy (CIDP)
Diabetic polyneuropathy

Neuromuscular transmission
Myasthenia gravis
Lambert–Eaton myasthenic syndrome
Congenital myasthenic syndrome
Neuromuscular blocking agents
Others: botulism, snake bites, fish toxins, organophosphates, hypermagnesemia, poisoning

Myopathy

Congenital

Periodic paralysis

Acid maltase deficiency

Myotonic dystrophy

Duchenne muscular dystrophy

Mitochondrial

Acquired

Inflammatory myopathy

PM, DM

Critical illness myopathy

Diffuse nonnecrotizing cachectic myopathy

Acute necrotizing myopathy of ICU

Others—HIV related, sarcoid, hypokalemia, hypophosphatemia, corticosteroids, rhabdomyolysis

Neuropathies

Acute inflammatory demyelinating polyneuropathy

About 1/3 of GBS pt require admission to the ICU because of respiratory insufficiency requiring observation or mechanical ventilation, severe bulbar weakness, treating pulmonary aspiration, or autonomic instability causing cardiac arrhythmias

Ventilatory failure is primarily caused by inspiratory muscle weakness. Weakness of the abd & accessory muscles of respiration, retained airway secretions contributes to pulmonary aspiration & atelectasis

Any associated bulbar weakness & autonomic instability reinforce the need for control of the airway & ventilation

Miller Fisher syndrome

Ataxia, areflexia, & ophthalmoplegia are the classical features

Diplopia is the most common initial complaint (in about 1/3), while ataxia is evident in about 1/5 of pt at onset

Facial weakness, bulbar impairments with dysphagia & dysarthria, along with facial & lip paresthesias may also occur & mild proximal limb weakness is found in 1/3 of pt

Acute motor and sensory axonal neuropathy and acute motor neuropathy

Axonal neuropathies that may present with paralysis developing rapidly over hrs leading to respiratory failure

There may be extensive total paralysis of all voluntary muscles of the body, including the cranial & ocular muscles

Cerebrospinal fluid (CSF) protein content is raised but there should be <10 WBC

In both, all peripheral nerves, including CNs, may be unresponsive to electrical stimulation, even when the stimuli are of high voltage & duration

Acute intermittent porphyria

Uncommon autosomal dominant dz characterized by recurrent episodes of abd pain, psychiatric disturbances, seizure, & motor axonal neuropathy with autonomic features

May mimic GBS causing bulbar & ventilatory failure

Attacks can be precipitated by heavy alcohol consumption & by numerous medications, many are commonly used in the ICU such as diazepam, theophylline, & barbiturates

Critical illness polyneuropathy

Acute sensorimotor axonal neuropathy develops in the stetting of sepsis, septic encephalopathy and/or multiorgan failure

The presence of insulin deficiency, hyperglycemia, hypoalbuminemia with or without corticosteroids, & neuromuscular blocking agents seems to place pt at a higher risk of developing this type of neuropathy

This dz is characterized by delayed weaning, severe distal flaccid wasting & weakness, areflexia, & sensory impairment in those pt who are able to cooperate with the examination

A pure motor neuropathy in association with neuromuscular blocking agents is a variant that has been reported. The clinical signs are difficult to obtain due to the difficulties in examining an uncooperative pt who is sedated or has coexistent septic encephalopathy

To compound the diagnostic problem, neuropathy, neuromuscular blockade, & myopathy may all coexist in the same pt

Nerve biopsy & autopsy studies have shown axonal degeneration of both sensory & motor fibers without evidence of significant inflammation or primary demyelination. Muscle shows scattered atrophic fibers in acute denervation & grouped atrophy in chronic denervation

Critical illness polyneuropathy is a self-limited dz & the prognosis is influenced by the severity of the underlying condition that itself accounts for most of the mortality

The outcome is also related to the severity of the sepsis & other factors, including the extent & severity of the neuropathy, the time in the ICU, & presence of hyperglycemia or hypoalbuminemia

When the neuropathy is mild or moderate, the recovery is relatively rapid & complete

Neuromuscular Disorders

Depolarizing agents

Physically resemble acetylcholine &, therefore, bind to activate & block acetylcholine receptors

Succinylcholine is short acting (2–5 min) & produces intense neuromuscular relaxation by causing prolonged depolarization of the postsynaptic receptors at the neuromuscular junction (NMJ). Its sole use is to facilitate tracheal intubation

It should be avoided in neuromuscular dz as hyperkalemia may follow & its use is a risk of the development of malignant hyperthermia

Nondepolarizing agents

Bind reversibly to the postsynaptic acetylcholine receptors antagonizing acetylcholine but do not activate them

They produce longer-lasting neuromuscular blockade & doses are cumulative, particularly if there is renal or hepatic failure

The effects are enhanced by hyperkalemia, hypophosphatemia, & hypermagnesemia

Prolonged neuromuscular blockade

Defined as recovery from NMJ blocking agents 50–100% longer than predicted by pharmacologic parameters

It is particularly associated with steroid-based NMJ blocking agents & occurs after either short- or long-term blockade with nondepolarizing agents

It may be associated with prolonged use or high doses of these drugs, metabolic acidosis, hepatic or renal insufficiency hypermagnesemia, or in association with corticosteroid, aminoglycosides, or other anesthetic agents

Weakness should not persist beyond 2 wks after stopping the blocking agents & typically lasts for only a few days

Prolonged blockade should be considered in any pt who remains weak after discontinuation of NMJ blocking agents

"Train of four" stimulation in which 4 equal pulses are delivered over 2 sec is used to assess recovery from acute block. Lack of an attenuated response indicates prolonged neuromuscular blockade but formal repetitive nerve stimulation is required for confirmation

Neuromuscular dz may be unmasked in previously undiagnosed cases by medications commonly used intraoperatively & in the recovery room or ICU

Pt with myasthenia gravis or the Lambert–Eaton myasthenic syndrome have extremely high sensitivity to subtherapeutic levels of agents that have minimal effect on neuromuscular transmission in normal people

Myasthenia gravis

Pt present with resp failure due to a myasthenic crisis (usually precipitated by infxn, surgery, or inadequate treatment)

Others may develop resp failure during the course of their dz, sometimes caused by a therapeutic cholinergic crisis

Associated bulbar weakness predisposes to pulmonary aspiration & acute resp failure, necessitating urgent tracheal intubation & ventilation

Repetitive simulation typically shows a decrement that is maximal after the 4th to 5th stimulus & is more marked at 3-Hz simulation. There is a postactivation repair of decrement immediately after exercise & postactivation exhaustion when retested after 3 min of rest

Botulism

Caused by toxins produced by *Clostridium botulinum,* an anaerobic gram-positive organism

Acts at the presynaptic region of the NMJ causing failure of release of acetylcholine

The classical form occurs after ingestion of food that contains toxin, but increasing numbers of pt are being seen as a consequence of using contaminated opiates or unclean needles to inject drugs of abuse into infected skin lesions

Pt develop CN deficits, including blurred vision, diplopia, ptosis, dysarthria, & dysphagia

The weakness often affects the arms before progressing to the legs

Autonomic sxs that include dry mouth, unreactive pupils, & ileus are frequent

The condition may be suspected by prominent & early ocular signs (dilated sluggishly reactive pupils & ophthalmoplegia) & dysphagia

Definitive dx requires detection of toxin in the pt's serum, stool, or food by bioassay

Electrodiagnostic may not be straightforward because the findings depend on the timing of the examination & the severity of the dz

Pt with relatively mild dz may have "normal" or low normal compound muscle action potentials amplitude, show no clear decrement at low rates of repetitive stimulation, but demonstrate an increment of >40% after exercise or after high rates of repetitive stimulation, consistent with this being a presynaptic disorder of neuromuscular transmission.

This increment is usually not as marked as in the Lambert-Eaton myasthenic syndrome (LEMS) & in general seen only in clinically weak muscles.

Unlike LEMS & myasthenia gravis, there is no postactivation exhaustion & the increment usually persists for 4–20 min. In more severe dz, the resting compound motor action potential (CMAP) is usually small, there may or may not be decrement at low rates of repetitive stimulation, & the incremental response to high rates to stimulation may be minimal or absent

Other neuromuscular transmission disorders

Organophosphate poisoning, tick paralysis, & black widow spider & certain types of snake envenomation

Muscle Disease

There are 3 major types of myopathies to be discussed: diffuse nonnecrotizing cachectic myopathy, myopathy with selective loss of thick (myosin) filaments (critical illness myopathy), & acute necrotizing myopathy of intensive care.

Diffuse nonnecrotizing cachectic myopathy

Common & presents as muscle wasting with associated weakness

The creatinine kinase (CK) & myoglobin (MG) levels are normal or show only mild changes

It is associated with prolonged ICU admission, sedation, or paralysis causing muscle disuse, & poor nutrition & with protein catabolism during critical illness

There is proximal or general weakness. Biopsy shows type 2 fiber & neurogenic atrophy

Critical illness myopathy

Distinct form of myopathy that occurs in pt with critical illness on the ICU

There are any other names that include myopathy with selective loss of thick filaments, acute quadriplegic myopathy, acute illness, acute myopathy of intensive care, rapidly evolving myopathy with myosin-deficient fibers

It is probably considerably more frequent than critical illness polyneuropathy

It is sometimes associated with prolonged exposure to high doses of corticosteroids & nondepolarizing muscle blocking agents used to treat acute pulmonary disorders such as asthma

It can occur in other situations including sepsis, a major organ transplantation, particularly liver, & it does not seem to correlate with the duration of intensive care

Other factors that may contribute include nutritional deficiencies; concurrent drug administration with aminoglycosides or cyclosporin; hyperglycemic, renal, & hepatic dysfunction; fever; & severe metabolic & electrolyte disorders

The limb weakness may be mild to severe & is predominately proximal although it may be generalized

There may be facial & neck weakness as well, but the ocular movements are often spared, reflexes are reduced, & sensation is not affected

Blood CK levels are raised in <50% & electrodiagnostic studies are neither sensitive nor specific for diagnosing myopathy in the critically ill

The outcome seems to be much better than after critical illness polyneuropathy, & most pt make a full recovery unless there has been severe & prolonged paralysis

Acute necrotizing myopathy of intensive care

Rare condition that may be a form on rhabdomyolysis

Develops after exposure to neuromuscular blocking agents with or without steroid therapy but may be associated with other infective or metabolic insults

Serum CK is markedly elevated, there is usually associated myoglobinuremia

Electromyography (EMG) confirms severe myopathy & biopsy shows patch or widespread necrosis with occasionally vasculitis or infarction within the muscle.

Prognosis for recovery of weakness is poor

Other myopathies include:

Steroid myopathy (e.g., in asthma or patients with chronic obstructive pulmonary dz)

This is a slowly evolving mild to moderate proximal weakness with mild elevation of CK & type 2 fiber atrophy

Sepsis may affect the muscles causing PM due to septic micrometastases

Inflammatory myopathies cause resp weakness & pt with DM may have a characteristic skin rash

Muscular dystrophy may present with ventilatory failure of developing resp insufficiency either as an early manifestation or as an inevitable feature of dz progression

Myotonic dystrophy is occasionally identified for the 1st time in the ICU

In adults, acid maltase deficiency may present with proximal weakness, scoliosis, & diaphragmatic paralysis

Rhabdomyolysis may be precipitated by trauma, compartment syndrome, ischemic arterial occlusion, or drugs & is associated with high-serum CK levels, myoglobinuria, & general weakness

Other conditions:

Tetanus

Neurologic manifestations are caused by tetanospasmin, a toxin contaminated by gram-positive spore forming bacilli *C. tetani* in unimmunized individuals

Toxin is transported via retrograde axonal transport in the spinal cord or brain stem or both

Migrates to the presynaptic terminals & inhibits the release of γ-aminobutyric acid & glycine, important inhibitory neurotransmitters

Most pt will be admitted to the ICU because of increased muscle tone & spasms

Resp compromise is caused by spasm of resp muscles or laryngospasm

Autonomic dysfunction occurs in severe cases & results in HR & BP lability, arrhythmias, fever, profuse sweating, peripheral vasoconstriction, & ileus

Muscle rupture & rhabdomyolysis can complicate extreme cases

Paralytic rabies

Produces neuromuscular weakness that can be difficult to differentiate from other causes of weakness such as GBS

May begin with local wound pain & paresthesias, followed by fasciculations near the site of inoculation

NEONATAL INTENSIVE CARE

STEVEN A. RINGER, MD, PhD

Resuscitation in the Delivery Room (Figure 32-1)

Apnea Is the Hallmark Sign of Neonatal Depression

Primary apnea: occurs shortly after a stress or insult to the infant & is easily corrected with stimulation

Primary apnea (untreated) will progress through period of gasping to **secondary apnea**

Secondary apnea requires vigorous resuscitation, including the provision of positive pressure breaths

Primary and Secondary Apnea May Initially Appear Similar

They cannot be distinguished by relation to delivery, as both may occur before, during, or after birth.

Therefore: always assume that apnea is secondary & be prepared to intervene ***IF INFANT IS APNEIC OR THE HR IS LOW,*** *the priority is to establish the airway & effective ventilation. Until this is done, chest compressions & medications are of little or no value!!*

Situations in which the likelihood of needing resuscitation is increased:

Prematurity

Evidence of nonreassuring fetal status

Category 3 (i.e., abnormal) tracing of fetal HR

Persistent bradycardia

Known or suspected anomalies

Meconium-stained amniotic fluid

Maternal conditions with potential effect on transition from fetal to newborn life

Factors associated with an increased risk of infxn in the newborn

Abnormal delivery—shoulder dystocia, breech, or abnormal lie

Preparation

Ensure that all resuscitation equipment is avail. & working

Ensure that delivery room temp is warm

Upon receiving the infant

Place on radiant warmer, GENTLY DRY infant, except:

Very low–birth-wt infants should be placed UNDRIED (head exposed) in plastic wrap/bag

Discard wet towels

Position head in slight extension, midline

Suction mouth, & then the nose with bulb, **only if needed**

If there is meconium-stained fluid, provide resuscitation **as usual.** Be vigilant for possible airway obstruction.

VIGOR = good HR, good respirations, good tone

Give tactile stimulation if apneic, repeat once (total of twice) if needed

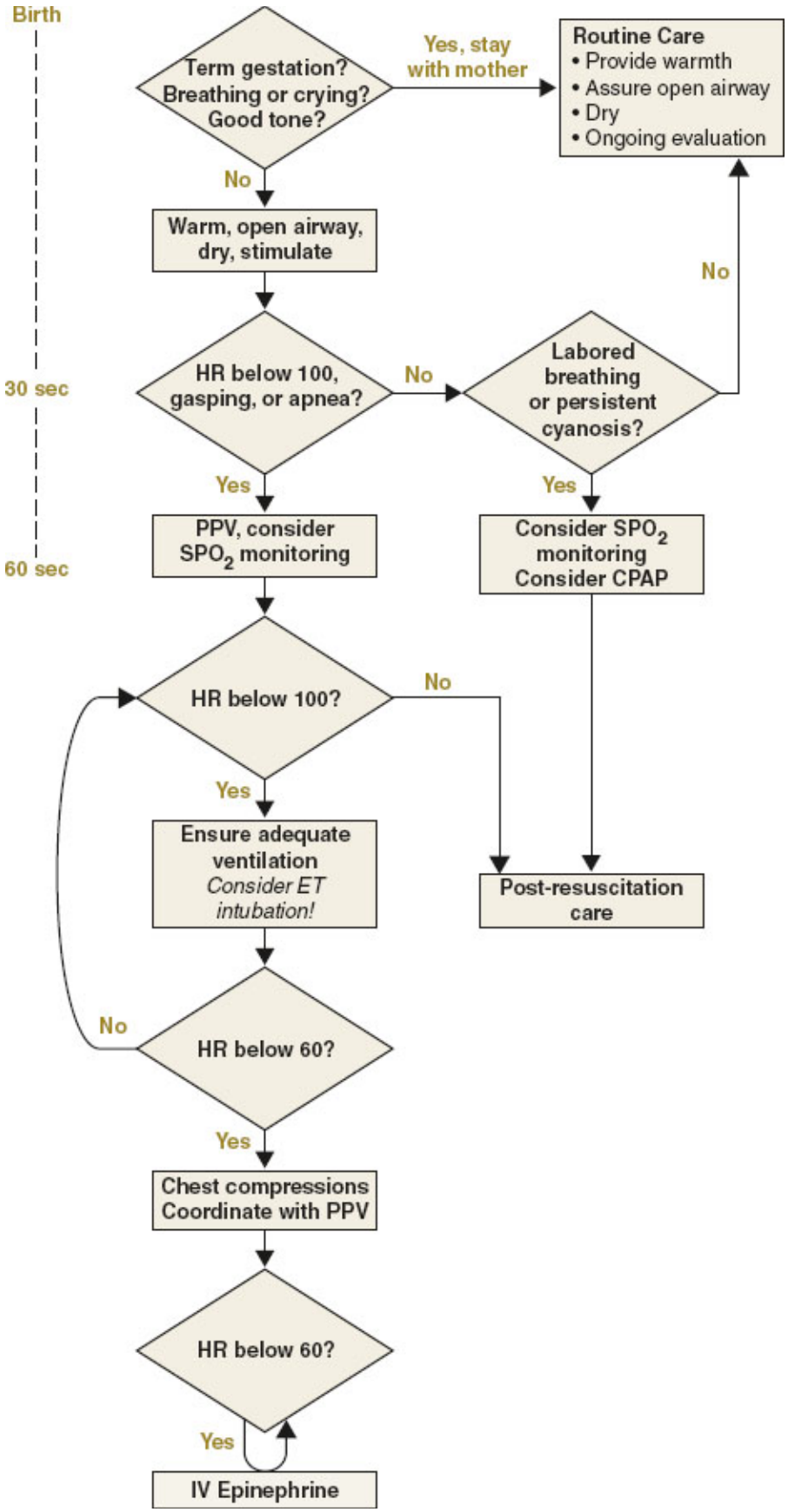
Acceptable methods: rub back, flick soles of feet

Apgar scores (see table): Assign them at 1 & 5 min of life. Repeat every 5 min until ≥7

Apgar Scores			
Criterion	**0**	**1**	**2**
HR	None	<100	>100
Respiration	None	Slow, irregular	Good cry
Muscle tone	Limp	Some flexion	Active movement
Reflex irritability	None	Grimace	Cough/sneeze
Color	Blue, pale	Pink body	Pink

Repeatedly evaluate breathing, HR, color (in that order), & base decisions for intervention on this evaluation as follows:

Figure 32-1. Overview of Ventilation–Perfusion Relationship


Birth
Term gestation?
Breathing or crying?
Good tone?
Yes, stay with mother
Routine Care
• Provide warmth
• Assure open airway
• Dry
• Ongoing evaluation
No
Warm, open airway, dry, stimulate
30 sec
HR below 100, gasping, or apnea?
No
Labored breathing or persistent cyanosis?
No
Yes
Yes
60 sec
PPV, consider SPO2 monitoring
Consider SPO2 monitoring
Consider CPAP
HR below 100?
No
Yes
Ensure adequate ventilation
Consider ET intubation!
Post-resuscitation care
No
HR below 60?
Yes
Chest compressions
Coordinate with PPV
HR below 60?
Yes
IV Epinephrine

Source: Textbook of Neonatal Resuscitation. In: Weiner G, ed. 7th ed. American Academy of Pediatrics/American Heart Association; 2016.

Assess: Is the Infant Breathing?

If the infant appears to be breathing, move to step 2

If the infant remains apneic, give breaths by bag/mask until respirations are spontaneous

For term infants, start resuscitation with room air

For premature infants <32 wks, start with blended oxygen 21–30%

For all infants, monitor SpO_2 & adjust concentration to ensure target saturations. These are considered the same for infants of all gestational ages

Target Oxygen Saturation ("Preductal" Measured on Right Upper Extremity)	
Time after Birth	**Target Saturation (%)**
1 min	60–65
2 min	65–70
3 min	70–75
4 min	75–80
5 min	80–85
10 min	85–95

Positive Pressure Ventilation

Indications:

Apnea

HR <100 despite spontaneous respirations

Persistent poor color/low SpO_2

Procedure

Begin positive pressure ventilation (PPV) with bag & mask at 40–60 breaths/min. Use adequate pressure/volume so as to result in chest expansion

The 1st breath may require 30–40 cm H_2O

Subsequent breaths usually require 15–20 cm H_2O but may require 20–40 cm H_2O in low compliance states (e.g., respiratory distress syndrome [RDS])

Bag–mask ventilation is often as effective as intubation. If not, check:

Mask seal

Reposition head to ensure open airway

Suction the airway

Open the mouth slightly

Increase the pressure used

Consider an alternative airway

Intubation

Laryngeal mask airway if infant is >1,500 g

Intubation

Indications:

Known or suspected diaphragmatic hernia

To deliver meds (epinephrine) if vascular access has not been achieved

To give surfactant in infants <28 wks gestation

Relative indications:

When PPV alone is not working

Airway stability during resuscitation or transport

Long-term ventilator support likely

Need for PEEP

Procedure—see later

Limit duration of each intubation attempt to 20–30 sec

Check tube placement by auscultation over lungs & stomach & presence of $ETCO_2$

Assess: Once Ventilation Is Ensured (or Spontaneous) Check the Heart Rate

HR is an excellent indicator of the efficacy of resuscitative efforts

Electrocardiographic monitoring of the HR is more reliable than clinical assessment & should be used during resuscitation esp. when chest compressions are given.

If HR >100, monitor. If respiratory support has been needed, observe for spontaneous breaths

If HR <100, or apneic, continue PPV as above, even if apparently breathing

If HR <60, start chest compressions (intubation recommended)

Encircle chest with both hands, thumbs meet over lower sternum. Stand at head of infant to 1 side of person providing ventilation.

Chest compressions are applied to the sternum below the nipple line at 90/min, depressing the sternum ½–¾ in. Supplied breaths continue at 30/min during compressions

Total of 120 events/min

Recheck HR every 45–60 sec to assess need for continuing compressions

Give medications (later) if HR does not improve above 60

Assess: Once Breathing and Heart Rate Are Ensured, Assess Oxygen Level

Clinical assessment of color is unreliable in the newly born infant

Pulse oximetry is more reliable & can aid in HR monitoring

Oxygen should be given in a concentration adequate to result in saturation within the target range for each minute after birth

For infants >32-wk gestation, start with room air & titrate up prn

For preterm infants <32-wk gestation, use blended oxygen (21–30%) & titrate up or down prn

Medications

If the HR remains <60 despite assisted ventilation, chest compressions, & 100% oxygen, resuscitation medications are indicated

Estimate pt's wt at 1, 2, or 3 kg: 1 kg < ~29 wks, 2 kg 29–33 wks, 3 kg 34+ wks

Epinephrine: often give 1st dose by ETT (0.3–1.0 ml/kg) while awaiting, obtain vascular access. IV dose: 0.1–0.3 ml/kg. Always use 0.1 mg/ml dilution (1:10,000 dilution)

Volume: 10 ml/kg of NS given IV. Can get emergency O negative blood if hemorrhage is known or suspected. Transfuse slowly

Resuscitation Medications in Delivery Room				
Med	**Indication**	**Route**	**Dose**	**Comment**
Epinephrine (0.1 mg/ml)	Low HR,	ET	0.3–1.0 ml/kg	IV dose is preferred
	Poor perfusion	IV	0.1–0.3 cc/kg q5min 1:10,000 dilution	
Volume	Volume loss, shock	IV	10 ml/kg	NS, blood Over 5 min

Drugs that are not used:

Sodium bicarbonate is not efficacious & may be harmful

Naloxone is not helpful. Apnea caused by maternal opioids should be treated with PPV

Stopping Resuscitative Efforts

If, after 10 min of properly performed resuscitative efforts with good chest rise, the HR remains undetectable, it is reasonable to stop efforts. Longer efforts may be indicated based on availability of therapeutic hypothermia and/or parental wishes

In other clinical situations the benefits & risks of continuing resuscitation must be weighed when considering whether to continue efforts

Some Common Mistakes in Resuscitation Include

Failure to introduce yourself upon entering room and get information

Failure to identify a team leader

Failure to define roles of team members

Focusing on low HR rather than correcting apnea

Failure to remove wet towels after drying the baby

Failure to position the head in midline

Flexion or hyperextension of the baby's neck during bag & mask ventilation

Too small an initial breath, & too large subsequent breaths

Tendency to bag-ventilate too fast & too shallow: AIM FOR RR of 40 (Count: Squeeze, 2, three…)

The NICU: The Initial Workup

Detailed maternal, obstetric, family hx

Physical examination:

Complete physical examination

Record the length, wt, & head circumference, & plot their percentiles

Dubowitz/Ballard examination to assess gestational age

Include retinal red reflex, hip examination for dislocation (even for premature infants)

Number & type of umbilical vessels

Detailed neurobehavioral examination

Lab data

Obtained as indicated by the clinical situation, none are routine

Common tests: include CBC w/diff, Ca, glucose, blood cx, type, & crossmatch

Cerebrospinal fluid (CSF) studies: if indicated, it is useful but not mandatory to obtain CSF before abxs have been administered

Radiographs

If possible, have all CVCs & tubes in place before getting a radiograph to minimize radiation exposure

It is usually possible to accurately ascertain correct ETT position by physical examination or CXR before surfactant therapy

Special Tests

Newborn screen

Varies from state to state but usually includes: phenylketonuria, maple syrup urine dz, homocystinuria, galactosemia, hypothyroidism, congenital adrenal hyperplasia, toxoplasmosis, Hb electrophoresis, cystic fibrosis

Kleihauer–Betke test:

Detects fetal red cells in maternal blood (i.e., fetomaternal hemorrhage)

Maternal blood is fixed on a slide

The adult Hb is eluted with acid

Fetal cells are visible after appropriate staining

The size of the transfusion is estimated from the percent of fetal cells

Apt test:

Determines whether GI blood is fetal or maternal (swallowed during delivery or breast-feeding) blood

Will not work on stool

Common Procedures

Thermal regulation: infants, esp. premature infants, will lose heat very rapidly while exposed for procedures. Minimize time with incubator open, add heat sources prn, esp. for low–birth-wt infants. Extremely low–birth-wt (ELBW) infants should be admitted to humidified incubator ASAP

Heelsticks: warm foot 1st, & avoid plantar aspect of foot. Electrolytes, Hct, BUN/Cr, capillary blood gases, some drug levels, bilirubin can be drawn this way. This method can give factitious results, esp. if flow is poor. Hct may be 5–15% higher than central venous Hct

Venipuncture: usually a small rubber band will suffice as tourniquet. Blood obtained in this manner is good for most studies

Scalp veins: avoid shaving the area if possible; combing is usually adequate. A rubber band placed around the head proximally is a helpful tourniquet

Arterial puncture: useful for ABGs, or other tests if venipuncture is not possible & a moderate volume of blood is needed

Ensure collateral flow via ulnar artery before puncturing the radial artery. The newborn hand is usually ulnar predominant, thus damage to this vessel can have dire consequences

The angle of approach to the radial artery is very shallow & is best accessed at the 2nd subthenar crease

Transillumination of the wrist to localize artery is often helpful

Umbilical arterial catheter (UAC):

Great for monitoring ABGs & other labs, infusing parenteral nutrition, BP monitoring

Use 2.5, 3.5, or 5F UAC catheter depending on infant size

Tip should be placed at T6–T10 (“high catheter”) or L3–L5 (“low catheter”)

The length of a high line is (approx.) umbilicus–shoulder distance +2 cm

Sterile technique & x-ray to check catheter placement are mandatory

Do not administer vasopressors or platelets via UAC

Dwell time should be as short as possible, depending on clinical needs

Monitor legs, esp. toes, for signs of vascular insufficiency or embolism (blue toes)

If present, warm other foot & consider pulling catheter. Monitor for HTN or hematuria with a “high” UAC & remove the catheter if present

Feeding with UACs in place is a matter of controversy, although it is agreed that gut priming is not harmful

Umbilical venous catheter (UVC):

Good for emergency access, exchange transfusions, monitoring of labs, & CVP

Tip must be placed above liver (cavo-atria (IVC-RA) junction) if used for continuous infusions

This is roughly distance from umbilicus to lower sternum above xiphoid

Dwell time should not exceed 10 days

A “low” UVC can be emergently placed for emergency drug or fluid administration or for exchange transfusion

Insert catheter just to the point of blood return, usually 3–5 cm in term infants, 2–4 in preterm infants

Dwell time should be limited to the length of the emergent need

Useful for emergency venous access in delivery room

Arterial catheters (peripheral)

Not for infusion other than flushes, normal or half-NS, or sodium acetate low-rate infusions

Intubation:

Small straight laryngoscope blades (Miller 0 or 00 for prematures, Miller 1 for term) are used

Uncuffed ETTs are almost always used, size

2.5 for birthweight <1,000–1,250 g

3.0 for birthweight 1,250–2,000 g

3.5 for 2,000+ g

4.0 rarely used in larger infants

Can be nasal—assisted by Magill forceps—or oral. Videolaryngoscopy is becoming avail.

On radiograph, tip of ETT should be below clavicles (thoracic inlet) & above carina

Initial *estimate* of tube insertion depth: Naso-tragal distance +1 cm

Neonates are commonly intubated awake

In elective procedure, sedate with narcotic and/or benzodiazepines

The neonatal airway presents special difficulties:

Larynx is small, anteriorly & superiorly placed

Cricoid pressure is often useful in pushing the larynx into view

The tongue is relatively large & the epiglottis, which is omega shaped, may conceal the cords

ETT position varies with head position: a flexed head results in a lower tube tip. “The hose goes with the nose!”

Chest tubes: usual site of insertion is 4th to 5th intercostal space above rib, at anterior axillary line. Watch for & avoid nipple/areola

Bladder tap:

The suprapubic area is prepped in a sterile manner

A 22- or 23-gauge needle attached to a syringe is introduced at the midline above the pubic bone, & slid in up to 3 cm aiming at the coccyx. If no urine is obtained, the bladder is empty

Some advocate directing the needle straight downward

Lumbar puncture:

The pt is placed in a lateral decubitus or sitting position, with the lower spine curved

The area is prepped & draped in a sterile manner

22-gauge spinal needle with stylet is introduced between L3 & 14 or L4 & L5, above Touffier's line

The needle is advanced toward the umbilicus. A "pop" is felt as it enters the subarachnoid space

In premature infants, this is only a few millimeters depth

CSF should be sent for cx & sensitivity, Gram stain, protein, glucose, cell count

Common Neonatal Problems

Respiratory Disorders

Tachypnea: RR >60/min

Cold stress
Sepsis/pneumonia
Respiratory distress (RDS)
Transient tachypnea of the newborn (TTN) due to retained fetal lung fluid
Metabolic acidosis
Polycythemia
Anemia
Hypoglycemia
CHF due to structural anomalies or patent ductus arteriosus (PDA)

Respiratory failure:

Diagnosed on clinical signs or defined as $PaCO_2$ >55, PaO_2 <50, pH <7.25.

Progression of treatment of hypoxemia

May give up to 60% oxygen by hood before considering other interventions.

With signs of distress, early use of CPAP (Continuous Positive Airway Pressure) is indicated based on distress & increased oxygen requirement

Begin CPAP (+4–6 cm H_2O) Late preterm or term infants may tolerate this poorly & need intubation

If there is decreased ventilation or apnea, CPAP may be inadequate

Intubation & mechanical ventilation. Also indicated for:

Severe apnea

Intractable seizures

Suspected persistent pulmonary hypertension (PPHN)

Surgical abdomen with respiratory compromise

Conventional ventilation is usually tried 1st: volume guarantee mode or SIMV (synchronized intermittent mandatory ventilation).

High-frequency ventilation (HFV) (high-frequency oscillatory ventilation [HFOV] or high-frequency jet ventilation [HFJV])

Failure of conventional ventilation modes:

HFOV useful for both hypoxemia & hypercarbia

HFJV often effective for hypercarbia & air leak syndromes

Local practice may favor earlier use of HFV of 1 or both types

Inhaled nitric oxide used in conjunction with mechanical ventilation for persistent pulmonary hypertension of the newborn (PPHN)

Extracorporeal membrane oxygenation (ECMO) may be effective in term & near-term infants for whom other modalities have failed

Resp management of the newborn:

Geared toward minimizing complications associated with hyperoxygenation & barotrauma **or** hyperventilation

Even short periods of low $PaCO_2$ may be harmful

The neonate usually tolerates pH >7.28, $PaCO_2$ 45–55, pO_2 45–65 very well, & these can be used as weaning parameters

Typically weaning is done by

Decreasing FiO_2, then peak inspiratory pressure (PIP) or tidal volume

Specifics depend on the dz & mode of support

For premature infants <32 wks who require supplemental oxygen, keep O_2 saturation between 90 & 94%

For more mature infants who require supplemental oxygen, keep SpO_2 between 87% & 97%

Respiratory distress syndrome

Primarily a disorder of prematurity (also rarely in term infants)

Underlying cause is deficiency (total or partial) of pulmonary surfactant, variable component of pulmonary HTN

Hypoxemia should be the major abnormality early on, if not, review dx

The pattern on CXR is usually a homogeneous "ground glass" opacification with air bronchograms

Difficult to distinguish from Group B streptococcal (*GBS*) pneumonia

In more mature infants, chest radiograph may be less homogenous, often patchy with air bronchograms

Treatment:

Fluids are monitored closely, may need to slightly restrict until diuresis occurs

First line is oxygen supplementation for mild cases

Most infants require some end-expiratory pressure—CPAP is effective, esp. when started as early as possible. In most cases, noninvasive ventilation with CPAP or NIPPV (noninvasive intermittent positive pressure ventilation)

Surfactant therapy may be indicated & should be administered as soon as the dx is made or highly suspected (soon after birth)

InSuRE method: intubation, surfactant & rapid extubation to CPAP mode

In more severe cases, surfactant used with mechanical ventilation

Conventional ventilator management includes a high rate, moderate tidal vol, or lowest possible PIP, & low I-time. End-expiratory pressure is needed. Specifics of therapy depend on mode of ventilation used

Repeated doses of surfactant may be given if FiO_2 >0.3–0.35, MAP >8 at the end of dosing interval. The inter-dose interval and the need for more than 1 dose depend on the particular product used

Additional doses often given to all extremely immature infants

Transient tachypnea of the newborn

Believed to be due to delayed resorption of fetal lung fluid

Infants with TTN are usually mature, often born by cesarean section, esp. those without labor. Typical features include:

Tachypnea

Mild cyanosis or low to moderate supplemental oxygen need

Mild respiratory distress

Typically improves in the 1st 4–6 hrs, & is usually resolved by 24 hrs after birth

Chest radiograph

Prominent vascular markings

Fluid in fissures

TTN is a dx of exclusion; abx should be considered in the absence of improvement or continued or increasing need for O_2 after 1st hours

Rarely requires specific therapy or support

Persistent pulmonary hypertension of the newborn

May develop after
Asphyxia, esp. chronic
Aspiration, such as meconium-stained or clear amniotic fluid
Pulmonary parenchymal or vascular dz or
Pulmonary hypoplasia
Congenital cardiac malformations
Sepsis
Persistent elevation in pulmonary vascular resistance results in:
Right-to-left shunting occurs at the level of the atria or ductus arteriosus
Cardiac dysfunction
Resultant hypoxemia
Chest radiograph may be clear or show decreased pulmonary blood flow
SpO_2 (& PaO_2) may show gradient between "preductal" sites receiving arterial supply from vessels proximal to the ductus arteriosus (right upper extremity) & measurements made "postductal" (in left or lower extremities)
ECG may show right ventricular hypertrophy (RVH) or strain, myocardial dysfunction, & a right-to-left shunt
Structural heart dz should be ruled out
Treatment:
The goal is to reduce pulmonary vascular resistance & decrease right-to-left shunting
May respond to administration of 100% oxygen
Systemic BP should be supported with vasopressors prn
Pt may be sedated or chemically paralyzed to prevent catecholamine release
Inhaled nitric oxide is mainstay of therapy, usually at 20 ppm to start
ECMO used in cases unresponsive to other therapies

Meconium aspiration syndrome

Chemical pneumonitis resulting from meconium aspiration before birth
Results from hypoxemia-induced gasping
Infxn, PPHN often associated
Often results in
Lower airway obstruction, air leak syndromes
Hypoxemia & decreased ventilation
Radiograph
Heterogeneous, patchy, “snow storm” with areas of hyperinflation & atelectasis
Treatment
Broad-spectrum abx coverage
Pulmonary toilet & close monitoring of resp status, BP, calcium, & glucose
Conventional ventilation may require high PIP, adequate PEEP, & longer expiratory time to avoid air trapping
HFOV: use lower Hz (6–12), higher amplitudes than used for pneumonia or RDS
ECMO for most severe cases
Concurrent treatment of PPHN prn

Air leak

May occur spontaneously (2–3% incidence after normal births)

These are often benign or unrecognized

Pathologic causes include excessive ventilation, progression of dz, & rarely due to trauma from procedure

Prevention focuses on minimizing barotrauma by avoiding excessive PIP & PEEP

Pneumothorax:

Clinical signs

Decreased breath sounds

Sudden decompensation

Positive transillumination of chest

Asymmetry of chest

Dx confirmed by

Radiograph, or

Diagnostic needle aspiration

Treatment

Not necessary in mild cases

Needle aspiration

Chest tube placement may be necessary if leak is recurrent or if lungs are abnormal/diseased

Pulmonary interstitial emphysema

Air leak from alveoli into interstitium

Can cause cardiovascular & resp instability

Most severe form is air block, when interstitium is gas filled & alveoli are compressed

Clinical signs

Worsening hypercapnia

Decreased breath sounds

Radiograph confirms dx

Cystic bubbles radiating linearly from hilum

Increased apparent lung size

Treatment is aimed at reducing mean airway pressure (MAwP) & PEEP (often to very low levels temporarily)

HFJV

Rarely, extremely severe cases can be improved by placing affected lung in dependent position or selective intubation of unaffected side

Pneumomediastinum

Dx suggested by distant heart sounds, respiratory distress

Lateral CXR is most helpful for dx best

Treatment

Reduction of MAwP & PEEP

Usually no specific treatment is needed, or possible

Analgesia may be helpful/required

Pneumopericardium

Rare, high mortality complication

Often associated with hypotension, bradycardia, cyanosis

Radiograph reveals heart looking like ball hanging on a string

Treatment

Emergent needle aspiration or pericardial tube placement

Systemic air embolism

Rare complication in which gas ruptures through into pulmonary veins & fills heart & circulation

Almost always rapidly fatal, with no specific treatment possible

Chronic lung disease (CLD) including bronchopulmonary dysplasia (BPD)

Usually occurs in premature infants exposed to mechanical ventilation

Etiology is multifactorial & incompletely understood

Often develops in ELBW infants who require little ventilator support or supplemental oxygen

Dx based on clinical or lab evidence of pulmonary dz, including need for supplemental oxygen at 28 days (CLD) or at 36-wk corrected gestational age (BPD)

Early signs often seen in ELBW infants at 7–10 days of age

H/o PDA & fluid overload are predisposing factors

Hypoxemia and/or hypercapnia may be present

Radiograph shows coarse reticular pattern, cystic structures, streaky densities, & hyperinflation

Prevention

Low ventilation pressure, early course of vitamin A & caffeine therapy

Avoidance excessive baro- or volutrauma early in course

Limited fluid intake

Preventing complications such as atelectasis, air leak or overdistention

Treatment

Limit fluid intake

Promote growth with adequate caloric intake

Low-level ventilator support often for prolonged periods

Supplemental oxygen

In very severe cases, short courses of corticosteroids may be needed

Cyanosis

Low PaO_2

Congenital heart dz, pulmonary dz, airway obstruction, extrinsic lung compression, CNS dz

Normal PaO_2

Polycythemia

Methemoglobinemia

Cold stress

Differential Diagnosis of Cyanotic Congenital Heart Disease		
	Cyanotic CHD	**Cyanotic with CHF**
PaO_2 on 100% O_2	<50 mm Hg	<150 mm Hg
Congenital heart dz	D-transposition of great arteries (±intact ventricualr septum) Total anomalous pulmonary venous return truncus arteriosus Ebstein's anomaly Tricuspid atresia Pulmonary atresia with IVS Severe pulmonic stenosis Severe tetralogy of Fallot	Hypoplastic left heart

Cardiac evaluation

Physical examination, vital signs (including 4 extremity BPs)

Radiograph: heart size, pulmonary vascular markings, major vessels, cardiac & visceral situs, other anomalies

ECG

Axis

Frontal plane loop (if suspicion of A–V canal defect or tricuspid atresia)

R wave progression

Hyperoxia test

A "postductal" PaO_2 150 mm Hg on $FiO_2 = 1.0$ is strongly suggestive of intracardiac or ductal R-L shunting due to structural anomaly

"Pre-" & "post"ductal PaO_2

Useful for distinguishing between intrapulmonary & cardiac/PDA shunting

Intrapulmonary shunting (e.g., V/Q mismatch), the measurements should be similar

Unoxygenated blood shunted R-L across an intracardiac lesion or PDA results in the preductal measurement being higher than the postductal (the O_2 Sat will be at least 10% higher)

Echocardiography

Usual standard that defines anatomy

Doppler studies yield flow rates & hence pressure gradients

Pressure, COs measured this way do not always correlate exactly with catheterization data

Catheterization

Exactly defines anatomy

Sometimes necessary for staging preoperatively

Rarely needed in initial evaluation

Used therapeutically in some cases

Balloon atrial septostomy

Clamshell ASD/VSD closure

Umbrella PDA closure in older children

Congestive Heart Failure

Signs:

Hypoxemia is initial sign. Other sx: tachypnea, tachycardia, hepatomegaly, inordinate wt gain, cardiomegaly

Radiograph

Cardiomegaly, congested lung fields

Treatment

Oxygen

Fluid restriction

Furosemide 1 mg/kg IV push or other diuretics

Cardiotonics, afterload reduction prn

Patent Ductus Arteriosus

Often manifested in 1–3-days-old premature infant

Systolic murmur at upper left sternal border

Often silent in ELBW infants

Bounding or wide pulses

Active precordium

CHF, hepatomegaly

Radiograph

Cardiomegaly, pulmonary congestion

Dx

Echocardiography (particularly with Doppler) provides definitive proof of PDA

Treatment

Characterization of hemodynamically significant PDA is unclear, as is benefit of treatment in overall population

Fluid restriction

Medical therapy: Indomethacin 0.2 mg/kg 1st dose, then 0.1 mg/kg q12h for 24 hrs if <48 hrs. 0.2/0.2/0.2 if 2–7 days; 0.2/0.25/0.25 if >7 days infant

Contraindications

Renal failure, severe thrombocytopenia, ongoing bleeding, necrotizing, enterocolitis, intraventricular hemorrhage

Surgical ligation rarely needed but may be indicated after failed medical therapy in hemodynamically significant cases

Blood Pressure

The normal BP in the premature neonate is not well defined

A MAP of >35 mm Hg is considered normal in term infants

For premature infants in 1st few days, normal MAP is considered to be more than the weeks of gestational age + 2

Some caregivers believe that a MAP of ≥30 mm Hg is needed to ensure cerebral perfusion independent of gestational age

Treatment of hypotension

10 ml/kg of NS given over 30 min

Blood transfusion if hematocrit is low

Vasopressors once fluid balance has been optimized

Dopamine at 3–30 mcg/kg/min

Dobutamine may be added up to 20 mcg/kg/min but is of questionable benefit

Epinephrine 0.1–1.0 mcg/kg/min for severe cases or vasodilation (warm shock)

Fluids and Electrolytes

General Facts

Total fluid per day varies from 40 to 150 ml/kg/d
Factors increasing fluid requirements include
Lower wt
Younger gestational age
Immature or injured skin integrity
Elevated urine output
Low-humidity environment
Anomalies with surface defects (omphalocele, myelocele, etc.)
Relatively dilute electrolyte solutions are used in neonates due to greater insensible water losses/kg
Fluid requirements tend to increase in days after birth
The normal neonate loses wt in the 1st few days of life & does not regain birth wt for up to 7 days
Phototherapy may increase insensible water losses
Wt loss up to 10% may be normal

Common Fluid Maintenance Regimens in Humidified Incubator

Day of life (DOL) #1.

Birthweight >1,200 g: birthweight: 80 ml/kg/d $D1_0W$

Birthweight <1,200 g: birthweight: 100 ml/kg/d $D1_0W$

Birthweight <1,000 birthweight: may require increased intake if losses are increased

Add calcium gluconate 200–400 mg/kg/d

Premature

Depressed infants

Infants of diabetic mothers (IDMs)

Glucose infusion rate

4–8 mg/kg/min in term infants

6–8 mg/kg/min for prematures

Adjust based on measured glucose

Monitor electrolytes but note that initially the infant's serum values are mostly reflective of the mother's. Smaller babies get earlier labs, usually 8–12 hrs of age, bigger ones at 24 hrs

DOL #2: & thereafter

20 ml/kg/d increase unless there is a supervening concern

Maximum usually 140–150 ml/kg/d

Na: 2–4 mEq/kg/d

K: 2 mEq/kg/d

Use chloride salts or acetate if there is metabolic acidosis

Calcium prn

Adjust intake to ensure urine output of 2–3 ml/kg/hr

Renal function

Little urine output in 1st 12–24 hrs is normal if no intake
Oliguria is defined as <1 ml/kg/hr in the neonate
Treatment
IV fluid bolus 10–15 ml/kg NS
Increased maintenance fluids
Assess renal function
US to r/o anatomic anomaly or obstruction
Serum creatinine
Assess cardiovascular status

Hypoglycemia (serum glucose <45)
Definition of hypoglycemia is not well established
Normal level usually will increase in 1st several days of life
Clinical signs
Often asymptomatic, jitteriness, tachypnea
Differential dx
Hyperinsulinemic states
Infant of diabetic mother, small for gestational age, sepsis, inborn errors of metabolism, birth asphyxia
Diminished stores
Small for gestational age
Inborn errors of metabolism
Other
Polycythemia/hyperviscosity
Treatment
Monitoring of at-risk infants after birth
Increased feeding frequency
Adding glucose to feeds
Acute management
200 mg/kg glucose IV push = 2 cc/kg $D1_0W$
Follow with continuous infusion at 8 mg/kg/min glucose
Adjust infusion based on repeat levels

Hyperglycemia

Causes

Excess glucose administration

Stress

Sepsis

Clinical presentation

Asymptomatic

Osmotic diuresis

Treatment

Insulin infusion

0.01–0.05 U/kg/hr

Adjust in increments of 0.005–0.01 U/kg/hr

Prime IV tubing with infusion before administering

Hypocalcemia (Ca <7 mg/dl, or use ionized calcium level)

Causes

Asphyxia, prematurity, infant of diabetic mother, hypoparathyroidism, diuretics, alkalosis

Clinical presentation

Jitteriness, apnea

Treatment:

Symptomatic, or the presentation is acute, give Ca gluconate 200 mg/kg IV slowly = 2 cc/kg 10% calcium gluconate

Asymptomatic: increase maintenance & monitor

Rapid IV infusion of calcium may cause bradycardia

Nutrition

Goals

Target wt gain is 10–15 g/kg/d
Actual wt gained will be lower for smaller infants
Length gain: 0.8–1.2 cm/wk
Head circumference growth: 0.5–0.8 cm/wk
Human milk is best substrate
For premature infants, milk usually requires supplementation in calories, protein, minerals

Requirements for growth

Calories: 110–150 kcal/kg/d
Protein: 3.5–4 g/kg/d
Fat: 2–3 g/kg/d

Method of feeding

Enteral feeds are optimal

Immature or compromised infants may initially feed via gavage tube, later PO

Bolus feeds every 3–4 hrs are the goal

In some infants (usually <1,000 g), continuous feeds are necessary

Feedings must initially be advanced slowly over days to ensure tolerance

In infants <1,000 g, feeds start as "gut priming"

Use human milk

Feed 0.5 ml every 4 hrs for 3 days

Then begin feeding advance as below

Advancement protocols vary widely, there is no 1 "correct" protocol: benefit appears to be in having a local standard

Start with 20 cal/oz feeds

Human milk is presumed to be 20 cal/oz

Increase feeding caloric density prn to promote growth

Fortification begun at vols of 80–100 ml/kg/d to maintain overall intake

Formulas made to increase density

Human milk fortified to caloric density

Most infants <1,500 g will need increased density

Begin iron supplementation when on full feedings (see the table below)

Remain vigilant for feeding intolerance or signs of GI dz

If present, hold feedings & evaluate

Suggested Rates for Initiation and Advancement of Nutritive Feedings

Birth Weight (g)	Initial Rate (ml/kg/d)	Volume Increases↑ (ml/kg Every 12 hrs)
<1,000	10	10
1,001–1,250	10–20	10
1,251–1,500	20–30	10–15
1,501–1,800	30	15
1,801–2,500	30–40	15–20

Total parenteral nutrition (TPN)

Used instead of enteral feedings

Infant is ill

During feeding advance to allow adequate nutrition without overloading gut

Should be started as soon as prolonged IV nutrition is anticipated

Begin right after birth for infants <1,200 g

Composition

Begin with total ml/kg allocated to TPN, order lipid infusion 1st

IV fat emulsion = 20% intralipid

Wt <1,000 g, start at 0.5 g/kg & advance by 0.5–1.0 g/kg/d to maximum of 3 g/kg/d

Wt >1,000 g, start at 1 g/kg/d & advance by 1 g/kg to maximum of 3 g/kg/d

Determine amino acid concentration

Amino acid solution = TrophAmine

Start at 2 g/kg/d & advance by 0.5–1 g/kg to maximum of 4–4.5 g/kg/d

Determine glucose infusion rate

Begin with 4–6 mg glucose/kg/min

Advance by 1–2 mg glucose/kg/min to maximum 11–12 mg glucose/kg/min

TPN also contains vitamin & trace minerals

Measure serum electrolytes, lipids, ALT, AST weekly

Urine glucose should be checked if there is a suggestion of hyperglycemia

Parenteral nutrition can begin at admission, esp. for infants <1,250 g, using a standard PN that has no added electrolytes or vitamin (to increase shelf life)

Neurology

Intraventricular–periventricular hemorrhage (IVH)

Common problem, esp. in infants <32-wk gestation
Most are mild
Exact etiology unknown
May be associated with shifts in BP
May follow large pneumothorax
Associated with more severe overall illness
Clinical signs
Often silent
Severe cases: signs of acute blood loss, szs, change in fontanel
Dx
Head US examination
Infants <32 wks screened
Days 1–2 for most immature infants
Days 7–10 for stable infants
Repeat at days 10, 30, & q30d
Treatment
Primarily supportive, prevention is important
Posthemorrhagic hydrocephalus may occur in severe cases
May require repetitive lumbar punctures to relieve pressure
May require shunt for long-term treatment
Prognosis
Overall positive in milder cases
Guarded with more severe cases
Intraparenchymal hemorrhage, early neurologic signs

Seizures

Distinguish from jitteriness
Szs do not extinguish with holding
Often subtle or incomplete in neonates
Lip smacking
Abnormal gaze
Etiology
Hypoxic ischemic injury
Usually tonic
Occur 12–24 hrs after injury in global injury
May occur early with acute brief injury
IVH (premature)
Usually tonic
Trauma/CNS hemorrhage
Stroke
Usually unilateral clonic
Infxn/meningitis
CNS malformations
Vascular malformation
Metabolic dz
Organic acidemia, urea cycle defect
Electrolyte abnormalities
HypoCa, hyponatremia
Hypoglycemia
Pyridoxine deficiency
Evaluation
Head US, MRI when avail., CT rarely needed, poses long-term risk, CBC w/diff, ABGs, electrolytes, glucose, calcium, ammonia
Treatment

Phenobarbital
Load with10–20 mg/kg
Maintain with 2–5 mg/kg/d
Therapeutic level = 20–40 mcg/ml
Fosphenytoin
Load 10 mg/kg
Infrequently used
Lorazepam

Birth Depression

Consider *Therapeutic Hypothermia* for infants ≥35 wks with concern for acute intrapartum hypoxic event. Remember that the therapy is based on concern—use of it does not indicate that an intrapartum event definitely occurred.

Eligibility criteria to be considered for cooling may vary locally—these are general criteria

Usually must fulfill all 3 criteria (A + B + C)

Evaluate in a timely manner to initiate cooling **as soon as possible, usually within 6 hrs after birth**

In some centers, an US or an EEG/aEEG is done prior to the commencement of hypothermia

A. Infants ≥35-wks gestational age

B. Any *one* of the following:

(1) Critical event prior to delivery such as uterine rupture, profound bradycardia, or cord prolapse
(2) Apgar score of ≤5 at 10 min of life
(3) Prolonged resuscitation at birth: Need for chest compressions and/or intubation and/or mask ventilation at 10 min
(4) Severe acidosis: pH ≤7.1 from cord or pt blood gas within 60 min of birth
(5) Abnormal base excess: ≤−10 mmol/l from cord gas or pt blood gas within 60 min of birth

C. Any *one* of the following:

(1) Seizure or any clinical event concerning for seizure
(2) Neonatal encephalopathy (defined as the presence of abnormal neurologic behavior). Use of a standardized scale is desirable.

Might consider turning warmer off during resuscitation

STOPPING RESUSCITATIVE EFFORTS

If, after 10 min of properly performed resuscitative efforts with good chest rise, the HR still remains undetectable by ECG, it is reasonable to stop efforts to resuscitate

The benefits & risks of continuing resuscitation, including availability of therapeutic hypothermia, must be weighed when considering whether to continue efforts

Discussion with the parents before birth should focus in part on parental wishes that can aid in these decisions

Apnea of prematurity

Common at <32 wks
May occur up to 35–36 wks
Typical onset days 2–3
Dx of exclusion
Differential dx
Atelectasis, sepsis, hypoglycemia, hypoCa, IVH
Seizures
Rare as sole presentation of seizures
Opioids
Electrolyte abnormalities
Airway obstruction
Vagal stimuli (indwelling feeding tube, moving ET tube)
Evaluation
CBC w/diff, platelets, glucose level, electrolytes, calcium, chest radiograph, head US screen
Treatment
Caffeine
Load with 20 mg/kg IV
Maintenance 5–10 mg/kg q24h
No levels need to be drawn
Oxygen supplementation
Nasal cannula
CPAP or high-flow nasal cannula
Intubation (rarely)

Periodic breathing

Up to 10 sec of apnea, followed by normal respiration
Occurs in many preterm infants
Low frequency after 36-wks gestational age
No specific therapy

Agitation

Sedation should be used with caution in newborns

Term infants

Phenobarbital

Benzodiazepines (diazepam, lorazepam)

Lorazepam may cause myoclonus in premature infants

Morphine or fentanyl is commonly used, particularity if there is a component of pain

Monitor for respiratory depression

Pain

Infants feel pain, at least after 22–24 wks of gestation

Oral sucrose can provide pain relief in mild instances

Ensure adequate analgesia for noxious, or painful procedures, or intervention

Assessment scales are used to guide therapy

GASTROENTEROLOGY

Feeding intolerance

Common problem in premature infants
Often occurs during feeding advance
Infant is otherwise apparently normal
Clinical signs
Increased gastric residuals, abd distention, distended bowel loops, no signs of ileus, difficult to initially distinguish from necrotizing enterocolitis (NEC)
Evaluation
Hold feedings
Radiograph may be helpful in ruling out pathologic condition
Observation for several hours
Sometimes progresses to more extensive evaluation to r/o NEC

Necrotizing enterocolitis

Idiopathic intestinal necrosis

Associated with prematurity

Presumed to be the result of bacterial action on an already compromised bowel

Most common in terminal ileum & ascending colon

Most suspected cases ultimately not confirmed

Clinical signs

Abd distention, tenderness, hematochezia, gastric aspirates before feedings, ileus, metabolic acidosis

Nonspecific signs

Apnea & bradycardia, shock

Dx

Radiographic

Pneumatosis intestinalis—gas bubbles in bowel walls

Air in biliary tree, pneumoperitoneum

Surgical

Peritonitis, bowel necrosis, perforation

Differential dx

Sepsis

Intra-abd catastrophes (midgut volvulus, etc.)

Infectious enterocolitis (rare)

Metabolic dz

Feeding intolerance

Allergic colitis (see below)

Evaluation

Should be done whenever there is heightened suspicion

Feedings should be held

Physical examination

KUB & left lateral decubitus. Repeat q6–8h as long as suspicion remains

CBC w/diff, blood cxs, & electrolytes

Sepsis evaluation

ABG if indicated

Surgical consultation if suspicion high or dx confirmed

Treatment—confirmed or clinically suspicious cases
The majority of cases are treated without need for surgery
Stop all enteral feedings for 14 days
Replogle tube for GI decompression
Broad-spectrum abx
Include coverage for potential anaerobic organisms
Repeat radiographs until stable
If perforation or clinical deterioration occurs—surgery is indicated
There is risk of intestinal stricture presenting weeks after acute course

HEMATOLOGY

Mean hematocrit at birth is 51% at term, lower in premature infants
Circulating blood vol is approx. 80 ml/kg

Anemia (Hct <30)

Cause

Blood loss

Fetomaternal, phlebotomy, hemorrhage

Hemolytic dz

Immune mediated

Blood-type incompatibilities

Nonimmune

Red cell defects (spherocytosis, etc.), enzyme deficiencies, G6PD, pyruvate kinase

Congenital infxns

Cytomegalovirus (CMV), rubella, parvovirus 19

Anemia of prematurity

Low reticulocytosis, phlebotomy, rapid growth

Evaluation

Smear, reticulocyte count, central hematocrit, type & Coombs
Kleihauer/Betke testing on maternal blood
Head US or other studies to locate bleeding may be needed

Treatment

DOL# 1–3: Transfuse for Hct <35–40 if

Hypotensive

Moderate or severe respiratory dz

DOL >3: transfuse if Hct <35 if

Sepsis, oxygen dependent, still requires ventilator support, tachycardic, tachypneic without other cause, poor wt gain despite adequate intake

Polycythemia

Hematocrit >65 with sx, >70 without
Confirm with central hematocrit
Higher risk in
Small for gestational age (SGA), infant of a diabetic mother (IDM), recipient twin in twin–twin transfusion
Clinical signs
Hypoglycemia, hypoCa
Abnormal neurologic examination
Treatment
Partial exchange transfusion to reduce Hct to 50–55
May reverse minor sx but will not change neurologic outcome

Hemorrhagic disease of the newborn

Coagulopathy & hemorrhage due to low vitamin K levels
Usually presents with severe & life-threatening GI hemorrhage at 3 days
May present at 1–2 wks, usually with acute CNS hemorrhage
Treatment
Preventative, 1-mg vitamin K IM at birth

Hyperbilirubinemia

Principles

Physiologic jaundice is common in newborns

Accelerated red cell destruction

Immature excretion pathways

Normally transient

Peaks on days 3–5, may decline slowly over weeks

Most bilirubin is bound to albumin in serum

Risk of bilirubin neurotoxicity exists from unconjugated bilirubin

Bilirubin not bound to albumin

Abnormal or injured blood–brain barrier

Pathologic causes can result in dangerously high levels

Hemolysis, enzyme deficiencies, defects in conjugation & excretion, metabolic disorders, hypothyroidism

Markedly elevated levels are dangerous

Otherwise, healthy term infants are at low risk with peak levels <22–25 mg/dl

Danger level in preterm not well established

Often considered to be level equal to 1% of birthweight (e.g., 1,400 g birthweight – danger level is considered to be 14)

Danger increased at lower levels when hemolysis or illness present

Monitoring

All term & late preterm infants should have screening level at 24–36 hrs

American Academy of Pediatrics (AAP) guidelines suggest repeat monitoring, when to start therapy (American Academy of Pediatrics Subcommittee on Hyperbilirubinemia. *Pediatrics.* 2004;114:297–316)

Premature infants should have screening level at 12–24 hrs

Base decisions on repeat monitoring on level, rate of rise, postnatal age

Goal: prevent serum concentration from exceeding determined danger level

Unusually high levels should prompt evaluation for pathologic cause

Type & Coombs, CBC, reticulocyte count, urine reducing substances, thyroid hormone levels

Treatment

Ensure normal hydration status

Phototherapy

Begin at levels about ½ of danger level

Efficacy depends on:

Intensity, wavelength of light (blue), exposed surface area, duration of therapy

Stop when level has dropped below trigger level

Level normally rebounds 0.5–1.0 mg/dl within 12–18 hrs

Exchange transfusion

Requires large IV or UVC

May be done with arterial & venous access

A volume twice the circulating blood volume is exchanged in aliquots

Level usually decreases by 50% immediately after procedure

Evaluation of the asymptomatic infant at risk for sepsis and meningitis

Newly born infants at risk for sepsis are initially asymptomatic

Evaluation done on the basis of historical factors

Known maternal GBS colonization, without treatment during labor (4 hrs)

Maternal fever >100.4°F (38.5°C)

Maternal chorioamnionitis

Prematurity <35 wks

Previous child with GBS dz—much higher risk

White cell count at birth of minimal value—better obtained at 6–12 hrs

Abnormal white cell count with elevated immature: total neutrophil count raises concern

Therapy

Indicated empirically for maternal fever >101°F, maternal chorioamnionitis, abnormal cell count, sx

Broad-spectrum abx

Ampicillin, gentamicin

Primary organisms are GBS, *Escherichia coli*, rarely *Listeria*

Alter choices based on local flora

Bacterial sepsis

A concern in any infant with consistent signs of:

Resp distress, hemodynamic instability, abnormal neurologic findings, temp instability, other signs without apparent cause

Evaluation

CBC w/diff, blood cx, CSF examination

May delay until decision to treat for full course

CSF Findings in Nonmeningitic High-Risk Infants				
	Preterm	Mean	Term	Mean
WBC (±SD)	0–25	9	0–22	8.2
% Polymorphonuclear leukocytes	57		61	
Protein (range)	65–150	115	20–170	90
Glucose (range)	22–63	50	34–119	52

CSF in the newborn may normally have 600–900 RBC/mm^3.

Therapy

Warranted when concern arises

Can be stopped after 48 hrs if evaluation negative

Likely organisms change with postnatal age

First several days—perinatal acquisition likely

Ampicillin/gentamicin as above

Late in 1st week to 3 wks of age

Add coverage for coagulase—*Staphylococcus* with indwelling lines/appliances

Consider coverage for *Staphylococcus aureus,* local flora

Hepatitis B prophylaxis

First dose of hepatitis B vaccine

Term infants—in 1st day

Premature infants given at 2-kg wt

If mother is known HbsAg (+), give hepatitis B immune globulin 0.5 ml in the 1st 12 hrs of life, along with the vaccine

Ophthalmia neonatorum (neonatal conjunctivitis)

Microbial causes include *Neisseria gonorrhoeae, Chlamydia, Staphylococcus*

All infants should receive eye ppx at birth (erythromycin ointment)

Congenital infections

CMV, rubella, other viruses

Clinical signs

Petechiae, hepatosplenomegaly, jaundice (conjugated), microcephaly, SGA, chorioretinitis, intracranial calcifications

Later onset cases of CMV may result from transmission via breast milk

Human immunodeficiency virus (HIV)

Most infected children are asymptomatic in the neonatal period

Lab dx is difficult because of persistence of maternal anti-HIV antibody

Viral cx & antigen p24 detection are useful

Antiretroviral therapy begun at birth for at-risk infants

Syndromes and Associations

VATER (VACTERL): Vertebral anomalies, **A**nal atresia, **C**ardiac defects (VSD or other), **TE** (tracheoesophageal) fistula, **R**enal dysplasia, **L**imb deformities (radial & other digital abnormalities).

Beckwith–Wiedemann syndrome. Macrosomia. Hypoglycemia macroglossia. May present difficulties eating or breathing visceromegaly, including pancreatic hyperplasia with excess islet cells (hence hypoglycemia)

Omphalocele & other abd defects.

Trisomy 21 (Down syndrome). 1:1,000 births hypotonia, brachycephaly, upslanting eyes, epicanthal folds, protruding tongue, redundant skin on neck, small ears □3 cm) Simian crease, short metacarpals, 5th finger clinodactyly. Increased space between 1st & 2nd toes, AV canal defect, VSD, PDA.

Trisomy 18 (Edward syndrome). 1:3,000 births. Growth deficiency, prominent occiput, low set ears, short palpebral fissures, clenched hand, overlapping index/3d, 4th/5th fingers, nail hypoplasia, short hallux. Rocker bottom feet. Short sternum, VSD, ASD, PDA umbilical hernia.

Trisomy 13 (Patau syndrome). 1:6,000 births holoprosencephaly, microcephaly, sloping forehead, microphthalmia, scalp defect, cleft lip/palate, abnormal/low set ears. Simian crease, polydactyly, PDA, VSD, & dextroposition. Single umbilical artery.

Antibiotics: Neonatal Dosing				
		Interval by Postconceptual Age or Weight		
Antibiotic	**Dose (Per Dose)**	**<30 wks**	**30–35 wks**	**36–42 wks**
Ampicillin	50–150 mg/kg	q12h q8h > 28 days	q12h q8h > 14 days	q12h q8h > 7 days
Gentamicin	3 mg/kg 4 mg/kg	<35 wks q24–36h		≥35 wks q24h
Cefotaxime	50 mg/kg	≤7 days q12h qh8 > 28 days	>7 days q12h q8h > 14 days	q12h q8h > 7 days
Clindamycin	7.5 mg/kg	≤29 wks q12h q6h > 1 mo	≥29 wks q8h	>29 wks
Amphotericin B	0.25–0.5 initial	q24–48h 0.5–1.0 mg/kg	<37 wks	≥38 wks
	Term		**Preterm**	
Azidothymidine (AZT)	2 mg/kg PO q6h 1.3 mg/kg IV		≤2 wks 1.5 mg/kg/dose PO q12h >2 wks 3 mg/kg/dose PO q8h	
Acyclovir	20 mg/kg q8h for 14–21 days		20 mg/kg q8h for 14–21 days	
Vancomycin	≤7 days < 1.2 kg 1.2–2 kg >2 kg >7 days ≤ 1.2 kg 1.2–2 kg >2 kg		15 mg/kg IV q24h 10 mg/kg IV q2h 15 mg/kg IV q2h 15 mg/kg IV q24h 15 mg/kg IV q12h 10 mg/kg IV q8h	

PEDIATRIC INTENSIVE CARE

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Key Principles for Pediatric Critical Care

Normal physiology, anatomy, & vital signs all change with age
Dosing of drugs, fluids, electrolytes is typically based on wt or body surface area (BSA)

Normal Physiologic Values

Age (yrs)	Weight (kg)	Systolic Blood Pressure	Heart Rate	Respiratory Rate	ETT Size (Cuffed)	ETT Depth (cm)
Newborn	3.5	60	100–180	30–40	3–3.5	9
6 mo	6	70	100–160		3.5–4.0	11
1	10	72			4	12
2	12	74	80–110	25–32	4.5	13
3	14	76			4.5	14
4	16	78	70–110		5	
5	18	80	65–110	22–28	5	15
6	20	82			5.5	
7	22	84			5.5	16
8	24	86			6	
9	26	88			6	18
10	28	90–120		20–24	6.5	

ETT, endotracheal tube.

Quick Calculations

Wt (kg) = 8 + 2 (age in yrs)
BSA (m^2) = [ht(cm) × wt (kg)/3,600]^{½}
Minimum acceptable SBP (systolic blood pressure) = 70 + 2 (age in yrs)
ETT (uncuffed) = 4 + (age in yrs/4)
If using a cuffed ETT, select 1 that is a half size smaller
ETT depth ≈ 3 × (ETT diameter)
Maintenance fluids
1–10 kg = 4 ml/kg/hr
11–20 kg = above plus 2 ml/kg/hr
>20 kg = above plus 1 ml/kg/hr
That is, 18 kg = (4 × 10 kg) + (2 × 8 kg) = 56 ml/hr
Fluid bolus = 20 ml/kg normal saline (NS) or lactated ringer's (LR)

Common Problems Encountered in Pediatric ICU

Shock

Tissue perfusion inadequate to meet metabolic needs

Phases of shock:

Compensated shock: tachycardia, vasoconstriction to maintain CO & BP (CO = stroke volume × HR)

Decompensated shock: hypotension AND weak central pulses, decreased UOP, altered mental status, metabolic acidosis, tachypnea

Types of shock:

Hypovolemic

Most common cause in pediatrics

Diminished intravascular volume; decreased preload

Dehydration, sepsis, blood loss, diarrhea, vomiting, 3rd spacing of fluids

Signs of dehydration: tachycardia, decreased UOP, tachypnea, decreased level of consciousness

Management: Intravascular volume repletion: isotonic crystalloids 10–20 ml/kg; assess & repeat fluid administration if required

Abx as soon as possible if suspected infxn

Cardiogenic

Various etiologies including myocarditis, cardiomyopathy, tamponade, arrhythmias, congenital heart dz, toxins

Diagnostic approaches: ECG, CXR, echocardiography, check electrolytes

Management:

Treat arrhythmia; inotropic support (dobutamine, dopamine, epinephrine)

Neurogenic

Hypotension with bradycardia. Weakness & flaccidity

Diagnostic approaches: C-spine films, CT/MRI

Management:

Immobilization, intravascular volume expansion, vasopressors

Anaphylactic

Tachycardia, tachypnea, bronchospasm, flushing, hypotension, urticaria

Management:

Epinephrine, IV fluid bolus, corticosteroids, antihistamines (H_1 & H_2)

Sepsis (also see Chapter 23 for definition & management of adult sepsis)

SIRS/septic shock

At least 2 of the following, 1 of which must be altered temp or WBC

Core temp >38.5°C or <36°C

Tachycardia (HR >2 SD above nl for age) controlled for external stimulus, pharmacologic stimulus, painful stimulus

Mean RR >2 SD above normal for age

Elevated or depressed WBC or >10% bands

Sepsis: sx of SIRS in the presence of proven or suspected infxn

Severe sepsis: sepsis with evidence of end-organ dysfunction

Septic shock: sepsis & CV organ dysfunction (sustained hypotension despite sufficient intravascular volume resuscitation)

Management:

Includes early & aggressive fluid resuscitation (20 ml/kg aliquots up to 60 ml/kg total)

Early institution of broad-spectrum abx

Vasopressor and/or inotropic support if fluid resuscitation not sufficient

Diabetic ketoacidosis (DKA)

Serum glucose >200 mg/dl with ketonemia/ketonuria & pH <7.30; accompanied by electrolyte abnormalities & hypovolemia

pH reflective of insulin deficiency; hyperglycemia reflective of hydration status

Cerebral edema #1 cause of mortality. Incidence of DKA: 1%, mortality: 20%, permanent neurologic deficit: 25% associated with resuscitation of >4 $l/m^2/24$ h

Avoid overly vigorous correction of dehydration & hyperglycemia

Artifactual hyponatremia, total body hypokalemia with initial normal/elevated serum K level, hypophosphatemia

Management:

Aimed at correction of hyperglycemia, acidosis, electrolyte deficits, & dehydration

Electrolyte & fluid requirements vary greatly

Guide to fluid resuscitation: initial isotonic fluid bolus (10 ml/kg) to correct impending shock. Correct remaining deficit over 36–48 hrs. Use normal or 0.45% NS. NS if Na remains low after glucose falls or if concerns about cerebral edema. Add K+ after 1st void (Kphos + Kacetate/KCl, avoid phos if Ca is low)

Insulin 0.1 U/kg/hr. Goal: decrease serum glucose 50–100 mg/dl/hr

When blood glucose (BG) is between 250 & 300 or if it falls >100 mg/dl/hr, add dextrose & titrate dextrose to maintain BG >100 to keep insulin infusing

Avoid bicarbonate

Monitor: BG q1h; venous blood gas, electrolytes, Ca, phos q2h until stable then q4h–q6h; urine ketones/glc. Consider ECG if electrolyte abnormalities

When pH >7.3 & BG <300, start PO intake & change to SQ insulin

Status asthmaticus

Accessory muscles, dyspnea, wheezing, pulsus paradoxus

Monitor O_2 sats & oxygenation, peak expiratory flow, hypercarbia (severe dz)

Management:

Supplemental O_2

Fluids: correct dehydration

Corticosteroids: methylprednisolone 2 mg/kg IV; then 0.5–1 mg/kg IV q6h–q12h (max 120 mg/dose). Oral prednisone for less severe cases

Inhaled β-agonists: continuous nebulized albuterol 0.15–0.5 mg/kg/hr = 10–20 mg/hr. Sinus tachycardia common but rarely problematic

IV β-agonists: terbutaline 10 μg/kg load over 10 min; then 0.1–10 μg/kg/min. Monitor for hypokalemia & supraventricular tachycardia (SVT) (avoid adenosine if SVT as can worsen bronchospasm). ECG, CK/troponin, electrolytes q12h

Consider:

Anticholinergic: ipratropium 125–500 μg neb/4–8 puffs MDI q4h–q6h

Magnesium sulfate 40 mg/kg/dose over 30 min, give fluid bolus prior to administration to prevent hypotension

Heliox decreases airflow resistance in small airways, cannot be used with hypoxemic patients given low FiO_2 with 70/30 or 80/20 mixture

Abx: usually viral or allergic provocation but might be bacterial (esp. mycoplasma)

Noninvasive ventilation

Mechanical ventilation: <1%. Refractory hypoxemia, hypercarbia, acidosis not responsive to pharmacotherapy. Severely depressed mental status

Ventilator management: avoid hyperinflation & air trapping. Dz of expiratory obstruction. Low positive end-expiratory pressure (PEEP), long expiratory time, slow rate. Adjust MV to keep arterial pH >7.25

Continue inhaled (& IV if used) β-agonists while intubated

Sedatives: ketamine continuous infusion 1 mg/kg/hr (side effect: increased secretions)

Bronchiolitis

Bronchiolar inflammation with obstruction of small airways

Peak incidence 12 mo (3 mo to 3 yrs)

High risk for complications: premature & ex-premature, congenital heart dz, bronchopulmonary dysplasia, immunodeficient, cystic fibrosis, age <3 mo

Respiratory syncytial virus most frequent cause

Management:

Hydration

Oxygenation: pulmonary toilet; nasal prongs; continuous positive airway pressure (CPAP); mechanical ventilation

Consider inhaled bronchodilator trial (albuterol, salbutamol, or racemic epinephrine): discontinue if no change or worsening

Treat secondary bacterial infxn if applicable

Acute respiratory distress syndrome (ARDS) (ARDS Definition Taskforce; Ranieri VM, et al. *JAMA*. 2012;307(23):2526–2533; also see Chapter 19)

Pt with pneumonia, sepsis, bacteremia, trauma, burns, pancreatitis, aspiration pneumonitis, fat embolism, near drowning, massive blood transfusion

High risk of mortality

Berlin Definition (ARDS Definition Taskforce):

Occurs within a week of insult or worsening respiratory sx

Bilateral pulmonary opacities not related to cardiac failure or fluid overload

Mild: 200 mm Hg < P_aO_2/F_iO_2 ≤300 mm Hg with PEEP/CPAP ≥5 cm H_2O

Moderate: 100 mm Hg < P_aO_2/F_iO_2 ≤200 mm Hg with PEEP ≥5 cm H_2O

Severe: ≤100 mm Hg with PEEP ≥5 cm H_2O

Management:

Early arterial access to evaluate & follow dz (P_aO_2/F_iO_2 & oxygenation index [OI])

CPAP/BiPAP/intubation for alveolar recruitment & respiratory failure

Lung protective ventilation strategies:

High PEEP & titrate to achieve F_iO_2 < 0.6% & S_pO_2 >88%, tidal volumes (Vt) 6 ml/kg & plateau pressure to <30 cm H_2O

Permissive hypercapnia unless contraindicated (i.e., pulmonary HTN)

Provide adequate sedation & analgesia, consider neuromuscular blockade

Optimize hemodynamics, maintain euvolemia

Consider high frequency oscillatory ventilation (HFOV) if high mean airway pressure & poor oxygenation; consider prone positioning

Extracorporeal membrane oxygenation (ECMO) if prior measures fail

Extracorporeal membrane oxygenation (see Chapter 21)

Venovenous or Venoarterial

Correct severe hypercapnia & hypoxemia and/or provide hemodynamic support

Allows lower FiO_2 & ventilator pressure thus decreasing pulmonary injury

Criteria for use:

Potentially reversible

Lack of response to conventional measures

Respiratory failure:

OI >40 [$OI = (FiO_2 \times MAP/P_aO_2)$]

P_aO_2 <50 mm Hg despite high FiO_2 & high ventilator pressure (PEEP & MAP)

CV failure:

During CPR (E-CPR)

Severe myocardial dysfunction (after cardiac surgery, myocarditis)

Anticoagulation with heparin to reduce clotting of circuits & potential thrombotic emboli, may require AT3 (esp. infants)

Complications: coagulopathy, intracranial hemorrhage, neurologic deficits, seizure

Acute chest syndrome

Pt with sickle cell dz

New or rapidly progressive infiltrate on CXR, fever, cough, chest pain (pleuritic), tachypnea, hypoxemia; mortality 25%. Can progress to ARDS

Usually provoked by infxn and/or pulmonary vaso-occlusion

Diagnostic tests: CBC, CXR, retic count, ABG, type & screen, blood/respiratory cx.

Management:

Generous but titrated hydration
Maintain adequate oxygenation to prevent increased sickling, supplemental O_2. Goal P_aO_2 > 80–100; S_aO_2 > 95%
Incentive spirometry & ambulation: decrease atelectasis & V/Q mismatch
Pulmonary toilet
Consider albuterol therapy
Analgesia: opioid-based, titrate. Monitor RR/effort
Consider CPAP, BIPAP, mechanical ventilation
Broad-spectrum Abx (including azithromycin)
Transfuse RBCs: decrease amount of sickled Hb (HgbS). Increases O_2-carrying capacity. Avoid hyperviscosity. Goal Hb >10 gm/dl
Partial exchange transfusion for severe or rapidly progressive dz
Consider inhaled nitric oxide (iNO), ECMO in severe cases

Tumor lysis syndrome

Acute leukemia, high-grade non-Hodgkin lymphoma (Burkitt's lymphoma), less commonly in solid tumors (neuroblastoma, hepatoblastoma)
Metabolic abnormality due to rapid lysis of tumor cells
Usually 12–72 hrs after initiation of chemotherapy (steroids, hormones, radiation might also trigger)
Characterized by elevated K+, phos, & uric acid. Low Ca++; acidosis

Management:
Hydration
Allopurinol or rasburicase (in severe cases)
Alkalinization of urine
Restrict K+ & phos, replace Ca only if symptomatic
Monitor K+, Ca, phos, uric acid q6h

Syndrome of inappropriate secretion of antidiuretic hormone (SIADH)

Pt with pneumonia, CNS disorders, cirrhosis, CHF, nephrotic syndrome, taking certain medications
Excessive antidiuretic hormone (ADH) secretion
Elevated total body water (TBW), hyponatremia, low serum osm (<280 mOsm/l), high urine osm (>500 mOsm/l)
Manage with fluid restriction
If severe hyponatremia or seizures occur, correct Na rapidly to 120 mEq/l (use 3% NS 1–2 ml/kg aliquots or consider infusion); then correct slowly by 0.5 mEq/l/hr to avoid central pontine myelinolysis

Cerebral salt wasting (CSW)

Pt with brain injury or brain tumor
Possibly due to abnormal secretion of natriuretic peptides
Diminished TBW, low serum Na, elevated UOP, elevated U_{Na}

Management:
Directed at replacing fluid & Na deficit
Consider fludrocortisone 0.2–0.4 mg/kg/d

Central Diabetes Insipidus (DI)

Pt with CNS dz/trauma/surgery
Impaired ability to concentrate urine due to lack of ADH
Elevated Na, elevated serum osm (>300 mOsm/l), low urine osm, low urine specific gravity (<1.005), elevated UOP (>4 ml/kg/hr)

Management:
Directed at replacing deficits & hormone replacement
Treat shock; then maintenance fluid + deficit + ongoing losses
Correct Na slowly over 48 hrs
Vasopressin (AVP) 0.5 mU/kg/hr (max 10 mU/kg/hr), titrate to UOP < 2 ml/kg/hr
Monitor UOP, Na, UOsm

Differences in Clinical Findings and Laboratory Results in Patients with Diabetes Insipidus, Syndrome of Inappropriate ADH Secretion, and Cerebral Salt Wasting			
	DI (central)	SIADH	CSW
TBW	Low	High	Low
UOP (cc/kg/hr)	>2–4	<0.5	>2–4
Serum Na	145–155	120–130	120–130
Serum Osm	>300 mOsm/l	<280 mOsm/l	Low
Urine Osm	Low	>500 mOsm/l	High
Urine specific gravity	<1.001	>1.025	<1.005

DI, diabetes insipidus; SIADH, syndrome of inappropriate antidiuretic hormone secretion; CSW, cerebral salt wasting; TBW, total body water; UOP, urine output.

Status Epilepticus (see Chapter 30)

Epilepsy, meningitis, traumatic brain injury, hypoxic ischemic encephalopathy

Single seizure or multiple seizures without return to baseline lasting >30 min

Management:

Antiepileptics:

If no IV access—diazepam or intranasal midazolam

IV access: Lorazepam IV × 2 doses every 5 min × 2, then fosphenytoin (or phenobarbital for infants), consider levetiracetam

Consider midazolam infusion or pentobarbital coma for refractory dz

Consider high-dose abx, acyclovir

Consider CT or MRI

Consider continuous EEG monitoring

Burns (see Chapter 44)

Pediatric Trauma

Leading cause of death in children >1 yo
Higher incidence of head trauma given large head-to-body ratio
May have little external evidence of internal injury
Greater risk of hypothermia due to large surface area-to-mass ratio
Type of trauma related to age
Infants: nonaccidental, home injury
1–5 yo: falls
Elementary school age: bicycle or car vs. pedestrian
Adolescent: motor vehicle crash, violent crime

Management:
Treat ABCs 1st
O_2, volume, consider PRBC
Vascular access can be more challenging than in adults. Consider intraosseous access

Head injury

High mortality. Diffuse axonal injury more common in pediatrics (clinical sx often out of proportion with radiologic findings). Skull fx more common than in adults
Nonaccidental trauma: always consider, esp if hx inconsistent with injuries
Perineal injuries, subdural hematomas, retinal hemorrhages, long bone fx, multiple fx of different age, burns, unusual bruising, repeated trauma
Full skeletal survey in children <2 yo. Ophthalmology evaluation for retinal hemorrhages
Child protective services/police involvement required

Management goals:
Rapidly treat intracranial HTN (mannitol, hypertonic saline, consider hyperventilation acutely, CSF drainage, consider barbiturate therapy, head positioning), ensure adequate oxygenation, maintain cerebral perfusion pressure (CPP) (avoid hypotension, treat elevated ICP), normothermia. Treat/prevent hypoxia, pain, fever, hypercarbia, seizure, hypo/hyperglycemia

Spinal cord injury and vertebral injury

Often difficult to diagnose radiographically

Often unique injury patterns due to developmental transition and/or pediatric dz/syndromes

Spinal immobilization if any concern. Maintain adequate perfusion & oxygenation

High index of suspicion. Timely dx & treatment

Spinal cord injury without radiologic abnormality. Pediatric spinal column more elastic than spinal cord. Obtain CT/MRI, proper immobilization, neurosurgical evaluation

Thoracic injury

Second to head trauma in mortality

Compliant mediastinum. Injury on 1 side can affect other

Pulmonary contusion: might not be seen on initial x-rays. Can progress to ARDS

Abdominal injury

Spleen (most common intra-abd organ injured), liver, kidney, pancreas, bowel injuries often managed nonoperatively with bed rest & close monitoring unless hemodynamically unstable and/or significant blood loss

Orthopedic injury

Growth plates can make radiologic dx more challenging

Consult orthopedics/vascular, esp. if neurologic or vascular compromise

Pediatric pain management

Pediatric differences: cognitive ability, communicative style, respiratory mechanics & airway anatomy, pharmacologic metabolism

Pain scales based on age

Wong–Baker (FACES) (for age 5–6 years) (see Chapter 8)

Number scale 1–10 (for age >7 years)

Pharmacologic modalities: (see page 33-7 for typical dosing)

Acetaminophen: Most commonly used drug for pediatric analgesia

NSAIDs: Use in >6-mo age. Side effects include GI irritation, plt dysfunction, acute kidney injury, closure of patent ductus arteriosus. Aspirin contraindicated in varicella/influenza—risk of Reye syndrome

Opioids: for moderate to severe pain not responsive to above medications. Cardiorespiratory depressive effects may be greater in children, esp. infants <3 mo, ex-prematures <60 wks postgestational age, children with airway anomalies, cardiac dz, neurologic dz, renal dz

Adjunctive analgesics: consider anxiolytics, antidepressants, anticonvulsants (gabapentin), NMDA receptor antagonist, neuroleptics, α_2 agonist (clonidine, dexmedetomidine)

Regional anesthetic blocks & catheters (pain/anesthesia service)

Local anesthetic cream: apply to intact skin 30–45 min prior to procedure. Avoid in infants (risk of methemoglobinemia)

Pt-controlled analgesia: requires pt/parental understanding, willingness, physical ability, & appropriate nursing/physician supervision; nurse-controlled analgesia is an alternative

Pediatric sedation

Practitioner must be familiar with & certified to administer drugs, monitoring depth of sedation/anesthesia, trained in resuscitation & airway management

Usually performed with reversible sedatives (benzodiazepines & opioids)

Hx & physical examination, airway evaluation prior to sedation

Obtain informed pt/parental consent; follow institutional guidelines

Monitoring requirements: O_2 Sat, EKG, BP, adequacy of respiration, $ETCO_2$

Must be available: resuscitation drugs (code drugs, reversal agents, intubation drugs), O_2 & positive pressure delivery system (e.g., bag valve mask), suction, intubation equipment (SOAP = suction, oxygen, airway, pharmacy)

Medications typically delivered IV, IM, PO, PR. Acquire IV access if feasible

Fasting guidelines:

Clear liquids (apple juice, water): 2 hrs

Breast milk: 4 hrs

Formula/juice (with pulp): 6 hrs

Solids/particulates/fatty meals/milk: 8 hrs

Procedures (also see Chapters 45 & 46)

Drug and Blood Product Dosing (Pediatrics)

Note: ***Drug dosing should be tailored to individual clinical scenarios.*** Dosages outside these guidelines might be clinically appropriate

Analgesics	IV Dose (max)
Fentanyl	0.5–2 µg/kg IV or 0.5–2 µg/kg/hr IV gtt
Morphine	0.05–0.1 mg/kg IV or 0.05–0.1 mg/kg/hr IV gtt
Hydromorphone	0.015 mg/kg IV
Ketorolac	0.25–0.5 mg/kg (30 mg) IV
Flumazenil	0.01 mg/kg (0.2 mg) IV
Naloxone	0.1 mg/kg IV
Ibuprofen	10 mg/kg q6h PO (40 mg/kg/d)
Acetaminophen	10–15 mg/kg q4h PO (75 mg/kg/d)

Anticonvulsants	IV Dose
Diazepam	0.1–0.2 mg/kg IV
Lorazepam	0.1 mg/kg (max 4 mg) IV; repeat 5 min
Fosphenytoin	20 mg PE/kg (max 1,000 mg) IV, PE = phenytoin equivalents, give over 7 min
Phenobarbital	20 mg/kg (max 1,000 mg) (load) over 20 min IV, repeat 5 mg/kg dose PRN. to max 40 mg/kg; then 2.5 mg/kg IV/PO q12h
Levetiracetam	30 mg/kg IV over 15 min, then 10–20 mg/kg/dose IV/PO q12h
Pentobarbital	Therapeutic coma: 1–5 mg/kg IV over 1–2 hrs (load); then 1 mg/kg/hr IV may ↑ to 5 mg/kg/hr to achieve burst suppression on EEG, monitor hemodynamics

Blood Products	
Albumin 5%	10 ml/kg (0.5 g/kg)
pRBC	10 ml/kg
FFP	10–15 ml/kg
Platelets	1 unit/10 kg to raise 50,000
Cryo	1 unit/10 kg

Bronchodilators	
Albuterol	Intermittent: (0.5%) <10 kg 0.25 ml INH; 10–30 kg 0.5 ml; >30 kg 1 ml q1h–q6h Continuous: 0.5 mg/kg/hr (max 20 mg/hr) INH
Ipratropium	0.25–0.5 mg INH × 3; then q4h–q6h
Racemic epinephrine (2.25%)	0.25–0.5 ml INH q1h
Terbutaline	Bolus: 10 µg/kg IV over 10 min; then 0.4–10 µg/kg/min
Magnesium sulfate	25–50 mg/kg (max 2 g) IV over 20 min

Code Resuscitation Drugs	Dose
Adenosine	0.1 mg/kg (initial max 6 mg) rapid IV; if no effect, 0.2 mg/kg (max 12 mg)
Amiodarone	5 mg/kg (max 300) IV/IO bolus; may repeat × 2
Atropine	0.02 mg/kg (min 0.1 mg/max 1 mg)
10% Calcium chloride	20 mg/kg (max 2 g) slow IV (central)
10% Calcium gluconate	100 mg/kg (max 2 g) slow IV (central)
Dextrose	D50W: 1–2 cc/kg D25W: 2–4 cc/kg: D10W: 5–10 cc/kg
Epinephrine	Cardiac arrest: IV/IO: 1:10,000 0.1 ml/kg (=10 µg/kg) (max 1 mg) q3min–q5min ETT: 1:1,000 0.1 ml/kg (100 µg/kg) Anaphylaxis: IM (1:1,000) 0.01 ml/kg (=10 µg/kg) (max 500 µg) Epi-pen 0.3 mg IM Epi-pen Jr. 0.15 mg IM
Lidocaine	1 mg/kg IV/IO/ETT (max 100 mg)
Magnesium sulfate	Torsades de pointes: 25–50 mg/kg IV/IO (max 2 g)
Sodium bicarbonate	(8.4% = 1 mEq/ml) 1 mEq/kg slow IV

Cardioversion/Defibrillation	
SVT or V tach with pulse	0.5–1 J/kg synchronized × 1; if no response, 2 J/kg
V fib or pulseless V tach	2 J/kg × 1; if no response 4 J/kg

Intubation Drugs	
Propofol	1–3 mg/kg IV
Thiopental	4–6 mg/kg IV
Ketamine	0.5–2 mg/kg IV; 3–7 mg/kg IM
Fentanyl	1–5 µg/kg IV

Neuromuscular Blockers	
Vecuronium	0.1–0.2 mg/kg IV
Rocuronium	0.6–1.2 mg/kg IV
Succinylcholine	1–2 mg/kg IV 3–4 mg/kg IM Consider atropine premed if <5 yrs

Sedatives	Dose
Midazolam	0.05–0.1 mg/kg IV or 0.05–0.1 mg/kg/hr IV gtt
Lorazepam	0.05–1 mg/kg IV/PO q4h
Propofol	25–100 µg/kg/min IV gtt (duration <12 hrs, monitor for propofol infusion syndrome)
Dexmedetomidine	0.5–2 µg/kg/hr IV gtt, consider 1 µg/kg bolus over 10 min (monitor for bradycardia, hypo- or HTN)

Steroids	Dose
Dexamethasone	0.1–0.6 mg/kg/dose (max 10 mg) IV/PO q8h Croup: 0.6 mg/kg IV/IM/PO × 1
Methylprednisolone	Load 2 mg/kg IV; then 1 mg/kg/dose IV q6h–q12h (max 120 mg)
Hydrocortisone	Stress dose 50 mg/m^2/dose IV (max 100 mg); then 20 mg/m^2 IV q8h

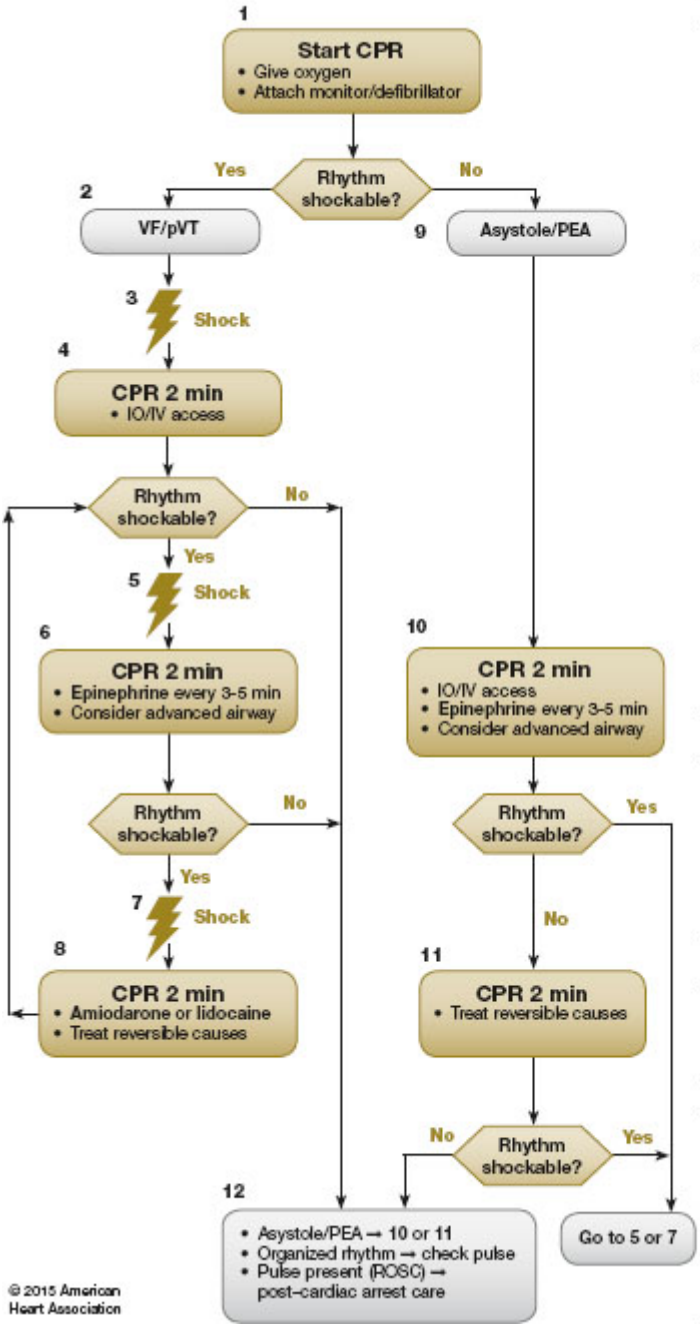
PALS (American Heart Association algorithms reused with permission from [Pediatric Advanced Life Support 2015 American Heart Association Guidelines Update for Cardiopul monary Resuscitation and Emergency Cardiovascular Care Allan R. de Caen, et al. *Circulation*. 2015;132: S526–S542]**)**

Sudden cardiac arrest in children is uncommon

Cardiac arrest usually terminal event of progressive respiratory failure or shock

Very high mortality

Pediatric Cardiac Arrest Algorithm—2015 Update



CPR Quality

- Push hard (≥⅓ of anteroposterior diameter of chest) & fast (100-120/min) & allow complete chest recoil.
- Minimize interruptions in compressions.
- Avoid excessive ventilation.
- Rotate compressor every 2 minutes, or sooner if fatigued.
- If no advanced airway, 15:2 compression-ventilation ratio.

Shock Energy for Defibrillation

1st shock 2 J/kg, 2nd shock 4 J/kg, subsequent shocks ≥4 J/kg, maximum 10 J/kg or adult dose

Drug Therapy

- **Epinephrine IO/IV dose:** 0.01 mg/kg (0.1 mL/kg of 1:10 000 concentration). Repeat every 3-5 minutes. If no IO/IV access, may give ET dose: 0.1 mg/kg (0.1 mL/kg of 1:1000 concentration).
- **Amiodarone IO/IV dose:** 5 mg/kg bolus during cardiac arrest. May repeat up to 2 times for refractory VF/pulseless VT.
- **Lidocaine IO/IV dose:** Initial: 1 mg/kg loading dose. Maintenance: 20-50 mcg/kg per minute infusion (repeat bolus dose if infusion initiated >15 minutes after initial bolus therapy).

Advanced Airway

- ET intubation or supraglottic advanced airway
- Waveform capnography or capnometry to confirm & monitor ET tube placement
- Once advanced airway in place, give 1 breath every 6 seconds (10 breaths/min) with continuous chest compressions

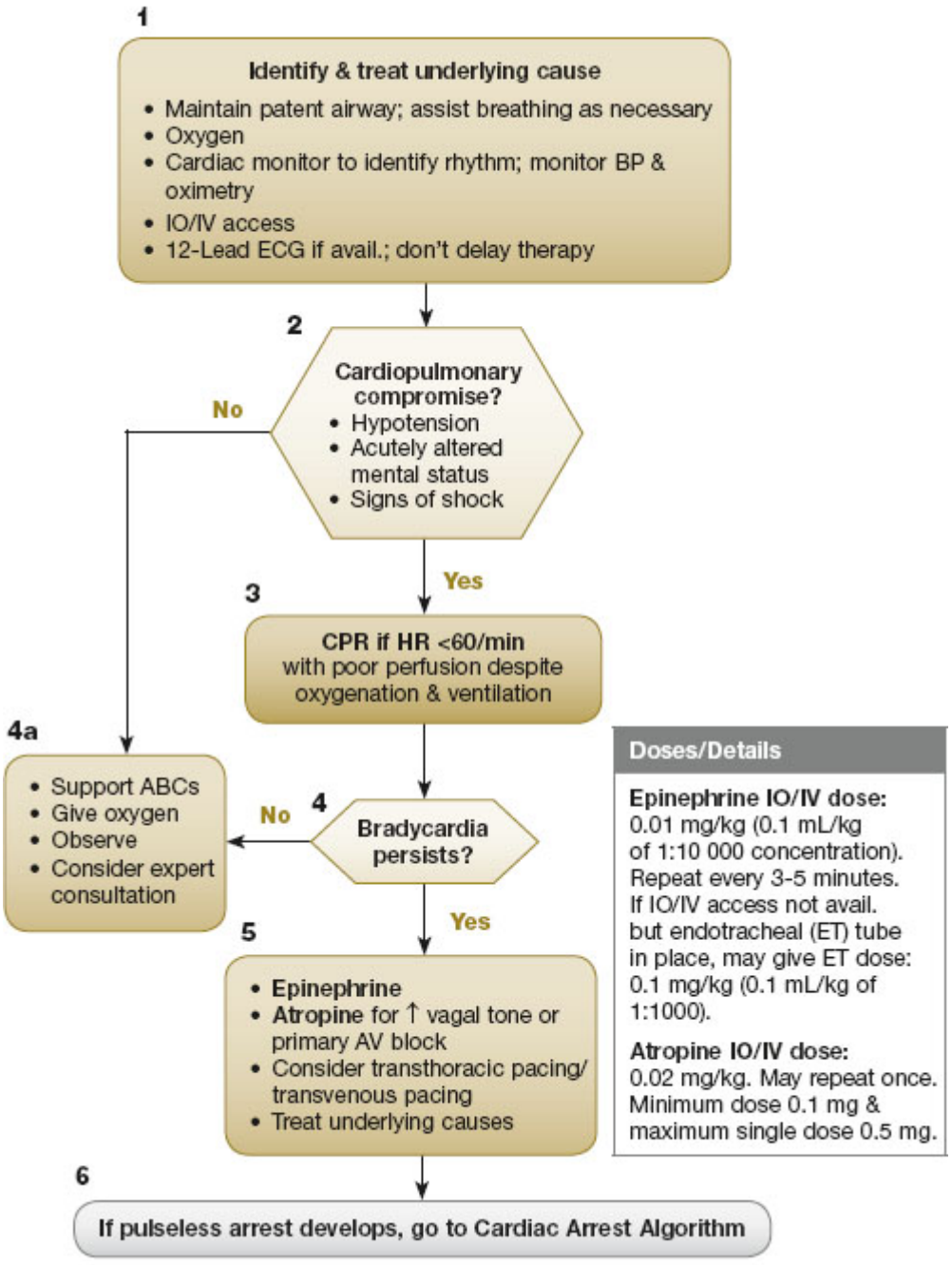
Return of Spontaneous Circulation (ROSC)

- Pulse & BP
- Spontaneous arterial pressure waves with intra-arterial monitoring

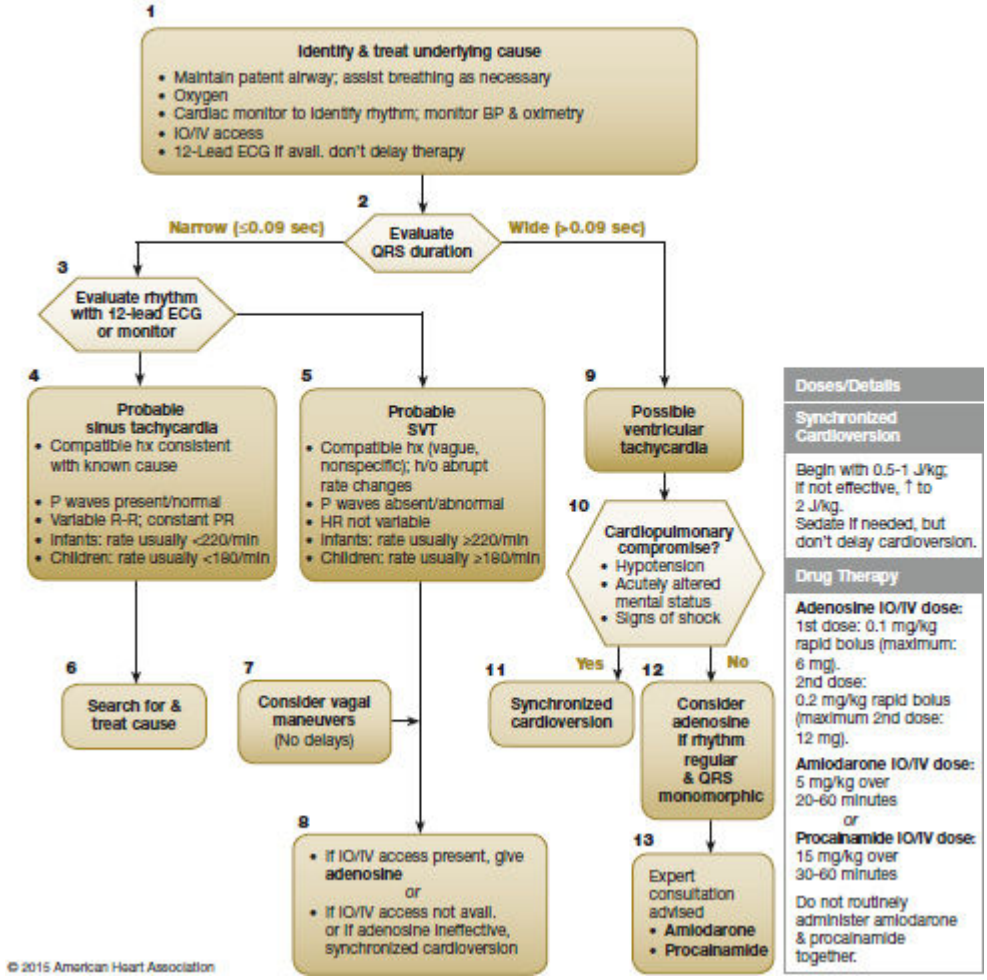
Reversible Causes

- **H**ypovolemia
- **H**ypoxia
- **H**ydrogen ion (acidosis)
- **H**ypoglycemia
- **H**ypo-/hyperkalemia
- **H**ypothermia
- **T**ension pneumothorax
- **T**amponade, cardiac
- **T**oxins
- **T**hrombosis, pulmonary
- **T**hrombosis, coronary

Pediatric Bradycardia With a Pulse and Poor Perfusion Algorithm



Pediatric Tachycardia With a Pulse and Poor Perfusion Algorithm



OBSTETRIC CRITICAL CARE

HOLLY R. ENDE, MD • DIRK J. VARELMANN, MD, DESA, EDIC

Introduction

Rate of ICU admission for pregnant/postpartum patient (pt): 0.17–1.1%.
Most due to obstetrical complications (47–93%): HTN, hemorrhage, sepsis, respiratory failure

Aortocaval Compression Syndrome

Compression of the inferior vena cava (IVC) & the aorta by the gravid uterus depending on position can occur after 16 wks of gestation

In supine position the IVC is nearly completely compressed resulting in decreased right atrial filling pressure (decreased right ventricular preload)

Sx: from mild hypotension to CV collapse

Lateral tilt of 30° increase IVC volume (Higuchi H, et al. *Anesthesiology.* 2015;122(2):286–293)

Tocolytic-Induced Pulmonary Edema

Complication of sympathomimetic therapy (β_2-mimetics, e.g., terbutaline; but also from calcium-channel blockers)

Sx

Dyspnea, tachypnea, hypoxemia

Cough, bibasilar crackles on auscultation (without heart failure)

Tachycardia, chest pain

Reduced hemoglobin concentration (hypervolemia from fluid resuscitation)

Chest x-ray: bilateral diffuse interstitial opacities (pulmonary edema)

Echocardiography: heart usually within normal limits for pregnant pt

Treatment

D/c offending agent, consider other tocolytics

Supplemental O_2, noninvasive ventilation in selected cases, intubation rarely required

Loop diuretics IV

Invasive hemodynamic monitoring rarely warranted

If pulmonary edema not improved within 12–24 hrs, exclude other causes

Mortality: very low

Aspiration

Dx

Frequently unnoticed, high level of suspicion required

Treatment

Milder cases resolve within 3–5 days with supportive therapy (abx treatment & corticosteroids usually not indicated)

Aspiration pneumonitis can progress to ARDS (see Chapter 19)

Venous Air Embolism

Sx

Diaphoresis, restlessness

Chest pain

Dyspnea, tachypnea, hypoxemia

Tachycardia, hypotension, cardiac arrest

Auscultation: “mill wheel murmur”

ECG: ST segment changes (depression more common than elevation)

Treatment

100% O_2 (to hasten nitrogen removal from air bubbles)

Cardiocirculatory/ventilatory support

Pt can be placed in left lateral decubitus with Trendelenburg position (preventing air bubbles from blocking right ventricular outflow tract)

If central venous catheter is in place, aspiration of air can be attempted

Consider hyperbaric O_2 therapy in case of paradoxical cerebral air embolism

Fetal Monitoring

Before a viable gestational age is reached, monitoring is limited to Doppler auscultation for fetal heart sounds

Starting at 26 wks of gestational age, twice weekly assessment of fetal heart tones is recommended for high-risk conditions

Testing should be performed for any changes in maternal status (e.g., inotrope/vasopressor requirements, maternal acidosis, increase in oxygen requirements)

Electronic fetal monitoring

For monitoring HR & uterine activity

Fetal HR variability occurs after 28 wks of gestational age

Maternal factors can lead to abnormal fetal HR without fetal distress

Biophysical profile scoring measures

Does not mature until 28–32 wks of gestational age

Recommended approach to assess fetal well-being

Measures (with US)

Amount of amniotic fluid

Limb movement, tone, breathing efforts

HR variability

Fetal growth

Pregnancy-related Diseases

Preeclampsia

Definition (American College of Obstetricians and Gynecologists; Task Force on Hypertension in Pregnancy. *Obstet Gynecol.* 2013;122(5):1122–1131)

Systolic BP ≥140 mm Hg or diastolic BP ≥90 mm Hg on 2 occasions at least 4 hrs apart in a previously normotensive pt (or systolic BP ≥160 mm Hg & diastolic BP ≥110 mm Hg, confirmation within minutes)

Proteinuria ≥300 mg/24 hrs or protein [mg/dl]/creatinine [mg/dl] ratio ≥0.3

Severe features of preeclampsia (any of these findings)

Systolic BP >160 mm Hg or diastolic BP >110 mm Hg

Thrombocytopenia (platelets <100 G/l)

Impaired liver function (liver transaminases >2 times normal), severe persistent right upper quadrant or epigastric pain

New development of renal insufficiency (serum creatinine >1.1 mg/dl or doubling of creatinine)

Pulmonary edema

New-onset cerebral or visual disturbances

Proteinuria not necessary to make the dx

Hyperuricemia is a predictor of poor fetal & maternal outcome (Hawkins TL, et al. *BJOG.* 2012;119(4):484–492)

Occurs after 20 wks of gestational age

Usually resolves within 6 wks postpartum

Cerebral complications if untreated (stroke, bleeding, edema)

Hemodynamic changes

HTN (high systemic vascular resistance, low CO)

Low cardiac filling pressure

Treatment

Manage BP

Typically used antihypertensives

Antihypertensives for the Treatment of Pregnancy-Induced Hypertension (PIH)	
Nifedipine	30–90 mg extended release PO qd
Hydralazine	10–40 mg IV q4–6h 10–50 mg PO q6h (max 300 mg/d)
Labetalol	20–80 mg IV q10min, max 300 mg 200–400 mg PO bid (max 2,400 mg/d)
Nicardipine	2.5–15 mg/h IV (may require arterial line)

- Maintain adequate volume status & urine output
- Treat pulmonary edema if necessary
- Renal failure is a rare complication, despite transient oliguria (resolves within 24–48 hrs postpartum)
- Consider urgent delivery for preeclampsia with severe features

Eclampsia

Preeclampsia + convulsions

Prodromal sx: headache, right upper quadrant pain

Treatment:

As with preeclampsia

Magnesium sulfate for prevention & treatment of seizures

4–6 g IV over 15–20 min (in 5 min if pt is seizing)

1–2 g/h IV as maintenance dose

2 g IV if seizures recur

Therapeutic level: 4–7 mEq/l (= 2–4 mmol/l, = 4.8–8.4 mg/dl)

Magnesium therapy can be monitored by repeatedly checking patellar reflexes & RR (toxicity: loss of reflexes, respiratory arrest, cardiac arrest)

If seizures persist after 2nd bolus of magnesium (2 g IV), use benzodiazepines or propofol. Intubation usually required

Expeditious delivery of the infant

HELLP

HELLP syndrome: hemolysis, elevated liver enzymes, low platelet count
Late findings: disseminated intravascular coagulation (DIC), pulmonary edema, placental abruption, retinal detachment, hepatic infarction/rupture
Sx
Right upper quadrant pain, N/V, wt gain/edema
Sx of preeclampsia (elevated BP, proteinuria)
Lab abnormalities
LDH >600 IU/l (hemolysis), increased bilirubin, ALT >70 IU/l, platelet count <100 G/l (Sibai BM. *Obstet Gynecol.* 2004;103:981–991)
Microangiopathic hemolysis: schistocytes, reduced haptoglobin
Potential increase in BUN & creatinine (renal impairment), hyperuricemia
Treatment:
Delivery of the fetus
Treatment of coexisting HTN (labetalol, hydralazine, nifedipine, nicardipine)
Magnesium (seizure prevention)
Cesarean delivery is not mandatory (vaginal delivery may be appropriate)
CBC including platelets, LDH should be monitored for 48 hrs postpartum

Anaphylactoid Syndrome of Pregnancy

Also known as amniotic fluid embolism (AFE)

Rapid onset, during labor or delivery (or within 30 min afterward)

Foreign substance (e.g., amniotic fluid, fetal cell debris) enters maternal circulation, triggering the release of histamines & arachidonic acid derivatives

Sx:

Restlessness, confusion, hypoxia, hypotension, cardiac arrest, coagulopathy

Treatment

Treatment is entirely supportive

Replacement of blood & clotting factors

Adequate volume replacement

BP support with vasoactive substances

Ventilatory support

Invasive monitoring (arterial & central venous catheters)

Cardiocirculatory assist may be beneficial (ECMO, cardioculmonary bypass) (Sultan P, et al. *Curr Opin Anaesthesiol.* 2016;29:288–296)

Peripartum Cardiomyopathy

Heart failure in the last mo of pregnancy or within 5-mo postpartum in the absence of identifiable cause/pre-existing heart dz

Sx/dx

Ejection fraction <45%

Shortening fraction <30%

Left ventricular end-diastolic dimension >2.7 cm/m^2 body surface area

Treatment

Reducing preload (diuretics), reducing afterload (vasodilators), improving contractility (inotropes)

Dietary sodium restriction

Cardiocirculatory assist devices, cardiac transplant

Prognosis is poor if cardiac function does not improve within 6-mo postpartum

Sepsis/Septic Shock (see Chapter 23)

Sepsis occurs in about 1 in 8,000 deliveries, mortality ~10%

Acute Fatty Liver of Pregnancy

Sx

Fulminant hepatic failure, coagulopathy, hepatic encephalopathy, coma

Renal failure

Biopsy: deposition of microvesicular fat in hepatocytes (rarely performed, because of invasiveness of procedure & concomitant coagulopathy)

Treatment

Delivery of the fetus

Severe cases: liver transplantation

Ovarian Hyperstimulation Syndrome (OHSS)

Associated with assisted reproductive technologies (ART), 0.2–1% incidence

Sx

N/V, diarrhea, hemodynamic instability

Multiorgan failure (ARDS, acute renal failure, ascites)

Thromboembolism

Treatment

Daily monitoring of weights

Periodic lab measurements (electrolytes, CBC, human chorionic gonadotropin hormone [hCG])

Fluid resuscitation (do not aggravate edema, ascites, pleural effusions)

Severe cases: repeated paracenteses, thoracenteses

Thromboprophylaxis (pneumatic compression stocking, heparin)

Most severe cases

Mechanical ventilation, invasive CV monitoring

Short-term hemofiltration/hemodialysis

Early termination of pregnancy in critical cases

OLDER ADULTS WITH CRITICAL ILLNESS: SPECIAL CONSIDERATIONS

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Introduction

1st-level assessment for functional, cognitive impairment, & polypharmacy at admission

Functional Status Assessment

Baseline disability is associated with in-hospital delirium, & ↑ 1-yr mortality. In addition, the inability to regain baseline function during hospitalization is an independent risk factor for 3-mo mortality in older pts

Activities of Daily Living (ADLs): bathing, dressing, transferring, toileting, continence, feeding (asking the pt or the family) (Katz S, et al. *Gerontologist.* 1970;10:20–30)

Scoring:

- Complete without assistance (score 1)
- Complete with assistance (score 2)
- Unable without assistance (score 3)
- Consider a pt as dependent if unable to complete daily tasks without assistance in >2 ADLs

***Action*:**

Consider a pt who receives assistance in ADLs as at risk of functional decline during & after the hospitalization. Order early physical & occupational therapy (Schweickert WD, et al. *Lancet*. 2009;373:1874–1882)

Instrumental Activities of Daily Living (IADLs): (asking the pt or the family) (Lawton MP, Brody EM. *Gerontologist.* 1969;9:179–186; Reuben DR, et al. *Geriatrics at Your Fingertips,* 18th Edition, American Geriatrics Society, New York, NY, 2016).

- Use of the telephone
- Operates phone on own initiative (score 1)
- Dials a few well-known numbers (score 1)
- Answers telephone but does not dial (score 1)
- Does not use the telephone (score 0)
- Shopping
- Takes care of all shopping (score 1)
- Shops independently for small purchases (score 1)
- Needs to be accompanied on any shopping trip (score 1)
- Completely unable to shop (score 0)
- Preparing meals
- Plans, prepares, and serves meals (score 1)
- Prepares meals if supplied with ingredients (score 1)
- Heats and serves prepared meals (score 1)
- Needs to have meals prepared and served (score 0)
- Housekeeping
- Maintains house alone or with occasional assistance (score 1)
- Performs light daily tasks (e.g., dishwashing) (score 1)
- Performs lightly daily task but no acceptable level of cleanliness (score 1)
- Needs help with all home maintenance (score 1)
- Does not participate in any housekeeping tasks (score 0)
- Doing laundry
- Does personal laundry completely (score 1)
- Launders small items (score 1)
- All laundry must be done by others (score 0)
- Using public transportation or driving
- Travels independently (public transportation or drives) (score 1)
- Arranges own travel via taxi (score 1)
- Travels on public transportation when assisted (score 0)
- Travels limited to taxi or automobile when assisted (score 0)
- Does not travel at all (score 0)
- Handling finances

- Manages financial matters independently (score 1)
- Manages day-to-day purchases but needs help with banking, etc. (score 1)
- Incapable of handling money (score 0)
- Handling medications
- Is responsible for taking medications (score 1)
- Takes responsibility if medications are prepared (score 0)
- Is not capable of dispensing own medications (score 0)

Scoring:
Give 1 point for each type of activity. Add the total points from each type of activity. The total score ranges from 0 to 8

Women
7–8 = high level of independence
5–6 = moderate level of independence
3–4 = moderate level of dependence
1–2 = dependence

Men
5 = independence
4 = moderate independence
3 = minimal independence/dependence
2 = moderate dependence
1 = dependence

Action:
Provide early occupation therapy for every pt but esp. for those with moderate independence, minimal independence/dependence, & moderate dependence (Schweickert WD, et al. *Lancet*. 2009;373:1874–1882.)

Cognitive Status Assessment

The presence of baseline cognitive impairment poses the pt at higher risk for delirium during the hospitalization, and increased mortality. Pts with dementia who experience delirium are more likely to have an accelerated decline in their cognitive performance & are more sensitive to polypharmacy

Ask the family if there is a known baseline cognitive impairment. If pt is communicative & not delirious perform a short evaluation of their cognitive abilities with the *Mini-Cog*. *Mini-Cog* combines a 3-item recall test with a clock-drawing test (CDT) (Borson S, et al. *Int J Geriatr Psychiatry.* 2000;15:1021–1027)

Step 1: instruct the pt to listen carefully to & remember 3 unrelated words (e.g., apple, penny, table) & then to repeat the words

Step 2: instruct the pt to draw the face of a clock on a blank sheet of paper. After the pt puts the numbers on the clock face, ask him or her to draw the hands of the clock to read a specific time, such as 11:20. These instructions can be repeated, but no additional instructions should be given. Give the pt as much time as needed to complete the task

Step 3: ask the pt to repeat the 3 previously presented words

Scoring:

Give 1 point for each recalled word after the CDT distractor

- A score of 0 indicates positive screen for dementia
- A score of 1 or 2 with an abnormal CDT indicates positive screen for dementia
- A score of 1 or 2 with a normal CDT indicates negative screen for dementia
- A score of 3 indicates negative screen for dementia

Action:

If the screening is positive without the presence of delirium, consider this pt at high risk for delirium & behavioral–psychological sx of dementia (BPSD)

Medications (Polypharmacy) Assessment	
Medications	Adverse drug events are frequent in older adults. Review preadmission medications, see Polypharmacy below

2nd level assessment within 24 hrs of admission

Frailty

Frailty is a clinically recognizable state characterized by a loss of physiologic reserve, resulting in an inability to maintain or restore homeostasis in response to acute stress. Persons with frailty are at ↑ risk of adverse outcomes such as onset of disability, morbidity, institutionalization, & mortality (Clegg A, et al. *Lancet.* 2013;381:752–762; Abellan van Kan G, et al. *J Nutr Health Aging.* 2008;12:29–37; Bagshaw SM, et al. *CMAJ.* 2014;186:E95–E102; Le Maguet P, et al. *Intensive Care Med.* 2014;40:674–682)

Define the presence and degree of frailty:

Obtain ADL and IADL information along with medical hx and then score the pt according to the Rockwood Clinical Frailty Scale (Rockwood K, et al. *CMAJ.* 2005;173:489–495)

Scoring:

Score	Category	Description
1	**Very fit**	Robust, active, energetic, well motivated & fit; these people commonly exercise regularly and are in the most fit group for their age
2	**Well**	Without active dz, but less fit than people in Category 1 (above)
3	**Well, with treated comorbid dz**	Dz sx are well controlled compared with those in Category 4 (below)
4	**Apparently vulnerable**	Although not frankly dependent, these people commonly complain of being "slowed up" or have dz sx
5	**Mildly frail**	With limited dependence on others for instrumental activities of daily living such as grocery shopping, cooking, & housekeeping
6	**Moderately frail**	Help is needed with both instrumental & noninstrumental activities of daily living
7	**Severely frail**	Completely dependent on others for activities of daily living, or terminally ill

Actions:

- If a pt is classified as frail then a referral should be made for a geriatrics-focused interdisciplinary management: geriatric evaluation & management (GEM), comprehensive geriatric assessment (CGA) (Stuck AE, et al. *Lancet.* 1993;342:1032–1036)
- The post-ICU in-pt management should be delivered in an Acute Care for Elderly Unit (ACE unit). (Landefeld CS, et al. *N Engl J Med.* 1995;332:1338–1344; Counsell SR, et al. *J Am Geriatr Soc.* 2000;48:1572–1581)

Risk of Falling

Assessing the Risk of Falling
1st level screening. Ask the pts or family: (Panel on Prevention of Falls in Older Persons, American Geriatrics Society and British Geriatrics Society. *J Am Geriatr Soc.* 2011;59:148–157) 1. If there have been 2 or more falls in the last 12 months 2. If there have been difficulties with balance or walking
Scoring: If the answer is positive to any of these questions then consider the pts at risk of falling
Action: If a pt is at risk of falling refer to the specific section on falls (geriatric syndrome) in this chapter for further advice

Assessing the Nutritional Status

Ask the pt or family if the pt has lost any wt in the year prior to the current admission (Wallace JI, et al. *J Am Geriatr Soc.* 1995;43:329–337)

Scoring:
Malnutrition if at least 5% loss of usual body wt

Action:
Refer to the section on malnutrition & Chapter 12

Vision and Hearing

Assessing Vision and Hearing	
Vision	Difficulty driving, watching television, reading, or doing any of your daily activities because of eyesight, even while wearing glasses? (Moore AA, Siu AL. *Am J Med.* 1996;100:438–443) ***Scoring:*** If yes, the screening is positive ***Action:*** Provide the pts with their glasses
Hearing	Ask the pt or the family the following questions screen (Reuben DB, et al. *J Am Geriatr Soc.* 1998;46:1008–1111): • Is the pt older than 70 yrs? (1 point) • Is the pt male? (1 point) • Does the pt have 12 or fewer years of education? (1 point) • Did the pt ever see a doctor about trouble hearing? (2 points) • Without a hearing aid, can the pt usually hear and understand what a person says without seeing his face if that person whispers to the pt from across the room? (If no, 1 point) • Without a hearing aid, can the pt usually hear and understand what a person says without seeing his face if that person talks in a normal voice to the pt from across the room? (If no, 2 points) ***Scoring:*** A score ≥3 represents a positive screening for hearing impairment ***Action:*** Provide the pts with hearing aids if screening positive

Depression

Assessing Pre-existing Depression

Ask the family or the pt if over the past 2 wks, how often the pt has been bothered by little interest or pleasure in doing things. Feeling down, depressed, or hopeless? (Kroenke K, et al. *Med Care.* 2003;41:1284–1292)

Scoring:

- A score of 0 if not at all
- A score of 1 if several days
- A score of 2 if more than half the days
- A score of 3 if nearly every day
- Total score ≥3, positive screen for depression

***Action*:**
Consider further evaluation or treatment

"FAST HUGS" Assessment

Daily Assessment: FAST HUGS

(Vincent JL. *Crit Care Med*. 2005;33:1225–1229; Landefeld CS, et al. *N Engl J Med*. 1995;332:1338–1344)

- **F**eeding: can the pt be fed orally, if not enterally? If not, should we start parenteral feeding?
- **A**nalgesia: the pt should not suffer pain, but excessive analgesia should be avoided
- **S**edation: the pt should not experience discomfort, but excessive sedation should be avoided; "calm, comfortable, collaborative" is typically the best level. Try to avoid benzodiazepine use
- **T**hromboembolic prevention: should we give low–molecular-wt heparin or use mechanical adjuncts?
- **H**ead of the bed elevated: optimally, 30° to 45°, unless contraindications (e.g., threatened cerebral perfusion pressure)
- **U**lcer prophylaxis: usually H_2 antagonists; sometimes proton pump inhibitors (consider the risk of ↑ clostridium difficile Infxn) (Linsky A, et al. *Arch Intern Med.* 2010;170:772–778)
- **G**lucose control: maintain a blood glucose target of 180 mg/dl or less & avoid hypoglycemic episodes (NICE-SUGAR Study Investigators, et al. *N Engl J Med.* 2009;360:1283–1297)
- **G**eriatric: delirium evaluation, ADL evaluation, early mobilization, early occupational & physical therapist, review of medications, removal of restraints (e.g., lines, physical restraints, chemical restraints, urinary catheters)
- **S**ocial: involvement of social worker, DNR/DNI orders

Geriatric Syndromes in the ICU

Delirium

Delirium management in the ICU (see Chapter 5)

Dementia: Differential Diagnosis

Use the following features to differentiate between delirium, dementia, & depression (Morandi A, et al. *Intensive Care Med.* 2008;34:1907–1915)

Clinical Characteristics of Dementia, Delirium, and Depression			
Feature	Dementia	Delirium	Depression
Onset	Slow	Sudden	Variable
Duration	Years	Day or weeks	Variable
Reversibility	Persistently progressive	Fluctuating	Variable during the day
Variation at night	Worse	Almost worse at night	Generally none
Level of consciousness & orientation	Impaired & worsening in the last stages	Fluctuates, disoriented	Generally normal
Attention & memory	Attention usually retained in the early phase, & early loss of short-term memory	Inattention & poor short-term memory	Intact memory, may have poor attention
Cognition	Global cognitive impairment	Focal to global cognitive deficits	Impaired in severe stage & may be misdiagnosed as dementia
Psychotic sx	Less frequent	Hallucinations might be present (mostly visual), delusions, & illusions	Rare: psychotic ideation is complex and related to the mood of the pt
Speech	Difficulty finding words	Often incoherent words	Normal
EEG	Variable	Generalized diffused slowing	None

If cognitive impairment is newly detected at ICU admission or at ICU discharge, consider referring the pt to a memory clinic or to geriatric clinic for further assessment

Behavioral and Psychologic Symptoms of Dementia

Agitation/aggression, psychosis (hallucinations or delusions) and mood disorders (depression) are the most common BPSD. In pts with Lewy body dementia & Parkinson dementia, visual hallucinations, delusions, & depression are more frequent

Step 1 (Donna LA, et al. *Am J Alzheimer's Dis Other Demen.* 1996;11:10–19)

Evaluate the presence of pain, new infection (e.g., respiratory or urinary tract Infxn), constipation, dehydration, hunger, thirst, sleep disruption, & environmental factors (noise, light); consider visual/auditory impairments

Perform a thorough evaluation of pharmacologic treatments. Review medication records because discontinuation of cholinesterase inhibitors (e.g., donepezil) might be associated with worsening BPSD (Holmes C, et al. *Neurology.* 2004;63:214–219)

Step 2: nonpharmacologic management of BPSD (Livingston G, et al. *Am J Psychiatry.* 2005;162:1996–2021)

Provide calming music and aromatherapy

Provide sensory stimulation (physical touch, gentle massage) through family members & create a home-like atmosphere

Decrease light and noise level

Approach the pt frontally and use a relaxed demeanor and a smile (Burgener SC, et al. *J Gerontol.* 1992;47:P242–P249)

If the presence of BPSD poses significant danger and nonpharmacologic approaches have not been beneficial, then consider a pharmacologic treatment

Step 3: pharmacologic management of BPSD

"Start slow and go slow" (Catterson ML, et al. *Psychiatr Clin North Am.* 1997;20:205–218)

In case of **Agitation/Aggressive Behavior/Psychosis** consider options:

Olanzapine: start with 2.5 mg/d and titrate up to 5 mg/d

Risperidone: start with 0.5 mg/d and titrate up to 1 mg/d

Citalopram: 20 mg/d

Careful use of antipsychotics in Lewy body dementia for higher risk of neuroleptic malignant syndrome (Sink KM, et al. *JAMA.* 2005;293:596–608)

Lower dose/discontinue antipsychotics when acute symptoms are controlled

In case of **symptoms of depression**:

Sertraline might be considered at 25 mg/d and titrate up to 150 mg/d (Lyketsos CG, et al. *Arch Gen Psychiatry.* 2003;60:737–746)

Malnutrition (see Chapter 6)

Falls

The **Morse Fall Scale Score** could be used to further stratify the risk of falls during the ICU course (Morse JM. *Can J Public Health.* 1986;77:21–25)

If a pt is at risk of fall, then activate the fall prevention system in place in your ICU

A pt who is at risk of falling should be referred to a geriatrician for a **multifactorial fall risk assessment** to evaluate the hx of falls, medications, gait-balance and mobility, visual acuity, other neurologic impairments, muscle strength, HR & rhythm, postural hypotension, feet & footwear, environmental hazard (Panel on Prevention of Falls in Older Persons, American Geriatrics Society and British Geriatrics Society. *J Am Geriatr Soc.* 2011;59:148–157)

Polypharmacy

Assess for polypharmacy and inappropriate medications at multiple times, including ICU admission, during the ICU stay, and at ICU discharge. D/c those that can be safely eliminated

Evaluate for the presence of potentially (PIMs) and actually inappropriate medications (AIMs) in particular anticholinergic drugs, antipsychotics, opioids (Morandi A, et al. *Arch Intern Med.* 2011;171:1032–1034). PIMs are judged as AIMs according to their indication, effectiveness, dosages, and drug interactions (Hanlon JT, et al. *J Clin Epidemiol.* 1992;45:1045–1051)

Pay attention to the number of medications since a pt taking 2 drugs faces 13% risk of adverse drug–drug interaction, 38% for 4 drugs, 82% if 7 or more drugs are simultaneously administered (Goldberg RM, et al. *Am J Emerg Med.* 1996;14:447–450)

Assess the anticholinergic burden for its potential effects on cognitive function

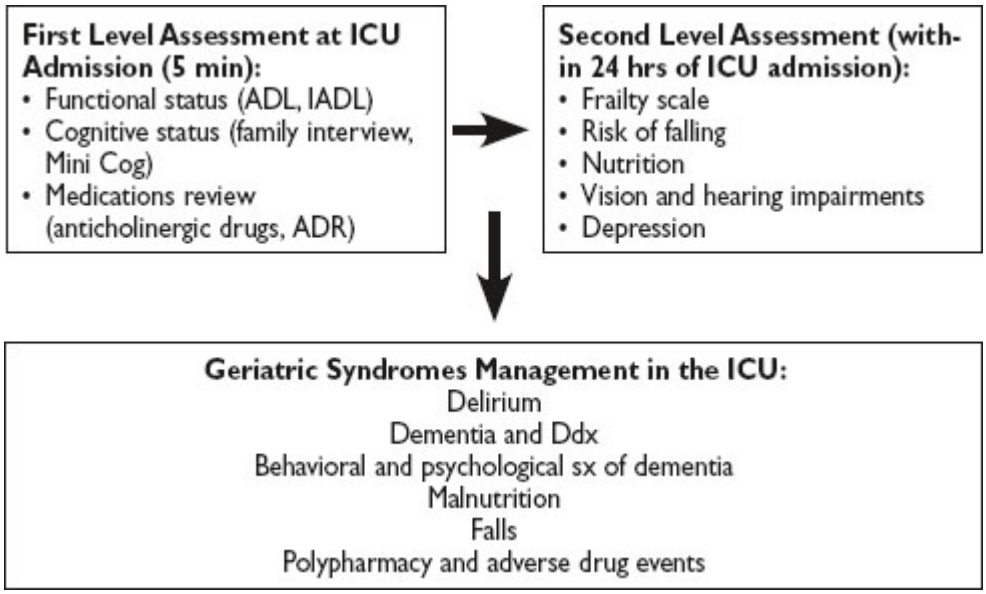
Assess the risk for adverse drug events with the following risk score

Assessing the Risk of Adverse–Drug Reactions (ADR)

Use the ADR Risk Score to Identify Patients Who Are at Risk of ADR during Hospitalization (Onder G, et al. *Arch Intern Med.* 2010;170:1142–1148)	
Variable	**Points**
≥4 comorbid conditions	1
Heart failure	1
Liver dz	1
Number of drugs	
≤5	0
5–7	1
≥8	4
Previous ADR	2
Renal failure[a]	1
Scoring: The risk of ADR ↑ from 2.0% with a score of 0–1 to 21.7% with a score ≥8	
Action: Revise each pt's medication list at ICU admission and discharge to identify those pts at risk for ADR	

[a]Defined a glomerular filtration rate <60 ml/min.

Summary of Geriatric Management in the ICU



ADL, activities of daily living; IADL, instrumental activities of daily living; ADR, adverse drug reactions.

OBESITY: SPECIAL CONSIDERATIONS

ALI A. EL-SOLH, MD, MPH

INTRODUCTION

The International Classification of Adult Underweight, Overweight, and Obesity According to BMI		
Classification	**BMI (kg/m^2)**	
	Principal Cut-off Points	**Additional Cut-off Points**
Underweight	<18.50	<18.50
Severe thinness	<16.00	<16.00
Moderate thinness	16.00–16.99	16.00–16.99
Mild thinness	17.00–18.49	17.00–18.49
Normal range	18.50–24.99	18.50–22.99
		23.00–24.99
Overweight	≥25.00	≥25.00
Preobese	25.00–29.99	25.00–27.49
		27.50–29.99
Obese	≥30.00	≥30.00
Obese class I	30.00–34.99	30.00–32.49
		32.50–34.99
Obese class II	35.00–39.99	35.00–37.49
		37.50–39.99
Obese class III	≥40.00	≥40.00

Source: Adapted from WHO, 1995, WHO, 2000 & WHO, 2004.

Metabolic Syndrome (MetS)

Constellation of clinical phenotypes linked to cardiovascular dz (see the table below). The core components are glucose intolerance or diabetes, obesity, HTN, & dyslipidemia

Other conditions associated with the syndrome include physical inactivity, aging, hormonal imbalance, & genetic predisposition

Prevalence: 25–34% of the US population depending on the definition used

Compared to those without the MetS, critically ill patients (pt) with this syndrome are at a higher risk of morbidity & mortality

Pt with the MetS have increased prevalence of obstructive sleep apnea (OSA), which can be as high as 87% (Coughlin SR, et al. *Eur Heart J*. 2004;25(9):735–741)

Perioperative β-block might improve outcomes in pt with a revised cardiac risk index ≥2

Although data in other high-risk groups suggest benefit, no clinical trials have addressed the perioperative use of statins in pt with MetS

Diuretics & β-blockers in high doses can worsen insulin resistance & atherogenic dyslipidemia

High serum glucose levels in pt with MetS are associated with higher risk of ICU acquired infxns

Adequate glycemic control is recommended with serum blood sugar target between 130 & 150 mg/dl. Tighter control runs the risk of hypoglycemia

Definitions of Metabolic Syndrome

Organization	Waist Circumference or BMI	Triglyceride Level	HDL-C Level	Blood Pressure Value	Fasting Glucose Level
American Heart Association/National Heart, Lung, & Blood Institute	Men: ≥102 cm (40 in) Women: ≥88 cm (35 in)	≥150 mg/dl (1.7 mmol/l)	Men: <40 mg/dl (1.03 mmol/l) Women: <50 mg/dl (1.29 mmol/l)	≥130/85 mm Hg or previous HTN treatment	≥100 mg/dl
European Group for the Study of insulin Resistance	Men: ≥94 cm (37 in) Women: ≥80 cm (31 in)	≥178 mg/dl (2.0 mmol/l)	<40 mg/dl (1.03 mmol/l)	≥140/90 mm Hg	≥110 mg/dl (6.1 mmol/l)
International Diabetes Federation	Men: ≥94 cm Women: ≥80 cm	≥150 mg/dl (17 mmol/l)	Men: <40 mg/dl (1.03 mmol/l) Women: <50 mg/dl (1.29 mmol/l)	≥130/85 mm Hg or previous HTN treatment	≥100 mg/dl (5.6 mmol/l)
National Cholesterol Education Program Adult Treatment Panel III	Men: ≥102 cm (40 in) Women: ≥88 cm (35 in)	≥150 mg/dl (1.7 mmol/l)	Men: <40 mg/dl (1.03 mmol/l) Women: <50 mg/dl (1.29 mmol/l)	≥130/85 mm Hg	≥110 mg/dl (6.1 mmol/l)
World Health Organization	Waist to hip ratio Men: >0.90 Women: >0.85 or BMI >30 kg/m^2	≥150 mg/dl (1.7 mmol/l)	Men: <35 mg/dl (0.90 mmol/l) Women: <39 mg/dl (1.00 mmol/l)	≥140/90 mm Hg	≥110 mg/dl (6.1 mmol/l)

Airway Management (also see Chapter 3)

Potentially more difficult mask ventilation & intubation although the association between BMI & difficult tracheal intubation is not consistent

Optimal pt positioning & airway/equipment prep is essential

Risk factors for difficult intubation

Limited neck mobility & mouth opening

A short sternomental distance

A receding mandible & prominent teeth

Neck circumference >40 cm

Mallampati score of ≥3

Prior hx of difficult intubation

Approach to Intubation (see Chapter 3)

Rapid Sequence Intubation Medications & Dosing Considerations for Obese Trauma Pt (Cullen A, et al. *Can J Anaesth*. 2012;59:974–996)

Agent	Dosing	Purpose
Etomidate	LBW or TBW	Sedation
Ketamine	LBW	Sedation
Midazolam	TBW (bolus), IBW (infusion)	Sedation
Propofol	IBW or LBW (bolus), TBW (infusion)	Sedation
Fentanyl	$52/(1 + [196.4 \times e^{-0.025\ ABW} - 53.66]/100)$	Analgesia
Remifentanil	IBW	Analgesia
Atracurium	IBW or TBW	Paralysis
Cisatracurium	IBW	Paralysis
Pancuronium	IBW	Paralysis
Rocuronium	IBW	Paralysis
Succinylcholine	TBW	Paralysis
Vecuronium	IBW	Paralysis

TBW = Total (Actual) Body Weight, IBW = Ideal Body Weight, LBW = Lean Body Weight

Mechanical Ventilation

There is also no clinical evidence suggesting superior clinical outcomes with intraoperative pressure control or volume-controlled ventilation use in obese pt. The mode of ventilation should be selected based on understanding of their different operation & characteristics to achieve the goals of lung protective ventilation & avoid both barotrauma & hypoventilation

Initial tidal volume calculated according to ideal body wt & then adjusted according to systemic ABGs

Addition of positive end expiratory pressure (PEEP 8–10 cm H_2O) facilitates alveolar recruitment & prevent atelectasis

Limit transpulmonary pressure to ≤35 mm Hg

Basilar atelectasis & VQ mismatch: most common causes of hypoxemia in intubated pt (may need to r/o PE, pneumonia, or pulmonary edema)

→ *Maintain trials of spontaneous breathing during mechanical ventilation even in pt with severe pulmonary functional disorders*

Since morbidly obese pt are at higher risk for postextubation stridor, may perform a cuff leak test for identifying laryngeal edema prior to extubation (has poor specificity)

Extubate in semirecumbent position

Use of bilevel noninvasive positive airway pressure at a level of 12/4 in the 1st 48 hrs postextubation improves pulmonary function & oxygenation

Application of CPAP should be initiated at the earliest opportunity postextubation in those with prior dx of obstructive sleep apnea

Fluid Loading Poorly Tolerated

Each 1 kg/m^2 increase in BMI is associated with a 0.08 l/min increase in CO & 1.35 ml increase in SV. Poor tolerance of IV fluid load may be due to right heart strain secondary to existing pulmonary HTN

Diagnostic Imaging

Ascertain radius & wt limit of the operating/procedure table

Chest radiograph shows limited diagnostic quality image with poor x-ray penetration & poor visualization of lung bases

Use the lowest frequency transducer avail. (2 MHz) during sonography & position the transducer within the range of the focal length of the transducer

MR scanners with a high signal-to-noise ratio (SNR) & strong gradients (≥1.5 T) cannot accommodate pt weighing >350 lb (159 kg). A vertical field open MRI system is needed for pt up to 550 lb (250 kg)

Venous Thromboembolism (VTE) Prophylaxis

Enoxaparin, 40–60 mg subcutaneously b.i.d.

Consider anti-Xa monitoring during LMWH treatment

With once-daily dose, target a level of 1.0–2.0 IU/ml at 4 hrs postinjection

For twice-daily administration, aim at a target of anti-Xa level of 0.6–1.0 IU/ml

Alternatively, 7,500 units of unfractionated heparin 3×/d for BMI >50; 5,000 units for BMI <50

No randomized controlled trials demonstrate efficacy or mortality benefit of IVC filter placement over sequential compression devices, ambulation, or anticoagulation alone

Indications for prophylactic filter placement include failure of anticoagulation therapy, known hypercoagulable state, decreased cardiopulmonary reserve, & BMI >55

Continuing chemoprophylaxis for 10 days after hospital discharge in high-risk pt may decrease the risk of VTE (Mechanik JI, et al. *Surg Obes Relat Dis*. 2013;9(2):159–91)

Nutrition

Although obese pt have excess body fat, they are more likely to develop protein energy malnutrition

Indirect calorimetry should be used to calculate energy expenditure

If indirect calorimetry is not avail., provide 20–30 kcal/kg of IBW/d

Protein requirements should be aimed at achieving nitrogen equilibrium: 1.5–2.0 g/kg of IBW

Pressure-Induced Rhabdomyolysis

Rare but potentially serious complications after prolonged surgery

Epidural anesthesia may mask sx of rhabdomyolysis of the lower limbs, gluteal or lumbar musculatures

Compartment syndrome, acute renal failure, & myoglobinuria are potential sequelae

When suspected, institute aggressive hydration & diuresis with mannitol to a target urine output of 1.5 ml/kg/hr

Alkalinize urine with sodium bicarbonate to a pH >7.0 (controversial)

Nursing Care

Provide instructions for the staff on avail. equipment & techniques & the importance of securing help before lifting the obese to avoid work-related injury

Do not rely on rotational mattresses to relieve pressure

Unconscious, immobile pt are prone to yeast infxns in the skin folds

It is advisable that morbidly obese pt be triaged to receive tests early in the day when the largest number of staff are avail. to move & secure the pt

Trauma

Obese pt suffering blunt trauma have fewer head injuries & liver lacerations, but extremity injuries & thoracic injuries (such as rib fx & pulmonary contusions) seem to be more prevalent & severe

Intra-abd pressure in the obese is chronically elevated at baseline, which could heighten the risk of abd compartment syndrome in obese pt receiving excessive fluid resuscitation

Obesity is an independent predictor of adverse events after burn injury; compared to nonobese pt, obese pt developed higher rate of wound infxn, urinary tract infxn, DVT in total body surface area (TBSA) ≥10% (3.1% vs. 1.1%), & PE. (Ray JJ, et al. 2015;198(2):450–455)

Recommendations for management of burns rely on visual estimation of body surface area (BSA) affected. The "rule of fives" has been suggested, in which the torso is assigned 50% of BSA, each leg is assigned 20%, 5% is assigned to each arm, & 2% is assigned to the head (Livingston EH, et al. *J Surg Res*. 2000;91(2):106–110)

Obesity is a risk factor for acute kidney injury. Each 5-kg/m increase in body mass index is associated with a 10% risk of worsening renal function (Danziger J, et al. *Crit Care Med*. 2016;44:328–334)

Dose Adjustments for Antimicrobial Therapy in Morbidly Obese	
Antibiotics	**Recommended Weight for Dosing**
β-lactam	IBW* + 0.3 (ABW – IBW)
Vancomycin	ABW
Fluoroquinolones	IBW + 0.45 (ABW – IBW)
Gentamicin	IBW + 0.43 (ABW – IBW)
Tobramycin	IBW + 0.58 (ABW – IBW)
Amikacin	IBW + 0.38 (ABW – IBW)
Erythromycin	IBW
Sulfonamide	IBW
Acyclovir	IBW
Amphotericin	ABW

Adapted from Wurtz R, Itokazu G, Rodvold K. *Clin Infect Dis*. 1997;25:112–118.
IBW, ideal body weight; ABW, actual body weight.
*IBW (kg) for men = 50 kg + (2.3 × ht in in over 60 in)
*IBW (kg) for women = 45.5 kg + (2.3 × ht in in over 60 in)

Increased ratio of adipose to lean body mass alters volume of distribution (Vd)

Accumulation of lipophilic drugs in adipose tissue increases the dose necessary to achieve effect, & prolongs the elimination half-life. Dosing of these drugs in obese pt is generally approximated best using actual body weight (ABW) rather than the ideal body weight (IBW)

The Vd of hydrophilic drugs in general relates better to lean body mass (approximated by IBW) because of poor penetration into adipose tissue

OPERATING ROOM: CARING FOR THE EXTREMELY CRITICALLY ILL PATIENT

EMILY NELSON, MD • GYORGY FRENDL, MD, PhD

Introduction

Key elements:

A rapid but thorough preoperative assessment of the acute process & associated organ dysfunctions

Understanding the patient's (pt) pre-existing comorbidities & their degree

Focus on the timely identification & management of the most life-threatening conditions

Deployment of strategies to prevent worsening of the pt's condition while providing a chance for improvement. Examples:

Applying lung-protective ventilation for a pt with inhalational injury, aspiration, or lung contusion

Switching to "damage control surgical management" for trauma pt when the anesthesiologist notices the development of the "triad of death: acidosis, hypothermia, hypercoagulability"

Deployment of interventions to restore/replace vital organ function. Examples:

Deployment of renal replacement therapy (i.e., CVVH) in the OR for a burned or septic shock pt with acute renal failure who is also suffering from severe fluid overload, intractable acidosis or a life-threatening electrolyte imbalance

Placement of a PA catheter with pacing ability to allow urgent surgery for a pt who suddenly developed 3rd-degree AV nodal block

Preoperative Assessment of the Severely Critically Ill Patient

A rapid but thorough assessment of the acute process & associated organ dysfunctions

Understanding the pt's pre-existing comorbidities & their degree

Specific organ systems should be evaluated for the following concerns:

Neuro: Determine & document the pt's preinjury mental status & basic neurologic exam, the changes the injury has caused, as well as any focal deficits. Assess if the pt is sufficiently sedated, & if his/her pain is treated. Plan to perform a neurologic exam at the end of the operation

Cardiovascular: Assess the pt's hemodynamic condition. Look for recent echo results: abnormalities in EF, pulmonary pressure, & valvular dz. Is the pt pressor dependent? Be aware of escalating doses. Hx of coronary dz or recent MI or arrhythmias? If the pt has a pacemaker/ICD, ask what kind & when it was last interrogated, or if ICD has fired recently. Pt with ventricular assist devices may need noncardiac surgical interventions. Assess volume status. Beware of cardiac contusion causing RV dysfunction or AV block

Pulmonary: Assess the status of lungs (use CXR, chest CT, ABG). Note preop ventilator settings & FiO_2. Evaluate if the pt will require transport ventilator to & from the OR or ICU ventilator during the procedure. Look for hx or signs of chronic and/or acute pulmonary HTN

Airway: Quickly assess airway for intubation (beware of C-spine injury, if unknown keep spine precautions). If the pt has been intubated, document if it was a difficult intubation; if trached, document when it was performed. What size ETT & type/size of tracheostomy tube is in place (cuffed or uncuffed—assess need to replace uncuffed trach)?

Renal/electrolytes: Does the pt have abnormal renal function? If in ESRD, when was last dialysis? What are most recent electrolyte values? Does the pt have an acidosis?

Heme: Is the pt actively bleeding? Does the pt have a coagulopathy & why? Document most recent hematocrit, platelets, & coagulation parameters. Ask for a type & cross to be performed, & ensure that blood is readily avail. (be aware of the presence of antibodies in the recipient's serum as they will make cross match more prolonged & difficult)

GI: Confirm NPO status. Trauma pt should be assumed to be full stomach & be intubated with rapid sequence intubation. Is the pt on TPN or should a CVC port be saved for TPN? Is the pt on tube feeds?

Endo: Check & manage blood sugars, keep in the 120–180 mg/dl range (NICE-SUGAR Study Investigators, Finfer S, et al. *N Engl J Med*. 2009;360(13):1283–1297). Look for chronic steroid use

ID: Provide appropriate perioperative abx coverage. If the pt is septic early, broad spectrum abx administration has significant benefits

Musculoskeletal: R/o recent orthopedic injuries or myopathy

Derm: Assess the area of burn or large BSA rash

Access: Assess vascular access & the need for additional access catheters for the procedure

Code Status/HCP: What is the pt's code status? Who is the pt's healthcare proxy (HCP) & have they been informed & have they given consent for the anesthetic?

Intraoperative Management of the Severely Critically Ill Patient

The timely identification & management of the most life threatening of the conditions

Deployment of strategies to prevent worsening of the pt's condition while providing a chance for improvement

Deployment of interventions to restore/replace vital organ function

Choice of monitors & access:

Physiologic monitors per standard of care

Consider invasive hemodynamic monitoring (arterial catheter; Swan–Gantz catheter vs. CVP monitoring), use of cardiac output monitoring (Vigileo or others), transesophageal or transthoracic echo

Assess special need for monitoring bladder (abd compartment) pressure or ICP monitor

Secure large bore IV catheters (RIC line, Cordis in central vein, need for hemodialysis catheters, etc.)

Airway management: as discussed above

Ventilator management

Use ARDSNet protective lung ventilation strategy for ARDS/ALI & septic pt

The use of inhaled prostacyclines may be necessary for lung injured pt with pulmonary HTN or very poor oxygenation

Use transport ventilators for pt with lung injury/contusion or at high risk for ALI/ARDS when in transit & ICU ventilators in the OR

Vasopressor management: we will refer to other chapters for detailed discussion on the use of vasoactive agents (pressors). Also see Chapters 20 & 38

Transfusion management: for discussion on transfusion goals & factor replacement for both actively bleeding pt & for pt who are NOT actively bleeding, please refer to Chapter 22

Fluid, electrolyte, & renal management:

For sepsis, see Chapter 23. For management of fluids & electrolytes, see Chapter 22

Assess degree of renal injury (most often ATN in sepsis & hemorrhagic shock). Manage fluids to minimize further injury to the kidneys & to support recovery. When renal failure occurs acutely in the OR, instituting intraoperative renal replacement therapy may be necessary (i.e., CVVH). Most common indications are intractable hyperkalemia, acidosis, & fluid overload leading to hypoxemia & heart failure

Pain management: Pt with chronic opioid use will require increased doses. Consider adding nonopioid adjuvants, such as ketamine, & use of regional anesthesia

Choice of anesthetic induction & maintenance agents

Etomidate has minimal effect on BP/CO, but may induce adrenal insufficiency. Propofol induction can be safe if dosed appropriately for the pt's hemodynamics (use reduced or incremental doses). Ketamine & opioid-based induction strategies can be used

Severely critically ill pt may not tolerate IV or inhaled anesthetics, & may need to be managed with a high-dose opioid strategy

Choice of muscle relaxant agents

Many procedures may be completed without muscle relaxation

Because kidney injury is very common in severely critically ill pt, small doses of nonrenally cleared muscle relaxants (cisatracurium or vecuronium) should be used as needed, titrated with the use of a nerve stimulator

Early, short-term muscle relaxation may improve recovery from ARDS. However, consider the risk of critical illness myopathy & neuropathy
(Papazian L, et al. *N Engl J Med*. 2010;363(12):1107–1116)

ACLS in the OR: acutely life-threatening conditions are managed in the OR according to ACLS (fatal arrhythmias) & ATLS (tension pneumothorax (PTX), hemothorax, pericardial tamponade, hemorrhagic/hypovolemic shock) guidelines for ACLS & ATLS protocols see Chapters 9 & 41

Communication with ICU team & pt's family: continuity of care & the need for family involvement requires that all caretakers from the OR both document & communicate the course of events, the intervention they made & their outcomes to both the next care provider in the ICU & the pt's family members

HEART AND LUNG TRANSPLANTATION

ANTONIO COPPOLINO III, MD • PHILLIP CAMP, MD • HARI R. MALLIDI, MD

Heart and Lung Transplant Postoperative Management

General Overview, Monitoring, and Key Concepts

Multidisciplinary team management is required for best results & outcomes
Specialized ICU & ICU critical care nursing team
Highly integrated protocol-based care algorithms
Transplant isolation precautions, positive pressure. room, thoroughly cleaned & sanitized prior to admission, universal precautions, 100% masks & gloves
Comprehensive invasive & noninvasive monitoring including:
Modern ventilators with flow pressure curves
PA catheter
Arterial catheter & noninvasive BP measurements
Urinary, gastric drainage catheters
Multilead continuous ECG monitors
Advanced vital sign monitors
Continuous and/or frequent monitoring of all drains, monitors, catheters

Lung Transplant Initial Postoperative Management

Ventilator Management

Modified lung protective strategy (for additional details, see Chapters 18 & 19)

Keep peak inspiratory pressure below 30–35 cm H_2O

PEEP of 8–10 (dual purpose: provide acceptable pleural tissue approximation to minimize soft tissue bleeding & to maintain lung recruitment & transcapillary gradient for improved oxygenation)

Tidal volumes: maintained 6–8 cc/kg of recipient ideal wt (note: Not the same as ARDSNet management with low tidal volumes, transplanted lungs have low initial compliance due to ischemia–reperfusion injury but uniform in nature, not patchy.)

There are no functional bronchial arteries (as they are not anastomosed), so PA perfusion & ventilation needed for tissue oxygenation

Fraction of inspired oxygen concentration (FiO_2): keep as close as possible to 0.21 to maintain arterial oxygen tension (PaO_2) 80–100 mm Hg

Patient (Pt) transfers from OR on 100% FiO_2

Check ABG frequently (q1h–q4h)

Allow modest hypercapnia in setting of good oxygenation & normal pH, overly aggressive correction delays normal respiratory drive

Extubation criteria

Pt is awake, alert, following commands

Has normal spontaneous respiratory effort

Has acceptable ventilation & oxygenation

Has good pain control with normal respiratory effort

Acceptable lower airway examination by bronchoscopy at bedside

Pt has weaned from full support to pressure support when stable & able to maintain ventilation

Augmentation of ventilation & oxygenation is required if:

Pulmonary Artery Pressures (PAP) are elevated above >50% of systemic BPs, or

Mean PAP is >30 mm Hg with other complications, or

CVP is >18 mm Hg, or

There is evidence of right ventricular failure and/or low CO

Use nitric oxide: 0–20 PPM, or

Use inhaled Flolan (epoprostenol sodium; doses of 2–70 ng/kg/min using simple nebulizers)

Monitor the pt's methemoglobin levels

Unique ventilation issues following lung transplantation

Single lung transplant

Differential response to ventilation strategy, e.g., new healthy but stiff lung & retained pathology of recipient original dz (COPD, pulmonary fibrosis)—must monitor to avoid overventilating or overpressurizing either lung

Barotrauma, air trapping with mediastinal shift, unanticipated dead space

Use volume control or pressure control ventilator modes, with larger (8–10 cc/kg) tidal volume with low RR, prolonged expiratory (E) time (COPD) or use prolonged I:E ratio (pulmonary fibrosis)

Possibility of lung isolation if ventilation is unmanageable without that

Either single or double lung transplant

Compromised lymphatics, fluid overload, ischemia–reperfusion injury

Need for regular & as needed bronchoscopy

Elevated PEEP

Postoperative bleeding: elevated risk in 1st 24–48 hrs due to common use of cardiopulmonary bypass (CPB) & systemic anticoagulation

Considerations and Treatment Options

Inadequately reversed heparin

Development of disseminated intravascular coagulation (DIC) due to CPB, transfusion reaction, profound inflammatory state (cystic fibrosis, pneumonia, etc.)

Fibrinolytic state secondary to retained blood & clot in chest; requires surgical evacuation

Administer antifibrinolytic agent—Amicar (ε-aminocaproic acid: 4–5 g loading dose IV over 60 min & continue 1 g/hr for 6–8 hrs or until bleeding subsides)

Decreased platelets due to CPB, response to induction agent

Poor tissue-to-tissue apposition in operative field

Increase PEEP if tolerated

Undetected small or medium bleeding vessels

Medical management

Increase PEEP as tolerated

Increase tidal volume

Ensure adequate pleural drainage

Correct incomplete replacement of coagulation factors

Low core body temp resulting in inability to establish normal clotting cascade

Warm patient to normothermia

Hemodynamics

Evaluate confounding factors that may be affecting pt hemodynamic status

Assess sequelae of other therapies or interventions

R/o hypotension & vasodilation related to the use of epidural analgesia

R/o narcotic & anesthetic-related hypotension & LV depression

Review medications & doses actually being delivered to pt (important concept as they may be changes or incorrectly set following transfer or major movement of pt)

R/o ongoing significant hemorrhage

Fluid Management

Lung transplant pt differ in management from standard postbypass cardiac pt; there is increased capillary permeability & nonfunctional lymphatic drainage of the graft

Goal: keep pt euvolemic during fluid resuscitation. Use colloid-rich solutions when able to use for secondary purpose, e.g., fresh frozen plasma

CVP goal: 4–14 mm Hg; urine output goal: 0.5 ml/kg/hr, keep BUN:Cr ratio at 30–40; monitor daily wt

Fluid resuscitate to functional clinical stability, e.g., urine output, CO, systemic vascular resistance (SVR), MVO_2, lactate level, & base deficit

No single parameter should drive care management decisions, continue monitoring the pt overall clinical status ("big picture") in 1st 24–72 hrs post transplant

Oxygen Delivery and Transfusion Management

Routinely maintain hematocrit above 22, with higher hematocrit goal of up to 30 based on need for improved DO_2 or associated pt comorbidity if those conditions are better served with elevated hematocrit

Close monitoring of postop hemorrhage with correction & replacement

Reverse all heparin effects

R/o & treat DIC associated with underlying pt condition & CPB

Maintain normothermia: 4°C drop in the pt's temp will double bleeding time & will not "correct" with added blood products until the pt's temp is normalized

Low platelet level, or, dysfunctional platelets secondary to CPB, other platelet-related medication

Transfuse platelets if <50,000, or active bleeding

Consider treating for platelet dysfunction if serum creatinine is elevated & renal dysfunction is suspected

DDAVP (will mobilize Von Willebrand factors from storage vesicles) & will temporarily restore platelet function

Cardiac Output

Maintain cardiac index 2.2–3.5 l/M^2
Maintain mixed venous saturation: 60–75%
Keep SVR: between 800 & 1,200
Keep pulmonary vascular resistance: between 80 & 150
Inotropic & vasoactive support
Epinephrine for primary cardiac support
Norepinephrine for primary cardiac support with associated vasodilation
Milrinone for biventricular support & RV dysfunction ± associated pulmonary HTN
Vasopressin (low dose) for isolated peripheral vasodilation
When using inotropes & vasoactive agents, a low-dose polypharmacy is preferred to high-dose monotherapy with side effects
Frequent, serial CO measurements & calculation of perfusion perimeters should be done. Measure serial MVO_2. Monitor response to changes at least hourly until pt is stable

Cardiac Rhythm Management

Sinus HR up to 110 bpm are typical & acceptable if stable perfusion
Sinus tachycardia should not be pharmacologically blunted until other causes are ruled out and/or treated, including:
Hypovolemia and/or hypotension
Inadequate pain control
Sequelae of other therapy or treatments
Generalized metabolic derangement, e.g., hypoxia, acidosis, etc.
Treatment: low-dose β-blockade titrated to effect. AVOID calcium channel blockers due to effect on calcineurin inhibitor drug levels

GI and Nutrition

Nutrition consult on admission to ICU

Consider early, low-volume ("trickle") enteric feed if no plan for extubation within 24 hrs posttransplant

Keep NPO when nearing extubation, allow sips of clears following extubation

If short-term intubation is planned following surgery, advance nutrition via tube feeding as tolerated

Secondary advantage of enteric feeding: many posttransplant medications can be given enterically & this can limit fluid administration

Aspiration is major cause of posttransplant infxn & respiratory compromise; precautions to prevent aspiration include head of bed >30° & use of Proton Pump Inhibitors (PPI)

Immunosuppression

Induction and Maintenance

Induction initiated in OR prior to recipient blood exposure to donor endothelium

Induction continues for up to a week following OR; goal is functionally negate chance of significant acute rejection, & blunt risk of ischemia–reperfusion injury

Concurrent treatment with high-dose steroids & antihistamines

Elevated risk for infxn

Maintenance

Begin calcineurin inhibitors once stable postoperatively, delay if there is nephrotoxicity due to metabolic derangement following transplant surgery

Convert to low-dose tapered steroids following induction

Additional immunosuppressive agents may be used on the basis of clinical stability & organ function; use oral route

Antimicrobials and Prophylaxis

Initial Postoperative Antimicrobial Therapy

Transplanted pt should be started on empiric antibacterial treatment pending airway sample cx results, unless the donor airway specimen gram stain is without neutrophils & organisms

For initial empiric coverage ciprofloxacin, metronidazole, vancomycin & micafungin

Inotropic and Vasopressor Drug Names, Clinical Indication for Therapeutic Use, Standard Dose Range, Receptor Binding (Catecholamines), and Major Clinical Side Effects

Drug	Clinical Indication	Dose Range	Receptor Binding				Major Side Effects
			α_1	β_1	β_2	DA	
Catecholamines							
Dopamine	Shock (cardiogenic, vasodilatory) HF symptomatic bradycardia unresponsive to atropine or pacing	2.0–20 μg kg^{-1} min^{-1} (max 50 μg kg^{-1} min^{-1})	+++	++++	++	+++++	Severe HTN (esp. in pt taking nonselective β-blockers) Ventricular arrhythmias Cardiac ischemia Tissue ischemia/gangrene (high doses or due to tissue extravasation)
Dobutamine	Low CO (decompensated HF, cardiogenic shock, sepsis-induced myocardial dysfunction) Symptomatic bradycardia unresponsive to atropine or pacing	2.0–20 μg kg^{-1} min^{-1} (max 40 μg kg^{-1} min^{-1})	+	+++++	+++	N/A	Tachycardia ↑ ventricular response rate in pt with atrial fibrillation Ventricular arrhythmias Cardiac ischemia HTN (esp. nonselective β-blocker pt) Hypotension
Norepinephrine	Shock (vasodilatory, cardiogenic)	0.01–3 μg kg^{-1} min^{-1}	+++++	+++	++	N/A	Arrhythmias Bradycardia Peripheral (digital) ischemia HTN (esp. nonselective β-blocker pt)
Epinephrine	Shock (cardiogenic, vasodilatory) Cardiac arrest Bronchospasm/anaphylaxis Symptomatic bradycardia or heart block unresponsive to atropine or pacing	Infusion: 0.01–0.10 μg kg^{-1} min^{-1} Bolus: 1 mg IV every, 3–5 min (max 0.2 mg/kg) IM: (1:1,000): 0.1–0.5 mg (max 1 mg)	+++++	++++	+++	N/A	Ventricular arrhythmias Severe HTN resulting in cerebrovascular hemorrhage Cardiac ischemia Sudden cardiac death
Isoproterenol	Bradyarrhythmias (esp. torsade des pointes) Brugada syndrome	2–10 μg/min	0	+++++	+++++	N/A	Ventricular arrhythmias Cardiac ischemia HTN Hypotension
Phenylephrine	Hypotension (vagally mediated, medication induced) ↑ MAP with AS & hypotension ↓ LVOT gradient in HCM	Bolus: 0.1–0.5 mg IV every 10–15 min Infusion: 0.4–9.1 μg kg^{-1} min^{-1}	+++++	0	0	N/A	Reflex bradycardia HTN (esp. with nonselective β-blockers) Severe peripheral & visceral vasoconstriction Tissue necrosis with extravasation
Phosphodiesterase Inhibitors							
Milrinone	Low CO (decompensated HF, after cardiotomy)	Bolus: 50 μg/kg bolus over 10–30 min Infusion: 0.375–0.75 μg kg^{-1} min^{-1} (dose adjustment necessary for renal impairment)	N/A				Ventricular arrhythmias Hypotension Cardiac ischemia Torsade des pointes
Amrinone	Low CO (refractory HF)	Bolus: 0.75 mg/kg over 2–3 min Infusion: 5–10 μg kg^{-1} min^{-1}	N/A				Arrhythmias, enhanced AV conduction (↑ ventricular response rate in atrial fibrillation) Hypotension Thrombocytopenia Hepatotoxicity
Vasopressin	Shock (vasodilatory, cardiogenic) Cardiac arrest	Infusion: 0.01–0.1 U/min (common fixed dose 0.04 U/min) Bolus: 40–U IV bolus	V_1 receptors (vascular smooth muscle) V_2 receptors (renal collecting duct system)				Arrhythmias HTN ↓ CO (at doses >0.4 U/min) Cardiac ischemia Severe peripheral vasoconstriction causing ischemia (esp. skin) Splanchnic vasoconstriction
Levosimendan	Decompensated HF	Loading dose: 12–24 μg/kg over 10 min Infusion: 0.05–0.2 μg kg^{-1} min^{-1}	N/A				Tachycardia, enhanced AV conduction Hypotension

α_1, indicates α-1 receptor; β_1, β-1 receptor; β_2, β-2 receptor; DA, dopamine receptors; 0, zero significant receptor affinity; + through +++++, minimal to maximal relative receptor affinity; N/A, not applicable; IV, intravenous; IM, intramuscular; max, maximum; AS, aortic stenosis; LVOT, LV outflow tract; HCM, hypertrophic cardiomyopathy; AV, atrioventricular.

- Hx of multidrug-resistant bacterial or fungal colonization or preexisting resistant gram-negative colonization (i.e., CF or other forms of bronchiectasis), tailor abx to the preoperative known bacterial isolates (follow cx sensitivities)
- Donor cx results must be checked at 24 & 48 hrs to further direct therapy. In cases in which no organism is identified & little or no purulence was observed during donor bronchoscopy, broad-spectrum empirical treatment can be discontinued after 72 hrs
- In cases in which significant purulence was observed bronchoscopically, antibacterials are often continued for 7–10 days

Posttransplant Infection Prophylaxis

PCP (*Pneumocystis jirovecii*)

There was a 10–20% incidence of PCP in the 1st 6 mo prior to the routine use of ppx (Rodriguez M, et al. *Clin Microbiol Rev*. 2004;17:770–782)

Trimethoprim–sulfamethoxazole 1 DS tablet PO M/W/F or 1 SS tablet OS daily indefinitely. In addition to providing ppx for PCP, trimethoprim–sulfamethoxazole provides ppx for *Listeria*, *Nocardia*, toxoplasmosis, & UTIs.

For those pt with documented allergy to sulfa, ppx alternatives include desensitization to trimethoprim–sulfamethoxazole (1 SS tablet PO daily), atovaquone 1,500 mg daily, dapsone 100 mg daily, & inhaled pentamidine 300 mg q2wk. Note: caution in choosing either dapsone or inhaled pentamidine as alternatives. Neither provides adequate ppx for toxoplasma IgG-positive recipients. Dapsone is associated with methemoglobinemia & hemolytic anemia, which can be severe in pt with G6PD deficiency. Significant cross-reactivity between dapsone & trimethoprim–sulfamethoxazole in non-HIV–infected pt.

Toxoplasmosis

Patients with positive IgG titers against toxoplasma receive lifelong prophylaxis with Bactrim; 1 double strength tablet daily.

Viral Prophylaxis

Among all solid organ transplant recipients, lung transplant recipients have the highest risk of cytomegalovirus (CMV) reactivation & dz in the absence of ppx. Active CMV infxn is associated with donor-positive/recipient-negative (D+/R−) CMV serostatus, rejection, & other invasive infxns (e.g., *Aspergillus* & PCP) & is also a risk factor for posttransplant lymphoproliferative dz. The duration of CMV ppx differs based on type of transplant, level of immunosuppression, & pretransplant serologic status. D+/R− recipients are at the highest risk while D−/R− lung transplant recipients are at the lowest risk & do not require specific CMV ppx.

Valganciclovir is our current drug of choice for CMV ppx. See table later for prophylactic valganciclovir regimen recommendations based on donor & recipient serologic status.

After the prescribed valganciclovir ppx course is completed, CMV virus load should be monitored every month for the following 3 months. Note that in addition to preventing CMV, valganciclovir also simultaneously prevents herpes simplex virus (HSV) & Varicella-Zoster Virus (VZV) outbreaks.

Pt who are D−/R− do not require valganciclovir ppx for the prevention of CMV but do require valacyclovir 500 mg PO BID for 3 mo after transplant for the prevention of VZV & HSV infxns.

CMV, VZV, HSV Prophylactic Strategy		
CMV Donor/Recipient Serologic Status	**Treatment PO Month 0–6**	**Treatment PO Month 6–12**
D+/R–	Valganciclovir (Valcyte) 900 mg daily	Valganciclovir (Valcyte) 900 mg daily
D+/R+	Valganciclovir (Valcyte) 900 mg daily	Valganciclovir (Valcyte) 900 mg daily
D–/R+	Valcyte 900 mg daily	None
D–/R–	Valtrex 500 mg bid	None

Pain Management

If no planned anticoagulation or heparin bolus associated with CPB, then place epidural catheter just before the operation

Generally, do not initiate infusion of epidural until hemodynamically stable & more alert, avoid confounding clinical picture with vasodilation & hypotension

If planned or likely need for systemic anticoagulation, consider placement of regional infusion catheters (e.g., "On-Q Catheter")

Begin infusion immediately postoperatively unless hemodynamically unstable

Systemic Pain Regimen

Used in combo with epidural or locoregional infusion catheters

Opioids;

NSAIDs short term only (risk of nephrotoxicity)

Anxiolytics, low dose as adjuvant to pain control agents

Primary Graft Dysfunction (PGD)

Syndrome consisting of lung injury during the 1st 72 hrs following lung transplant defined as a decreased PaO_2/FiO_2 ratio & the presence of diffuse infiltrates on CXR

Clinically important PGD occurs in about 17% of lung transplant pt & associated with 23% increase in death at 1 yr (Diamond JM, et al. *Am J Respir Crit Care Med*. 2013;187: 527–534)

Consider extracorporeal membrane oxygenation (ECMO) support when ventilatory requirements reach a peak inspiratory pressure of 35 cm H_2O or F_iO_2 surpasses 60% in order to minimize lung injury from aggressive mechanical ventilation & oxidative stress (Gulack BC, et al. *J Thorac Dis*. 2014;6(8):1070–1079)

LIVER, KIDNEY, AND PANCREAS TRANSPLANTATION

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Liver Transplant Patient

Liver transplant is the only treatment for end-stage liver failure

In 2015 7,127 liver transplants were performed in the United States each year including whole or split orthotopic (from a recently deceased donor) & living donor transplant

Immediate Postoperative Management

All liver transplant patients (pt) are transferred directly from the OR to the ICU with NGT in place

Postoperative Lab Work

Immediate BMP (Chem 7), Ca, Mg, PO_4, LFTs, LDH, CBC & PTT/PT/INR

Potassium—monitor for hyperkalemia, due to preservation fluid entering into the circulation & a temp-impaired sodium–potassium transporter

Calcium—monitor for hypoCa & hypomagnesia as transfusion of citrate-containing blood products may drop levels

Magnesium, phosphorus—keep Mg & PO_4 levels high to avoid muscle weakness & seizure

Lactate—lactate levels should normalize quickly but if persisting, suggests hypoperfusion or poor graft function

Every 6 hrs: INR, transaminases for 24 hrs

Every 4 hrs HCT for 24 hrs

Postoperative Imaging

CXR once arrives in ICU, assess for pleural effusions, ETT position

Doppler US once arrives in ICU to assess for fluid collections & liver perfusion/liver parenchyma (assess for preservation injury)

T-tube cholangiogram on POD7 for detection of anastomotic stricture or leakage

Ventilation

Immediate postoperative extubation is the goal if transplantation was uneventful, as intrapleural pressure is lower in spontaneously breathing pt & linked to improved portal, venous & hepatic artery blood flow

Barriers to extubation:

Early graft dysfunction, hypervolemia, hemodynamically instability, pleural effusions, retransplantation, multiorgan transplants

Hemodynamics and Fluid Balance

Intraoperative fluid restriction is necessary, however, postoperative goals are net negative to reduce pulmonary complication & assist with extubation, Goal CVP 5 (not higher than 10 mm Hg)

Sources of hypervolemia include sodium/water retention due to liver cirrhosis, intraoperative "third spacing," & steroid application

Recommend colloid for resuscitation, avoid LR as pt likely have an elevated lactate level

If using resuscitation with D5 monitor for hyperglycemia

Hemodynamic instability may also be caused by myocardial dysfunction during the reperfusion phase & may persist postoperatively, if concerned, obtain an ECHO & assess for an appropriate preload & afterload, & use inotropes (dobutamine, dopamine) if necessary

Daily Management

Daily BMP (Chem 7), Ca, Mg LFTs, LDH, CBC, & PTT/PT/INR should be checked in addition to immunosuppressant monitoring

Daily CXR to assess for pleural effusion, ETT position until extubated

Daily Doppler US to assess for fluid collections (hematoma, abscess) & liver perfusion/liver parenchyma—preservation injury, subcapsular hematoma

Drain Care

Traditionally, 3 Jackson–Pratt (JP) drains are left in place postop (lateral to right lobe, at the common bile duct anastomosis, at the left lobe) in addition to the T Tube

JP drains should be to closed bulb suction

Change in drain quality (color, clarity) & quantity may be signs of complications

T Tube cholangiogram on POD7, overall will remain in place 2–6 wks

Postoperative Complications

Bleeding

10–18% of pt will require reoperation for continued bleeding (Thompson MA, et al. *HPB Surg*. 2014;2014:816246) (DiNorcia J, et al. *J Am Coll Surg*. 2001;219(5):993–1000)

Attributable to lack of clotting factors, fibrinolysis, thrombocytopenia

Be suspicious for bleeding in case of postoperative hypotension or oliguria

Assess drains & hematocrit/Hb frequently after transplantation

Avoid LMWH & prophylax with unfractionated heparin

Hepatic Artery Thrombus

Incidence of approx. 3% in adults, overall mortality is 34% (Bekker JPS. Am J Transplant. 2009;9:746–757)

Risk factors for early HAT included prolonged hepatic artery anastomosis time (>80 min), >7U PRBC intraop, or postop PRBC transfusion (Yang Y, et al. *World J Gastroenterol.* 2014;20(30):10545–1052)

Presentation ranges from asymptomatic pt to markedly rising transaminases, clinical deterioration, fever, & increasing WBC

Dx: Immediate Doppler US, & if findings are suspicious, perform CT angiogram

Normally diagnosed with imaging, if biopsy performed: Foamy hepatocyte degeneration, features of ischemic cholangitis (Limaye AR. In: Tagaya N, ed. *Liver Biopsy After Liver Transplantation, Liver Biopsy—Indications, Procedures, Results*. InTech; 2012)

Tx: Operative management often required with either thrombectomy or correction of arterial anastomosis to restore blood flow. Consider early retransplantation

For mild cases, trials of conservative management including thrombolysis, percutaneous angioplasty, & stent placement have been attempted

Required postop anticoagulation with unfractionated heparin

If thrombosis persists without management, there is a high risk of hepatic abscesses, necrosis of intrahepatic & extrahepatic biliary tree, sepsis, & in the long term, ischemic biliary lesions with nonanastomotic strictures

Restrict platelet transfusion (threshold 20,000) & avoidance of graft swelling (fluid restriction) increase hepatic artery flow

Portal Vein Thrombus or Stenosis

Incidence of approx. 2% incidence in adults (Duffy JP, et al. *J Am Coll Surg.* 2009;208:896–903)

Risk factors include previous portal vein thrombosis or previous portacaval surgery & pt with portal vein reconstruction with an interposition graft

Presentation (POD0-7) includes rapid clinical deterioration & is associated with: severe graft dysfunction, hemodynamic instability, & kidney failure

Dx: Immediate Doppler US, & if findings are suspicious, perform a CT angiogram

Normally diagnosed with imaging, if biopsy performed: normal appearance, may show focal nodular hyperplasia (Limaye AR. In: Tagaya N, ed. *Liver Biopsy After Liver Transplantation, Liver Biopsy–Indications, Procedures, Results*. InTech; 2012)

Tx: Consider early retransplantation, 50% of pt with PVT require retransplantation

Rejection and Graft Dysfunction

Preservation/Reperfusion Injury

Incidence of up to 30%, 2–7% severe in adults

Presentation (POD0-3)

Acute Cellular Rejection

15–25% of liver transplant recipients experience cell-mediated rejection (Maluf DG, et al. *Am J Transplant.* 2005;5(1):149) (Gruttadauria S, et al. *Transplant Proc.* 2005;37(6):2611)

Presentation (POD2-7) may vary from asymptomatic transaminase elevation to fever, graft tenderness, graft dysfunction, jaundice

Dx: Biopsy, portal inflammation, biliary inflammation, endothelitis (Limaye AR. In: Tagaya N, ed. *Liver Biopsy After Liver Transplantation, Liver Biopsy–Indications, Procedures, Results.* InTech; 2012)

Tx: Steroid pulse therapy & increase of immunosuppression, if mild may be treated with increasing of maintenance immunosuppression alone

Any treatment must consider the severity of rejection, the original dz, & the particular medical h/o the pt

Hepatitis C Infection and Acute Rejection

Dx: Biopsy (portal inflammation, lobular activity—may be difficult to distinguish between acute cellular rejection) (Limaye AR. In: Tagaya N, ed. *Liver Biopsy After Liver Transplantation, Liver Biopsy–Indications, Procedures, Results.* InTech; 2012)

Tx: Requires special consideration as treatment with high-dose steroids or T-cell depleting therapy may cause a flare up of HCV progression—may defer treatment (increasing baseline immunosuppression or adding an adjuvant agent) if dx of rejection is unclear or if only mild rejection is suspected

Acute Humoral Rejection

Rare after liver transplantation

Mediated by preformed antibodies against ABO antigens, HLA antigens, or endothelial antigens

Dx: Biopsy (complement fixation & fixation of antibodies, necrosis, neutrophil infiltrates)

Tx: includes B-cell depletion using rituximab (anti-CD20 mab) and/or plasmapheresis

Primary Nonfunction

Reported incidence about 5% with a variation between 1% & 24%, accounting for about $^{1}/_{3}$ of early graft losses after liver transplantation

Risk factors may include increased donor age (reduced repair capacities), graft macrosteatosis (reduced liver flow due to narrowing of the sinusoidal space), long cold ischemia time, small-for-size grafts (i.e., in pediatric transplantation), & other factors (endotoxins from the gut or hepatotoxic agents)

Presentation includes steep rise of transaminases (often on POD2 or 3) constant increase of bilirubin, severe coagulopathy, lactate acidosis, & hypoglycemia

Clinical picture: signs of liver failure such as lack of bile production, hepatic encephalopathy & brain edema, renal failure, & instable hemodynamics

Hyperdynamic circulation. The pt may have either hypotension or HTN, metabolic acidosis, organ hypoperfusion, the clinical picture may mimic signs of sepsis

Dx: Biopsy, centrilobular hepatocyte dropout with hepatocellular necrosis, zone 2 hepatocyte, & bile ductular proliferation

Note: Before a diagnosis of primary nonfunction can made one must rule out HAT, PVT, immunologic or infectious causes. May require imaging including CT, Dopler, Angiography

Tx: Retransplantation, high risk of mortality without retransplantation as a consequence of severe brain damage, sepsis, & multiorgan failure

Sx management:

Detoxification through albumin dialysis (MARS system) that removes albumin-bound & water-soluble toxins leads to improvement of encephalopathy & renal function

Hypoglycemia: constant glucose substitution

Metabolic acidosis (sodium bicarbonate 50–180 mEq diluted in 1L D5W, depending on severity of acidosis)

Bleeding: check coagulation parameters & thromboelastography, administer fresh frozen plasma &, if necessary, replace factors VII, IX, X through factor concentrates

Intracranial edema/HTN: place pt in head up position, check for need of ICP monitoring, use 20% mannitol 0.25 gm/kg infusion, note: hyperosmolality

Encephalopathy: avoid neomycin, administer lactulose via NGT every 6–8 hrs, intubated pt require a CCT scan & EEG follow-up

Renal failure: continuous venovenous hemodiafiltration

Hypotension: initially challenge with colloids & replace red blood cells, then use inotropes such as dopamine, followed by noradrenaline if necessary

Sepsis management:

Ventilation: keep PEEP as low as possible (5 cm H_2O) (negative effects on cerebral edema & hepatic perfusion)

Treat hypoalbuminemia (20% albumin, fresh frozen plasma)

GI bleeding ppx (IV high-dose PPI, 20–40 mg once daily)

Nutrition: enteral nutrition (EN) using liver-specific formulas, avoid IV nutrition

Discontinue all potentially hepatotoxic agents

Antimicrobial Management (see Table 39-1; Antimicrobial Agents for Liver Transplant)

Antifungal

Fungal infxns usually occur within the 1st wks after transplantation

Pt at increased risk: those requiring reoperations or renal replacement therapy, retransplanted pt

Distinguish between colonization (often in bronchial washings, sputum, nasal secretions) & infxn & ppx should be limited to high-risk pt, treatment based on cx data

Table 39-1. Antimicrobial Agents for Liver Transplant

			Organism	Dosing
Antifungal	PROPHYLAXIS	**Fluconazole**	Candida albicans	400 mg PO QD × 6 wks (*for high risk pts*)
		Co-trimoxazole	Pneumocystis	480 mg PO QD × 3–6 mo For renal tx start QOD until Cr <0.5
	THERAPY	**Fluconazole**	Candida albicans	Must be monitored with tacrolimus
		Caspofungin	Noncandida	70 mg IV × 1 then 50 mg IV QD
Antibacterial	PROPHYLAXIS	**Isoniazid** *(If h/o TB, born in Asia/Africa)*	Tuberculosis	200 mg PO QD × 1 yr
		Pyridoxine *(If h/o TB, born in Asia/Africa)*	Tuberculosis	10 mg PO QD × 1 yr
Antiviral	PROPHYLAXIS	**Valganciclovir**	CMV	450 mg BID PO (if normal renal fx) For renal tx start QOD until Cr <0.5
		Valacyclovir	CMV	1 g TID PO
		HBV-Ig	HBV	Can be given as monotherapy but improved with lamivudine
		Lamivudine	HBV	150 mg PO BID or 300 mg PO QD
		PEG-interferon Given with Ribavirin	HCV	Monitored dosing in conjunction with pharmacy support
	THERAPY	**Ganciclovir**	CMV	5 mg/kg IV QD × 2 wks for low change of recurrence × 3 months if high chance of recurrence
		CMV-IgG	CMV—severe infection	2 ml/kg
		Adefovir	HBV	10 mg QD (may be given with HBV-Ig)
		PEG-interferon Given with	HCV	1.5 mcg/kg/wk
		Ribavirin	HCV	400–1,200 mg/d

Antibiotic Prophylaxis

Broad-spectrum abx ppx consisting of meropenem, piperacillin/tazobactam or ampicillin, & gentamicin are commonly used for 3–5 days posttransplant or until all catheters are removed

Note: abx ppx should be kept to a minimum, i.e., 24–48 hrs maximum transplantation due to the risk of increasing drug resistance (gram-negative bacteria!)

TB Prophylaxis

Pt at risk (h/o TB, born in Asia/Africa) may receive ppx × 1 yr

PCP Prophylaxis

Pneumocystis Pneumonia (PCP) ppx posttransplant period for 3–6 mo

CMV Prophylaxis

Cytomegalovirus (CMV) infxn occurs primarily in the 1st 3 mo causing graft dysfunction & is associated with the development of opportunistic infxns, acute rejection, & vanishing bile duct syndrome

Often applied to all recipients except D−/R− recipients

CMV Infection

Presentation includes graft dysfunction, mononucleosis-like sx may include leucopenia, fever, night sweats, arthralgia, neutropenia, thrombocytopenia, & CMV viremia, often affects the GI tract

Dx: Quantitative CMV–RNA detection in blood, biopsy

Tx: Decrease of baseline immunosuppression, addition of ganciclovir

Consider treatment of asymptomatic pt with high viral load (>10,000 copies)

Hepatitis B Prophylaxis

Pretransplant HBV therapy can prevent posttransplant recurrence

Check for anti-Hbs titers & HBV DNA (PCR, blood)

Ppx of pt with mutant HBV forms should include drugs with better resistance profile (tenofovir or adefovir)

Recurrent HBV Infection

As a consequence of posttransplant immunosuppression, HBV recurrence may progress rapidly if prophylactic therapy fails

Dx: Quantitative PCR detection in blood, biopsy

Tx: Adefovir with HBV-Ig

Hepatitis C Prophylaxis

HCV-associated liver cirrhosis is the most common indication for orthotopic liver transplant (OLT)

Posttransplant recurrence is almost certain, resulting in 10- to 20-fold increase in HCV RNA levels after the 1st week, 20–30% cirrhosis after 5 yrs, & a lower long-term outcome compared to other indications for OLT

HCV Prophylaxis after Orthotopic Liver Transplant

Few studies are avail. showing mixed results regarding the efficacy of PEG-interferon alfa-2a ppx ± Ribavirin with sustained viral response (SVR) rates between 0% & 33%

Adverse effects (mostly anemia) are common (up to 50%)

While PEG-IFN + Ribavirin, if tolerated, may have beneficial effects on histologic changes & HCV–RNA levels, standard preemptive therapy cannot be recommended

Recurrent HCV Infection

Generally, response rates to treatment are low due to the combined bone marrow suppressive effects of interferon & immunosuppressants & side effects of ribavirin frequently requiring dose reduction or discontinuation of treatment

Consider decrease of immunosuppression in case of severe HCV infxn (adjust tacrolimus levels depending on time after transplantation & individual immunologic risk) & avoid steroid bolus treatment for mild acute rejection if possible (increase/add MMF)

Early virologic response (EVR) defined as negative HCV–RNA or 2-log decrease of HCV–RNA is a positive predictor of SVR

Standard therapy: PEG-interferon (1.5 mcg/kg/wk) + Ribavirin (400 mg–1,200 mg/d) offer good results (SVR >30% on average) with an EVR >50%

However, interferon intervention is associated with a higher risk of acute & chronic rejection

Side effects include myelosuppression, hemolysis, rejection, infxn, & depression

Immunosuppression

Immunosuppressive protocols vary with center preference.

Induction Therapy

Traditionally, induction therapy has been minimized transplant recipients out of concern for recurrence of or HCV. However recent literature has begun to support induction therapy.

Agents generally used for induction include antithymocyte globulin or IL-2RA (Table 39-2; Immunosuppressive Agents). With appropriate antimicrobial ppx, recent literature does not show increased rates of infxn (including CMV), & there may be a role for expanding induction therapy for liver transplants in order to minimize use of steroids or Calcineurin inhibitor (CNI) agents (Rostaing L, et al. *Transplant Rev.* 2012;26(4):246–260)

Immediate Postoperative Immunosuppression

Either tacrolimus is started within 12 hrs of OLT or alternatively simulect.

In addition, methylprednisolone is started at high dose & tapered over the 1st week

Maintenance Immunosuppression

Maintenance immunosuppression usually consists of tacrolimus & steroids, often combined with MMF (see Table 39-2; Immunosuppressive Agents)

Table 39-2. Immunosuppressive Agents

	Agent	Mechanism of Action	Dosing	Side Effects
INDUCTION AGENTS	**Corticosteroids**	Inhibit formation of arachidonic acid through binding to intracellular receptors Broad effects on cellular response although little specific	High dose (500 mg Prednisolone IV) induction, with subsequent taper	Osteopenia, hypertension, hyperlipidemia, hirsutism, ulcer disease, glucose intolerance, cataracts, psychosis, weight gain, and many more
	Basiliximab (Simulect)	Inhibits activation and proliferation of T-cells	20 mg IV induction and POD4	hypersensitivity
	Antithymocyte globulin (ATG/ Fresenius)	Polyclonal, purified IgG fraction directed against human lymphocytes—complement dependent lysis of AICD	8 mg/kg IV induction	infusion reaction, anaphylaxis, serum sickness (rash, joint, and muscle aches), thrombocytopenia, leukopenia, antibody formation, increased risk of malignancies
	Thymoglobulin		1.5 mg/kg IV induction	
	Alemtuzumab (Campath 1H)	Humanized monoclonal CD52-specific IgG1 that rapidly depletes not only T-cells but also NK-cells, B-cells	30 mg IV inuduction and POD1 (give with chlorpheniramine 30 mg IV or diphenhydramine 30 mg IV)	Severe pancytopenia
MAINTENANCE AGENTS	**Tacrolimus** (Prograf)	Binds to FK-binding protein and inhibits calcineurin (calcineurin inhibitor: CNI), which ultimately inhibits IL-2 production and production of proinflammatory cytokines, thus inhibiting T-cell proliferation	0.15 mg PO bid (or 0.01–0.05 mg/kg/ 24 hrs IV) Target trough levels 8–12 ng/ml	nephrotoxicity, neurotoxicity, hypertension, hyperglycemia, hyperkalemia, hypomagnesemia, posttransplant lymphoproliferative disorder (PTLD) CYTOCHROME 450 inhibitor—fluconazole will increase tacrolimus levels
	Mycophenolate mofetil (MMF/ CellCept)	Inhibition of inosine monophosphate dehydrogenase and production of guanosine nucleotides prevents T-cell and B-cell proliferation	1 mg PO BID (renal)	Side effects are myelosuppression, gastrointestinal symptoms (nausea, vomiting, diarrhea, abdominal pain)
	Mycophenolate sodium (Myfortic)		1.5 mg IV BID (liver)	

Steroid withdrawal or minimization is common with goal being to avoid prolonged use given side effect profile

Nutrition

Preoperative malnutrition is common, TPN may be required

EN should be started as soon as possible

In the intubated pt, OGT/NGT/NJT may be used for enteral feeds but residuals need to be determined to assess volume absorbed

Glucose Management

Strict glucose control is important in all postoperative pt, may require insulin gtts in the initial postoperative period

Kidney Transplant Patient

Kidney transplantation is the treatment of choice for pts with end-stage renal disease (ESRD)

The 5-yr survival rate for transplant pt (85.5%) if more than twice that for dialysis pt (35.8%)

In 2015, 17,878 kidney & 719 combined kidney/pancreas transplants were performed in the Unites States

Immediate Postoperative Management

In general, kidney transplant pt are transferred from the OR to the PACU & then to a transplant floor, rarely kidney transplant pt require OR to ICU management

Postoperative Lab Work

Immediate BMP (Chem 7), Ca, Mg, PO_4, CBC

Potassium—monitor for hyperkalemia, due to preservation fluid entering into the circulation, a temp impaired sodium–potassium transporter & preexisting renal failure

Repeat lab work at 6 hrs postop

Postoperative Imaging

If arriving in ICU for vent management, CXR to assess for pleural effusions, ETT position

Immediate postop Doppler US to assess for fluid collections & resistive indices (Goal <0.6)

Ventilation

Rarely are postop renal transplant pt ventilated but if requiring respiratory support often secondary to volume overload but unlike liver transplants, renal transplant requires a higher level of resuscitation

Hemodynamics and Fluid Balance

Maintain intravascular volume at normal or slightly increased levels with a (CVP) goal of 10 mm Hg

Replace urine output with half-NS on a milliliter per milliliter basis

Half-NS is chosen because the sodium concentration of the urine from a newly transplanted kidney is 60–80 mEq/l

If the pt is noted to be hypovolemic, isotonic/NS boluses are given in 500 ml increments—living related donors tend to produce more urine more rapidly than deceased donors

Hypervolemia is managed by the use of diuretics, most commonly furosemide

Dialysis may be required for fluid overload not responsive to diuretics & for hyperkalemia in delayed graft function

Daily Management

Daily BMP (Chem 7), Ca, Mg, PO_4, CBC in addition to immunosuppressant monitoring

Doppler US to assess for fluid collections & renal perfusion/parenchyma based on clinical factors (i.e., decrease in urine, rising creatinine)

Postoperative Complications

Bleeding

Hemorrhage is uncommon, if from the vascular anastomosis (arterial & venous) may require continued resuscitation in the ICU even after primary control was obtained in the OR

Ongoing bleeding may be from unligated vessels in the hilum of the transplanted kidney or from the retroperitoneal surface

Graft Thrombosis

Presentation of graft thrombosis includes rapid decrease in urine output, rise in creatinine, & tenderness over graft. Generally presents on POD0-2. The occurrence graft thrombosis is low (<1%)

Dx: US of graft

Tx: Operative management with thrombectomy & revision

Rejection and Graft Dysfunction

Delayed Graft Dysfunction

Presentation includes anuria or oliguria postoperatively, creatinine does not decline
Dx: R/o rejection & thrombosis with biopsy & US
Tx: supportive care, dialysis

Acute Cellular Rejection

Presentation includes (POD) decreasing urine output, rising creatinine, tenderness over the graft
Dx: Biopsy
Tx: Steroid pulse therapy & increase of baseline immunosuppression

Acute Humoral Rejection

Presentation includes (POD) decreasing urine output, rising creatinine, tenderness over the graft
Dx: Biopsy (complement fixation & fixation of antibodies, necrosis, neutrophil infiltrates)
Tx: includes B-cell depletion using rituximab (anti-CD20 mab) and/or plasmapheresis

Antimicrobial Management

Ppx against PCP & CMV is initiated on POD1 unless D-/R-

Immunosuppression Management

Induction

The goal of induction therapy is to prevent acute rejection during the early posttransplantation period by providing a high degree of immunosuppression at the time of transplantation. Induction treatment allows delaying the application of calcineurin inhibitors, thus reducing nephrotoxic side effects in the early period after transplantation.
All of the induction immunosuppressive agents currently used are biologic agents & are either monoclonal (daclizumab, basiliximab, alemtuzumab) or polyclonal (antithymocyte globulin [equine] or antithymocyte globulin [rabbit]) antibodies

Maintenance

The level of chronic immunosuppression is slowly decreased over time to help reducing the overall risk of infxn & malignancy

The major immunosuppressive agents that are currently being used in various combination regimens are calcineurin inhibitors (tacrolimus, cyclosporine), MMF, mycophenolate sodium (Myfortic), corticosteroids (primarily oral prednisone), azathioprine, & rapamycin (sirolimus)

Triple immunosuppression consisting of tacrolimus, MMF, & prednisone is the most widely used maintenance immunosuppressive regimen

Tacrolimus levels must be carefully monitored. Initially, levels can be kept in the range of 10–15 ng/ml &reduced after 3 mo (5–10 ng/ml) to reduce the risk of nephrotoxicity

Glucose Management

Strict glucose control is important in all postoperative pt, may require insulin gtts in the initial postoperative period

Pancreas Transplant Patient

In 2015, 228 pancreas transplants and 719 combined pancreas/kidney transplants were performed in the States

Pt survival rates at 1 yr were >95% in each recipient category

Pancreas transplant recipient fall under 3 categories

SPK, usually from the same deceased donor in a pt who has both ESRD & insulin-dependent diabetes

PAK, in a pt with nephropathy corrected by a kidney transplant & is now waitlisted for a pancreas transplant

Pancreas transplant alone (PTA), in a pt with normal kidney function. PTA should be considered a therapy in pt only who exhibit

Immediate Postoperative Management

All pancreas transplant pt are transferred directly from the OR to the ICU, regardless of ventilator requirements

Kept NPO with OGT if ventilated, NGT if extubated

Postoperative Lab Work

BMP (Chem 7), Ca, Mg, PO_4, CBC, urinary amylase (in bladder drained recipients), serum amylase & lipase, & C peptide levels

Repeat lab work at 6 hrs postop

Postoperative Imaging

If arriving in ICU for vent management, CXR to assess for pleural effusions, ETT position

Immediate postop Doppler US to assess for fluid collections & parenchymal perfusion

Ventilation

Rarely are postop pancreas transplant pt ventilated but if requiring respiratory support, often secondary to volume overload

Hemodynamics and Fluid Balance

Avoid dextrose-containing solutions as this may cause elevation in blood glucose & make it more difficult to assess endocrine function of the allograft

Daily Management

Daily BMP (Chem 7), Ca, Mg LFTs, LDH, CBC, urinary amylase (in bladder drained recipients), serum amylase & lipase, & C peptide levels

Daily CXR to assess for pleural effusion, ETT position until extubated

Daily Doppler US to assess for fluid collections (hematoma, abscess) & perfusion

Postoperative Complications

Graft Thrombosis

Presentation (POD1-2), often VT. Prevention with aspirin often employed.

Dx: Doppler US

Tx: Thrombectomy

Pancreatitis Secondary to Ischemia during Preservation

Dx: Pain over graft site elevated lipase/amylase

Tx: Conservative management with octreotide, bowel rest, supportive care

Rejection

Rejection in pancreas transplant is subtle, only 5–20% of pt reporting any sx (Sutherland, *Gut and Liver* 2010;4:450)

Acute Rejection

Dx: Biopsy, bladder-drained transplants monitor urine amylase, enteric-drained transplants monitor glucose disappearance

Tx: 7- to 14-day course of mono- or polyclonal antibody therapy (Sutherland, *Gut and Liver* 2010;4:450)

Antimicrobial Management

Prophylaxis

IV antimicrobials are administered with coverage to include bacterial, viral, & fungal infxns (vancomycin, piperacillin-tazobactam, Ganciclovir/acyclovir fluconazole), course is dependent by institution & may range from 24 to 48 hrs to 7 days

Ppx against PCP & CMV is initiated on POD1 unless D−/R−

Immunosuppression Management

Induction

The most common agents used are Thymoglobulin, alemtuzumab, basiliximab, or daclizumab

Maintenance

The majority of recipients receive tacrolimus, MMF, & steroids as maintenance immunosuppression

Glucose Management

Goal blood–sugar monitoring performed q1h to maintain blood glucose below 150 mg/dl with aggressive utilization of gtt if levels >150 mg/dl>150 mg/dl, as uncorrected hyperglycemia may be deleterious to the pancreatic β-cells of the allograft

BONE MARROW AND STEM CELL TRANSPLANTATION

BRETT E. GLOTZBECKER, MD • EDWIN PASCAL ALYEA, III, MD

Background

Curative therapy for patients (pt) with inborn errors of metabolism, bone marrow failure syndromes, immune deficiencies, & hematologic malignancies

Increasing use of bone marrow & stem cell transplantation

Increasing number of transplants in older adults older than 65 yrs

As of 2014, in the United States, there were an estimated 11,000 autologous & 8,000 allogeneic stem cell transplants/year (CIBMTR, 2016)

Definitions

Autologous Stem Cell Transplant

Use of an individual's own hematopoietic progenitor cells to reestablish hematopoiesis after exposure to high doses of chemotherapy or chemoradiotherapy

Allogeneic Stem Cell Transplant

Use of an HLA matched donor's hematopoietic progenitor cells

Efficacy derived from (1) infusion of tumor-free graft & (2) graft versus dz effect mediated by donor lymphocytes

Comparison of Autologous to Allogenic Bone Marrow Transplantation		
	Autologous	**Allogeneic**
Advantages	No need for HLA match	Graft vs. tumor activity
	No need for immune suppressive medications	Stem cells free of tumor & unharmed by chemotherapy
	Lower risk of complications	Lower risk of relapse
Disadvantages		Donor availability
		Risk of graft vs. host dz (GVHD)
	Higher risk of relapse	Higher risk of complications

Other General Considerations

Stem Cell Source

Peripheral blood results in faster count recovery

Bone marrow & cord blood stem cells are also used

Cord blood stem cells recover slowly. Pt tend to be at greatest risk of complications resulting from prolonged neutropenia & immature T cell phenotype.

Neutrophil engraftment

Absolute neutrophil count (ANC) ≥500 cells/ml on 2 consecutive days or 1,000 cells/ml on 1 day

Platelet engraftment

Unsupported platelet count >20,000 cells/ml

Comparison of 3 Potential Stem Cell Sources			
Characteristic	**BM (Bone Marrow)**	**PBSC (Peripheral Blood Stem Cells)**	**UCB (Umbilical Cord Blood)**
HLA matching requirements	≥5/6 or 9/10	≥5/6 or 9/10	≥4/6
Time to neutrophil engraftment	22–24 days	10–14 days	1 Cord—40 days 2 Cords—12–24 days
Total nucleated cells (TNC)	$\geq 3 \times 10^6$ cells/kg recipient	$\geq 6 \times 10^6$ cells/kg recipient	$1.5–2 \times 10^7$ cells/kg recipient
Time to identify & collect cells	~2 mo	~2 mo	<1 mo
Risk of acute GVHD	Intermediate	Highest	Lowest
Risk of chronic GVHD	<PBSC	Highest	<PBSC

Indications

Malignant

Acute lymphoblastic leukemia, acute myelogenous leukemia, myelodysplastic syndrome, non–Hodgkin's lymphoma, Hodgkin's lymphoma, chronic myelogenous leukemia, chronic myelomonocytic leukemia, neuroblastoma

Nonmalignant

Bone marrow failure syndromes, hemoglobinopathies, immunodeficiencies

Complications

Infusion Reactions Associated with Stem Cell Infusion

Fevers

May be due to cryopreserving agent (DMSO), contaminated product, cytokines released during processing, or coincidental coinfxn

If fevers >100.5°F, send blood cx + stem cell cx & start broad-spectrum abxs until cx are negative

Dimethyl Sulfoxide (DMSO) Toxicity

Autologous stem cells are routinely cryopreserved with DMSO

Sx—nausea, vomiting, headaches, dizziness, itching, erythema

Signs—hypotension, arrhythmias, anaphylaxis

Lab abnormalities—mild intravascular hemolysis due to remaining red blood cells (RBCs) in marrow, RBC in urine, elevated LDH

Treatment—saline for volume expansion & then dopamine drip for continued hypotension, if sx persist, remove DMSO from product

Special Circumstances

Patent foramen ovale—in pt with elevated right-sided pressure, there may be right-to-left shunting of blood flow

Clinical scenario—infusion of stem cell products may result in a paradoxical cerebral emboli due to cellular aggregation

Prevention—standard blood filter for all stem cell products

Posttransplantation

Engraftment Syndrome

Definition

Inflammatory condition that usually occurs within the 1st 2 wks

Etiology

Mediated by activated leukocytes & release of proinflammatory cytokines

Sx

Fevers, manifestations of vascular leak including hypotension, shortness of breath, hypoxia, organ dysfunction including renal or hepatic, or diarrhea without another cause

Examination

Erythematous rash, wt gain & peripheral edema or ascites suggestive of 3rd spacing

Imaging

CXR: bilateral infiltrates, noncardiogenic pulmonary edema

Differential

Dx of exclusion

Other etiologies—infxn & hyperacute GVHD

Treatment

Methylprednisolone—typically start at 1 mg/kg/d & taper over 7–10 days

Acute GVHD

General

Most common morbidity of allogeneic stem cell transplantation

Incidence

Standard ppx (calcineurin inhibitor [CI] & methotrexate)

10–50% matched sibling; 50–80% matched unrelated donors

Onset

Previously assigned to all allogeneic manifestations before day 100. Now recognized that there can be late-onset aGVHD (frequently after reduced-intensity transplantation)

Risk factors

Increasing HLA disparity, older age of recipient or donor & female donor, cytomegalovirus (CMV) status of the donor & host

Clinical

Principal target organs of acute GVHD are the skin, gut, & liver

Acute GVHD Scale Based on Signs/Symptoms by Organ System

Organ	Stage	Description
Skin	1	Maculopapular rash: <25% skin. No Sx
	2	Maculopapular rash: 25–50% skin with pruritus or sx
	3	Macular, papular, or vesicular eruption with bullous desquamation on >50% skin
	4	Generalized erythroderma with bulla
Gut	1	Diarrhea: >500 mg/d or persistent nausea
	2	Diarrhea: >1,000 mg/d with or without N/V
	3	Diarrhea: >1,500 mg/d
	4	Diarrhea: >2,000 mg/d or >90 ml/kg or Severe abd pain with or without ileus
Liver	1	Bilirubin 2.0–3.0 mg/dl
	2	Bilirubin 3.1–6.0 mg/dl
	3	Bilirubin 6.1–15.0 mg/dl
	4	Bilirubin >15.0 mg/dl

Acute GVHD Cumulative Grading Scale

Overall Grade	I	II	III	IV
Skin	1–2	3	–	4
Gut	0	1	2–3	4
Liver	0	1	2–4	–

Treatment

Corticosteroids most effective: complete remission rates ~50%

Grades II–IV GVHD: Methylprednisolone: 2 mg/kg/d

Retrospective studies support methylprednisolone: 1 mg/kg/d in pt with Grade II GVHD (Mielcarek M, et al. *Blood.* 2009;113(13):2888–2894). Current response & survival data do not support adding other immunosuppressants to corticosteroids as standard of care for aGVHD

Add 2nd agent if progressive dz on steroids within 3–5 days or no improvement at 1 wk

Options include mycophenolate mofetil, antithymocyte globulin, infliximab, etanercept, pentostatin, or extracorporeal photopheresis

Current response & survival data do not support the choice of any specific agent for secondary therapy of steroid refractory aGVHD.

Prognosis: Pt with moderate to severe aGVHD have significantly higher mortality rates than those with mild dz

Infectious Complications

Neutropenic Fever

Definition

Single temp of >38.3°C (101°F) or

Sustained temp >38°C (100.4°F) for more than 1 hr in

Pt with an ANC <500 cells/μl or <1,000 cells/μl with an expected nadir of <500 cells/μl

Treatment

Standard empiric therapy in high-risk pt includes coverage for gram-negative bacteria including Pseudomonas → antipseudomonal B-lactam (cefepime), carbapenem (imipenem or meropenem), or piperacillin–tazobactam

Pt who are colonized with *Staphylococcus aureus,* have indications of a central line, skin, or soft tissue infxn or are clinically unstable should be started on vancomycin

If febrile after 96 hrs on these agents, 1–3-β-glucan & galactomannan (aspergillus) assay should be sent, & an antifungal agent should be started

Pt on piperacillin–tazobactam may have false-positive galactomannan assays

Pt treated with intravenous immunoglobulin (IVIG) or albumin may have false-positive glucan tests

Granulocyte transfusions in granulocytopenic pt in whom gram-negative bacterial or fungal infxns are not controlled by antimicrobials remain controversial & are not currently recommended

Infections (Figure 40-1 and Figure 40-2)

Based on time posttransplant & if on medications to prevent or treat GVHD

Days 0–30

Infxns related to conditioning therapies & neutropenia—bacterial infxns from the GI tract or catheter related, aspergillosis, candidemia

Day 30–80

Opportunistic infxns—CMV, PCP, toxoplasmosis, nocardia, aspergillosis

Day 180+

Encapsulated organisms (*Streptococcus pneumoniae, Haemophilus influenzae, Klebsiella pneumoniae*), varicella zoster virus (VZV), *Pneumocystis jiroveci*

Days 0−180+

Respiratory viruses—parainfluenza, influenza, respiratory syncytial virus (RSV), adenovirus

Figure 40-1. Timeline for Typical Infections after Autologous Stem Cell Transplant

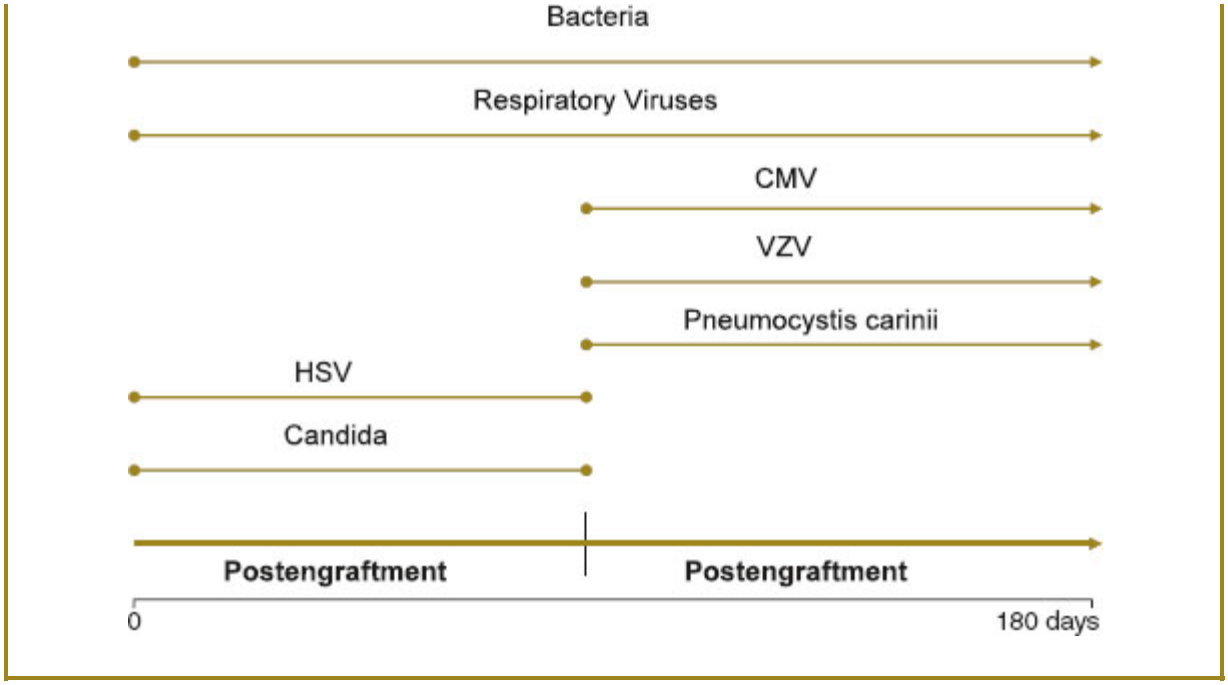
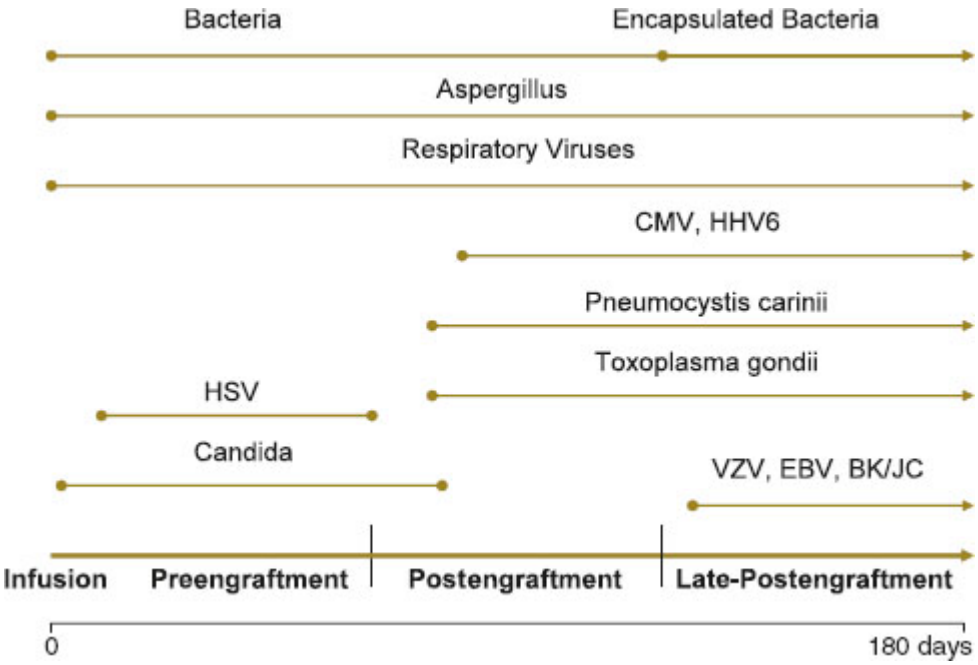


Figure 40-2. Timeline for Typical Infections after Allogeneic Stem Cell Transplant


Bacteria
Encapsulated Bacteria
Aspergillus
Respiratory Viruses
CMV, HHV6
Pneumocystis carinii
Toxoplasma gondii
HSV
Candida
VZV, EBV, BK/JC
Infusion
Preengraftment
Postengraftment
Late-Postengraftment
0
180 days

Prevention

Ppx with acyclovir to prevent herpes simplex virus (HSV)/VZV reactivation & TMP-SMX or atovaquone to prevent *P. jiroveci* pneumonia is standard of care at most centers

Ppx with a fluoroquinolone to prevent gram-negative rod infxns & an azole to prevent fungal infxns is widely practiced

Treatment

CMV dz (viremia + organ toxicity – colitis/pneumonia)

Ganciclovir 5 mg/kg IV every 12 hrs until sx resolve & viral load negative × 2 → followed by suppressive dose – valganciclovir 900 mg/d

IVIG 500 mg/kg 3 times/wk × 6 doses (may be useful in pneumonia)

HSV—severe mucositis, cutaneous dz, hepatitis

Acyclovir—5 mg/kg every 8 hrs; may need Foscarnet if acyclovir resistant

VZV—reactivation as shingles is common; also at risk for dissemination

Limited involvement dz

Valacyclovir 1,000 mg TID or famciclovir 500 mg TID

Disseminated VZV (or pulmonary or liver involvement)

Acyclovir—10 mg/kg IV TID

Adenovirus—pharyngitis, pneumonitis, enteritis, hepatitis, hemorrhagic cystitis

No effective proven treatment

Cidofovir—5 mg/kg IV qwk × 2 wks, followed by 4 doses every other week (prehydrate & administer probenecid prior to each dose)

RSV—pneumonia causes high morbidity/mortality posttransplant

No proven treatment in adults

Consider IVIG 500 mg/kg QOD for 5–7 days

Influenza

For influenza A or B—oseltamivir 75 mg PO BID

Pneumocystis jiroveci pneumonia (PJP)—goal to start steroids within 72 hrs of PJP therapy

High-dose Bactrim—15–20 mg/kg/d divided every 6–8 hrs + prednisone 40 mg PO b.i.d. days 1–5, 40 mg daily days 6–10, then 20 mg daily days 11–21

Or atovaquone 750 mg PO t.i.d.

Or dapsone 100 mg daily + primaquine 15 mg daily

Candidemia

Echinocandins—caspofungin—70 mg IV daily, followed by 50 mg IV daily or micafungin 100 mg IV daily

Azoles—fluconazole—800 mg load then 200–400 mg daily; voriconazole 6 mg/kg IV q12h for 2 doses & then 3 mg/kg IV q12h

AmBisome—3–5 mg/kg/d IV over 120 min

Invasive aspergillosis

Azoles—voriconazole (preferred)—6 mg/kg IV q12h for 2 doses & then 3 mg/kg IV q12h; isavuconazole—372 mg q8h for 6 doses & then daily)

AmBisome—3–5 mg/kg/d IV over 120 min

Zygomycosis

AmBisome—3–5 mg/kg/d IV over 120 min. Dose could be increased to 7.5–10 mg/kg

Isavuconazole—372 mg q8h for 6 doses & then daily; posaconazole—800 mg/d divided b.i.d. or q.i.d.

Hepatic Complications

Hepatic veno-occlusive disease (VOD)

Alternative name

Sinusoidal obstruction syndrome

Incidence

5–60% of pt following stem cell transplantation

More common after allogeneic transplants

Usually occurs days 0–30 but may be as late as day 90

Etiology

Initial: Endothelial injury of the sinusoids of hepatocytes in zone 3 by cytokines & free radicals

Cascade of events including thickening of the subintimal zone of the sublobular venules leading to hepatic congestion, hepatocyte necrosis, & centrilobular sinusoidal fibrosis

Risk factors

Pretransplantation related factors:

Liver dysfunction, h/o viral hepatitis, prior liver radiation, tumor in the liver, estrogen use, iron overload, recent gemtuzumab ozogamicin use, previous transplant

Transplantation-related factors

High-dose conditioning regimens including total body irradiation or busulfan (with cyclophosphamide), sirolimus use in combination with high-dose conditioning, allogeneic donor

Clinical criteria for dx of VOD

Seattle criteria

Presence of 2 or more of the following before day 30 post-hematopoietic stem cell transplant (HSCT):

Hyperbilirubinemia (>2 mg/dl)

Right upper quadrant pain/hepatomegaly

Ascites ± wt gain >2% baseline

Baltimore criteria

Bilirubin ≥2 mg/dl by day 21 + at least 2 of the following:

Hepatomegaly

Ascites

Wt gain >5% baseline

Imaging—noninvasive testing can support the dx

US with Doppler to look for reversal of flow/ascites

Dx

Liver biopsy & wedged hepatic venous pressure gradient gold standard

Risk in the setting of the pt being coagulopathic

Biopsy by the transvenous route

Prevention

Use of ursodeoxycholic acid for prevention has been associated with a decreased incidence of VOD (Tay J, et al. *BBMT.* 2007;13:206–207). It is most effective if started 2 wks before conditioning therapy in pt at high risk of developing VOD.

Treatment

Recently, FDA approved defibrotide

Single-stranded oligodeoxyribonucleotides derived from porcine mucosal DNA

Treatment has been associated with day +100 posttransplant survival rates of 32–79% (vs. 10–25% expected) (Richardson PG, et al. *Blood.* 2016;127:1656–1665)

Supportive—diuresis, transfusion, continuous veno-venous hemofiltration, pain control

Prognosis

50–80% of pt' sx with mild dz resolve over 2–3 wks

Untreated VOD with multiorgan failure is associated with >80% mortality

Idiopathic Pneumonia Syndrome (IPS)

Definition

Widespread alveolar injury following hematopoietic stem cell transplantation (HSCT) in the absence of lower respiratory tract infxn & cardiac causes

Incidence

Incidence is 3–15% with median time of onset at 6–7 wks

Etiologies

Direct toxic effect of the conditioning regimens

Undiagnosed pulmonary infxns

Release of inflammatory cytokines

Association between IPS & severe GVHD in several studies

IPS is less common after autologous HSCT

Diagnostic criteria

Widespread alveolar injury (must meet all):

Multilobar infiltrates on CXR or CT scan

Signs & sx of pneumonia

Evidence of abnormal pulmonary physiology (increased alveolar–arterial oxygen gradient or the need for supplemental oxygen)

Absence of lower respiratory tract infxn

Negative bronchoalveolar lavage or lung biopsy

Ideally negative test 2–14 days later

Treatment

Supportive therapy

Supplemental oxygen, mechanical ventilation

Empiric abx coverage while awaiting cx data

Immunosuppressive therapy

High-dose steroids—1–2 mg/kg/d for 3 days, followed by a taper by 50% every 3 days

The addition of etanercept—25 mg subcutaneaosly twice weekly × 4 wks associated with improved response rates & overall survival (Tizon R, Frey N, Heitjan DF, et al. *BMT.* 2012;47:1332)

Prognosis

Mortality is 50–85% in pt not requiring ventilation & ~95% in pt requiring ventilation

Diffuse Alveolar Hemorrhage

Definition

Acute form of noninfectious respiratory failure

Usually occurs within the 1st month of stem cell transplantation

Incidence ranges from 1% to 21% in autologous stem cell transplant

2–17% in allogeneic stem cell transplant recipients

Etiology

Not well-established

Possible cytokine release by engrafting cells

Diagnostic criteria

Multilobar pulmonary infiltrate

Sx & signs of pneumonia

Abnormal pulmonary physiology with increased alveolar to arterial oxygen gradient & restrictive ventilatory defect

Absence of infxn compatible with the dx

Dx

Bronchoalveolar lavage with bloodier return from 3 subsegmental bronchi or

20% or more hemosiderin-laden macrophages or

Blood in ≥30% of the alveolar surfaces of lung tissue

Risk factors

Toxic effects of the conditioning regimens, older age, h/o thoracic irradiation, & renal insufficiency

Treatment

No prospective, randomized trials

Steroids 1,000 mg/d × 3 days; taper by 50% every 3 days

Small studies of up to 2,000-mg steroids/day show no survival benefit (*Am J Respir Crit Care Med.* 2002;166:641)

Prognosis

Majority require mechanical ventilator support

Reported mortality rate is between 64 & 100%

Bronchiolitis Obliterans Syndrome

Definition

Inflammatory dz of the small airways, granulation in bronchioles leading to airway obstruction & air trapping

Occurs anytime from 3 mo to 10 yrs after transplantation

Incidence ranges from 2 to 26% in allogeneic stem cell transplant recipients

Sx

Insidious onset—dry cough, dyspnea, wheezing

Dx

Chest radiograph may show hyperinflation or be normal

High-resolution CT is the best radiographic study. Shows narrowing of small airway bronchiectasis, centrilobular nodules, & mosaic attenuation

Pulmonary Function Tests (PFTs)—Obstructive pattern—decrease in FEV1 by ≥10% from pretransplant with FEV/FVC <0.7

Lung biopsy is gold standard. Shows fibrinous obliteration of the lumen of the bronchioles

Risk factors

Usually occurs in association with hypogammaglobulinemia & chronic GVHD

Early posttransplant respiratory viral infxns, older age, busulfan-based conditioning, peripheral blood stem cell source, female donor to male recipient, previous pneumonitis, low FEV1/FVC at the time of transplant

Treatment

Prolonged steroids, FAM (Flovent, azithromycin, montelukast) with some benefit (*BBMT.* 2016;22:710); some centers report benefit with extracorporeal photopheresis

Prognosis

Poor—only 8–20% have improvement in PFTs with 3-yr mortality of 65%

Bronchiolitis Obliterans Organizing Pneumonia (BOOP)/Cryptogenic Organizing Pneumonia (COP)

Definition

Inflammatory dz resulting in granulation tissue within ducts & air sacs

Onset 1–12 mo (median—4 mo) after transplantation

Sx

Fever, dry cough, shortness of breath, crackles on exam

Dx

Chest radiograph/CT may show nodular ground glass opacities

PFTs—Restrictive pattern, reduced DLCO & lung volumes

Lung biopsy is gold standard. Shows Masson bodies—organized polypoid granulation tissue in distal airways extending to alveoli

Risk factors

Acute & chronic GVHD, unrelated donor

Treatment

Prednisone—1–2 mg/kg/d with slow taper over several mo

Prognosis

About 80% of pt with BOOP/COP after hematopoietic stem cell transplantation will respond to treatment

Pulmonary VOD

Definition

Intimal proliferation of fibrous tissue in the pulmonary venules

Usually occurs 6–8 wks after stem cell transplantation

Incidence

Very rare, incidence unknown as overlap exists with pulmonary HTN

Etiology

Endothelial injury from infxns, carmustine, & bleomycin

Clinical features

Nonspecific—dyspnea on exertion, lethargy, cough, chest pain, cyanosis, orthopnea, hemoptysis, diffuse alveolar hemorrhage (DAH)

Dx

Studies—x-rays—pleural effusions, Kerley B lines

Right-sided heart catheterization—difficulty obtaining PA wedge pressure (if obtained normal or low)

Lung biopsy—shows intimal proliferation

Presence of 20% or more hemosiderin-laden macrophages

Risk factors

Exposure to BCNU, bleomycin

May be associated with hepatic VOD

Treatment

Steroids—1–2 mg/kg/d—anecdotal reports

Prognosis—grim

2003—case report—40 pt—4 survivors (*J Pediatr Hematol Oncol.* 2003;25:405)

Neurologic Complications

Posterior Reversible Encephalopathy Syndrome

Etiology

Unique complication of CIs

Often occurs in association with new-onset HTN

Development is not directly correlated with drug level

Cessation of the drug does not always lead to resolution

Sx

Insidious onset of headache, confusion or decreased consciousness, visual changes, cortical blindness, or seizures

Radiographic evaluation

MRI—white matter edema in the posterior circulation

Treatment

Changing to another agent such as mycophenolate mofetil

BP control is crucial

Prognosis

The majority of cases are reversible within days to wks with withdrawal of the inciting agent & BP control

MRI findings of hyperintense signals on DWI or more extensive brain stem involvement predict worse or irreversible outcomes

CNS Infections

Toxoplasma gondii

Incidence

Up to 1.4% in centers with high seroprevalence

Occurs within the 1st month of transplantation

Clinical

Focal neurologic sx & encephalopathy

Radiology

MRI—multiple mass lesions in the basal ganglia that are typically enhancing but in this population may be nonenhancing or hemorrhagic

Dx

PCR on the CSF for *T. gondii* may also be positive

Treatment

Combination—pyrimethamine, sulfadiazine, & folinic acid

Prognosis

Fair—2003—review of European Group for Blood & Marrow Transplantation data suggests with appropriate therapy up to 40% clinical or radiographic response

CNS aspergillosis

Clinical

Angioinvasive fungal dz

New stroke-like sx or meningeal sx in addition to headaches, focal neurologic signs, or seizures

Radiology

MRI—lesions are often associated with edema, hemorrhage, infarction, & ring enhancement

Dx

Evaluation of spinal fluid is usually not helpful

Risk factors

Early posttransplant (<40 days)—age, HLA mismatch

Late posttransplant (>40 days)—GVHD, CMV infxn

Any time point—neutropenia, lymphopenia, iron overload

Treatment

Antifungal ± neurosurgical procedure

Voriconazole achieves CSF levels → trough plasma levels

Retrospective study suggested lack of clinical efficacy for CNS aspergillosis with amphotericin B

Prognosis

With use of voriconazole ± neurosurgical procedure, reports of survival rates of ~20% (Schwartz S, et al. *Blood.* 2005;106:2641–2645)

Viral encephalitis

Etiology

Human herpesvirus-6 (HHV-6)

Clinical

Limbic encephalitis

Short-term memory loss, seizures, confusion, & behavioral changes

Radiology

MRI—hyperintense T2 lesions in the medial temporal lobes primarily in the hippocampus & amygdala

Dx

PCR of the CSF for HHV-6 variant B

Treatment

Foscarnet

Other considerations

Consider PCR on the CSF, HSV, & VZV (reactivation less common in the era of acyclovir ppx)

Progressive multifocal leukoencephalopathy

Etiology

JC virus

Clinical

Motor deficits, limb or gait ataxia, & visual sx

Radiology

MRI—increased signal on T2 images bilaterally in the periventricular regions & subcortical white matter

Dx

Gold standard for dx is brain biopsy

PCR can be sent on CSF for JC virus

Treatment

Steroids or CIs should be stopped

No other proven efficacious treatment

Prognosis

Usually progressive & often fatal

Renal Complications

Posttransplant Thrombotic Microangiopathy (TMA)

Incidence

0.5–76% in different series (no uniform definition)

Etiology

Multifactorial—factors that damage endothelium, CIs, sirolimus, chemotherapy and/or total body irradiation, stages III/IV GVHD, hepatic VOD, & fungal/bacterial infxns

Clinical

Clinical spectrum of thrombotic thrombocytopenic purpura (TTP)/hemolytic uremic syndrome syndromes

One of the causes of acute & chronic kidney injury

Diagnostic criteria

De novo prolonged or progressive thrombocytopenia, defined as a platelet count <50,000/μl or ≥50% ≤ previous values

RBC fragmentation ≥2 schistocytes/high-powered field

Decrease in Hb or increase in transfusion requirement

Decreased haptoglobin

Persistently & unexplained elevation in LDH

Treatment

Reduce or stop CIs

Plasmapheresis for posttransplant TMA unlike in idiopathic TTP is controversial & has not proven to be effective (*BBMT.* 2005;11:571)

Prognosis

With intervention, recovery of renal function in ~90%

Acute Renal Failure (ARF)

Incidence

42–84% after myeloablative allogeneic stem cell transplant

Usually occurs within the 1st month following transplant

Etiology

Infxns—CMV, polyoma virus

Posttransplant complications—GVHD, VOD, TMA

Medications—CIs, antibiotics/antifungals

Acute tubular necrosis

Diagnostic criteria

Rise in creatinine 2 × baseline/decrease in CrCL to 50% baseline

Treatment

Depends on etiology—stop possible causative agent; start fluids if secondary to volume depletion; treat possible infxn

BK virus nephropathy—unclear benefit of cidofovir, leflunomide, fluoroquinolone

Hemodialysis

Prognosis

Mortality is 2–3 times higher in pt with ARF

If pt need dialysis, mortality rates may rise to >80%

Cardiac Complications

Arrhythmias

Incidence

Relatively uncommon—2–10%

Usually occurs during conditioning, DMSO infusion, or 1st 1–2 wks after transplant

Etiology

Conditioning—cyclophosphamide, infxn, volume overload, electrolyte abnormalities, DMSO, thyroid dz

Diagnoses

ECG, electrolyte panel, thyroid stimulating hormone, ± echocardiogram

Treatment

If due to DMSO, slow the rate of infusion, hydrate, & observe. If severe, give diphenhydramine & hydrocortisone

If atrial fibrillation with rapid ventricular response & uncontrolled by treating infxn, repleting lytes, fluids; consider IV lopressor 1st (amiodarone/diltiazem are metabolized by the CYP450 & interact with many agents used in transplant)

Prognosis

Permanent antiarrhythmic is usually not needed (Hidalgo JD, et al. *Bone Marrow Transplant.* 2004;34(7):615–619)

Myopericarditis

Incidence

Cyclophosphamide toxicity is idiosyncratic

Occurs within 1–10 days of cyclophosphamide or infxn

Etiology

Cyclophosphamide, infxn

Syndromes

Severe—associated with high doses—tamponade & pulseless electrical activity arrest

Moderate—CHF sx

Mild—myocardial edema—reduction in ECG voltage

Clinical manifestations

Shortness of breath, pleuritis, cough, fevers, tachycardia

Diagnoses

Physical exam—pericardial rub

ECG—diffuse ST segment elevation, PR depression, decreased voltages in the precordium

Echocardiogram—effusion, tamponade, diastolic indentation, or collapse of the RV

Pericardial biopsy or aspiration of fluid

Treatment

Stop possible causative agent; treat infxn

If due to cyclophosphamide, no specific intervention

No NSAIDs if thrombocytopenic

Pericardiocentesis or pericardial window for tamponade

Prognosis

Cyclophosphamide-induced myopericarditis commonly leads to asymptomatic effusion/ECG voltage reduction

Rarely the toxic metabolites extravasate → myocyte necrosis/death

Transplant-Related Complications

Summary of Transplant-Related Complications	
Organ System	**Complication**
Immune	GVHD
	Engraftment syndrome
GI	Hepatic VOD
Pulmonary	Idiopathic pneumonia syndrome (IPS)
	Diffuse alveolar hemorrhage (DAH)
	Pulmonary VOD
Renal	Thrombotic microangiopathy
	Acute renal failure
Cardiac	Arrhythmia
	Myopericarditis
Neurologic	Posterior reversible leukoencephalopathy
	CNS infxn (toxoplasma/aspergillosis/progressive multifocal leukoencephalopathy)

GENERAL TRAUMA I

ALEXANDRA B. COLUMBUS, MD • JOAQUIM M. HAVENS, MD

Trauma Organization and Advanced Trauma Life Support (ATLS) Guidelines

Over 60 million injuries occur in the United States each year
Trimodal death distribution: Immediate, early, & late deaths
For every trauma death, 3 patients (pt) suffer permanent disability

	Time Frame	Typical Injury
Immediate deaths	Sec to min after injury	Apnea due to severe brain injury, high spinal cord injury, rupture of heart or great vessels
Early deaths	Min to several hrs after injury	Subdural or epidural hematoma, hemopneumothorax, intra-abd organ injury, pelvic fx
Late deaths	Several days to wks after injury	Sepsis & multiple organ system dysfunction

Principles of ATLS

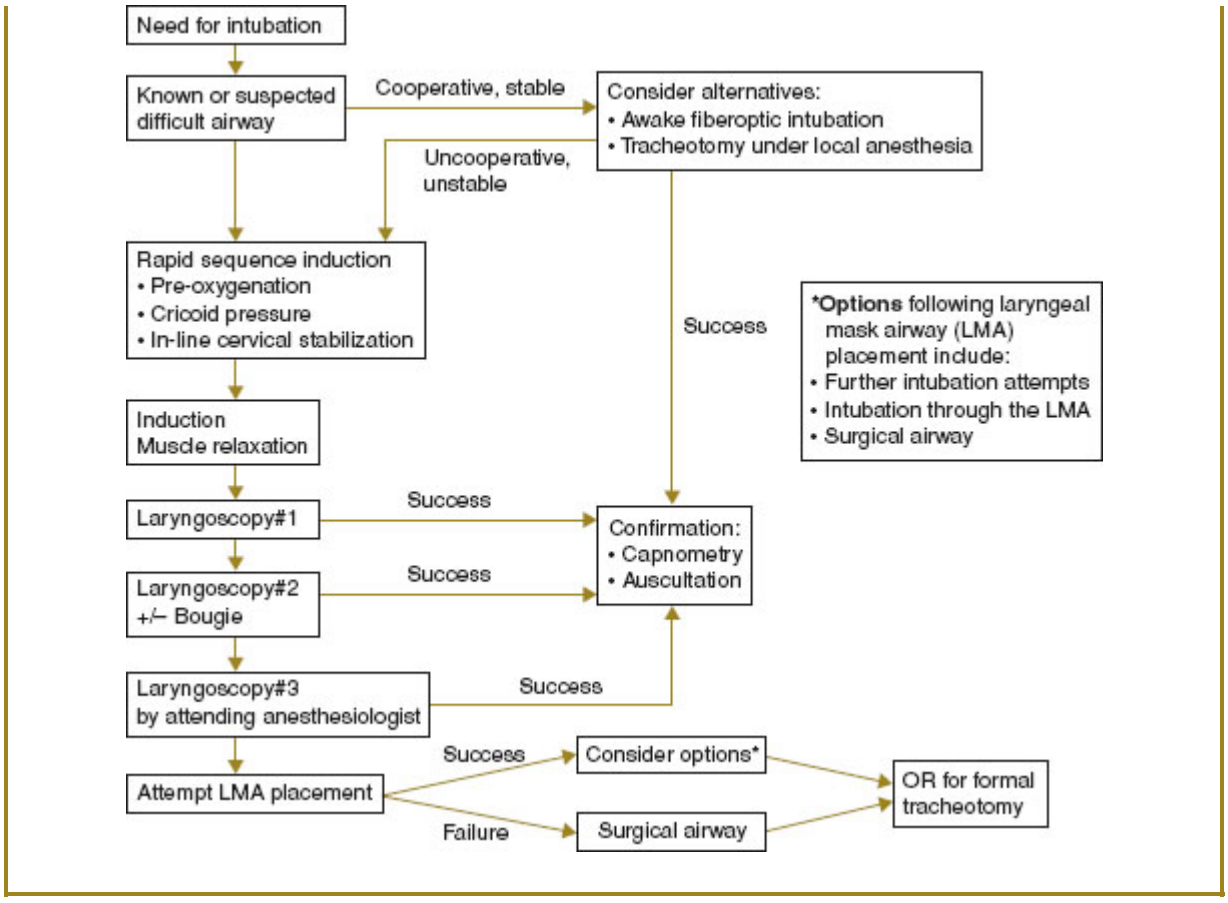
Treat the greatest threat to life 1st
The lack of a definitive dx should never impede the application of an indicated treatment
A detailed hx is not essential to begin the evaluation of an acutely injured pt

Initial Assessment and Management

Prep → triage → primary survey (ABCDEs) → resuscitation → adjunct to primary survey & resuscitation → secondary survey (head-to-toe evaluation & hx) → adjuncts to secondary survey → continued postresuscitation monitoring & reevaluation → definitive care
Primary Survey: lifesaving measures are initiated when the problem is identified

Components of Primary Survey (ABCDEs)		
A	**A**irway maintenance with cervical spine protection	Patency, Glasgow Coma Scale (GCS) score <9 requires definitive airway, assume C-spine injury
B	**B**reathing & ventilation	Observe bilateral rise & fall & auscultate
C	**C**irculation with hemorrhage control	Assess blood volume & CO (level of consciousness, skin color, pulse) & control external hemorrhage
D	**D**isability: neurologic status	GCS, pupillary size & reaction, lateralizing signs & spinal cord injury level
E	**E**xposure/**E**nvironmental control	Completely undress pt but prevent hypothermia

Figure 41-1. Emergency Airway Management Algorithm Used at the R. Adams Cowley Shock Trauma Center



(From Stephens CT, et al. *Anesth Analg.* 2009;109:866–872.)

General Approach to the Trauma Patient

Primary Survey

The sequence for the primary survey is remembered with the acronym "*ABCDE*"

A: (Airway; Fig. 41-1) rapid assessment of the airway, including inspection for foreign bodies & facial, mandibular, or tracheal/laryngeal fx

The most common cause of airway obstruction is altered level of consciousness, allowing the tongue to block the posterior pharynx

Emergency ET intubation is indicated for:

Airway obstruction, hypoventilation, severe hypoxemia (despite supplemental oxygen), GCS <8, cardiac arrest, severe hemorrhagic shock

Emergency airway management algorithm

Rapid sequence intubation is the standard of care for securing the airway in trauma pt

The need for a surgical airway has been reported to be as low as 0.3% (Stephens CT, et al. *Anesth Analg.* 2009;109:866)

Key points in modified algorithm for maxillofacial & neck trauma: stopping is seldom an option, a surgical airway may be the best choice in certain situations, an awake intubation can be used in a pt with a known difficult airway if the pt is cooperative & stable (Pierre EJ, et al. *Anesthesiol Clin.* 2007;25:1)

B: (Breathing) contingent upon the integrity of the phrenic nerve & brain stem, the bony chest, & chest contents

Exam findings suggestive of a thoracic injury: penetrating wound, shortness of breath, resp distress, chest wall crepitance/tenderness, tracheal deviation, JVD

If unstable hemodynamically, place chest tube on injured side

Do not wait for CXR

Consider cefazolin 2 g IV prior to insertion

C: (Circulation) palpation of pulses provides immediate information regarding circulatory status

sBP estimations:

Radial pulse: 90 mm Hg

Brachial pulse: 80 mm Hg

Femoral pulse: 70 mm Hg

Carotid pulse: 60 mm Hg

HR >120/min can represent approx. 30% blood loss; rates >140 can represent >40% blood loss

Emergency-release blood products should be administered for hemodynamically unstable pt who have failed to respond to 2 liters (2L) of crystalloid infusion or have ongoing blood loss

If type-specific blood is unavailable, give type O packed cells

To avoid sensitization in women of childbearing age, give type O, Rh-negative cells

Type-specific blood is usually avail. within 10 min

Type-specific blood is compatible with ABO & Rh blood types (not tested for other antibodies)

Hypovolemic shock should NOT be treated with vasopressors, steroids, sodium bicarbonate, or continued crystalloid infusion. It should be treated with blood products & operative control

For further transfusion guidelines, see Chapter 22 for transfusion guidelines for hemorrhagic shock

D: (Disability) assess gross motor movement in all extremities & calculate a GCS score

GCS: Eye (4 points), Verbal (5 points), Motor (6 points)

Eye: (4) eyes open spontaneously (3) eye opening to verbal command (2) eye opening to pain (1) no eye opening

Verbal: (5) oriented (4) confused (3) inappropriate words (2) incomprehensible words (1) no verbal response

Motor: (6) obeys commands (5) localizes pain (4) withdrawals from pain (3) flexion to pain—decorticate response (2) extension to pain—decerebrate response (1) no motor response

E: (Exposure) removal all of the pt's clothes, including underwear

Stabilize the cervical spine

Perform rectal exam to evaluate for gross blood or a high-riding prostate

Immediately cover & warm pt to prevent heat loss

Adjuncts to primary survey: cardiac monitoring, urinary & gastric catheter, anteroposterior CXR & pelvis x-ray

Secondary Survey

Secondary survey: begins when primary survey is complete, resuscitative efforts well established, & the pt demonstrates normalization of vital signs

Head-to-toe evaluation

Each region of the body completely examined

Reassessment of all vital signs

Complete neurologic examination is performed

Hx (AMPLE) **A**—**A**llergies, **M**—**M**edications, **P**—**P**ast illness/**P**regnancy, **L**—**L**ast meal, **E**—**E**vents/**E**nvironment related to injury

Adjuncts to the secondary survey: specialized diagnostic tests, x-rays, CT scans, urography, angiography, ultrasound, bronchoscopy, & esophagoscopy, as indicated

Reevaluation: after any intervention & frequently to ensure that new findings are not overlooked

Definitive care: the closest appropriate local facility should be chosen on the basis of its overall capabilities (See Section B. Triage & Surveillance)

Cervical Spine Clearance

CT scan is indicated for the following:

Age >65 yrs, fall >3 ft or 5 stairs, motor vehicle crash at high speed, motor vehicle rollover or ejection, bicycle crash, motorcycle crash, motorized recreational vehicle crash

If no injury or fx is seen on cervical spine CT, cervical collar must remain on if a pt has any of the following:

Altered mental status, intoxication with drugs or alcohol, traumatic brain injury, midline cervical tenderness, focal neurologic deficit, numbness or paresthesia of any extremity without direct injury, painful distracting injury

An MRI should be considered in these instances if the pt remains obtunded to r/o ligamentous injury

If no ligamentous injury is identified with MRI, & the CT finding for the cervical spine is negative, the collar may be removed in obtunded pt

If a pt is cooperative & does not meet any of the abovementioned conditions, a clinical exam may be performed

The cervical collar may be removed in the absence of:

No midline cervical pain or limitation with active flexion or extension

No midline cervical pain or limitation with active rotation to the left or the right

If there is pain with active range of motion, a spine surgery consult should be obtained, flexion/extension radiographs may be considered

If the radiographs are negative for evidence of subluxation or fx, the collar may be removed

If a fx or ligamentous injury is identified at any point with the abovementioned studies & clinical exams, a spine surgeon should be consulted

Focused Assessment with Sonography for Trauma (FAST)

Four-view abbreviated US technique

View 1: right upper quadrant—hepatorenal fossa (Morrison's pouch)

View 2: subxiphoid view—to detect pericardial fluid

If unable to obtain, may position probe in left 2nd intercostal space, midclavicular line

View 3: left upper quadrant—to detect perisplenic fluid

View 4: pelvis—retrouterine pouch (pouch of Douglas) & retrovesical pouch

Interpreted as positive, negative, or indeterminate

Exam is directed at identifying the presence of free intraperitoneal or pericardial fluid, usually due to hemorrhage

Sensitivity varies between 42 & 96%

Specificity is often higher

Potential benefits of FAST (Smith J. *Postgrad Med J*. 2010;86:285):

May reduce the number of diagnostic peritoneal lavages (DPL)

Marginal reduction in need to obtain CT

Reduces time to initial dx & time from ED to OR

Potential pitfalls of FAST:

Is a "rule-in" triage tool for pt with blunt abd trauma

CT remains the gold standard for blunt abd trauma

May be noneffective or misleading in untrained hands

Some have recommended 200 scans to obtain proficiency (Scalea TM, et al. *J Trauma.* 1999;46:466)

Images are not as complete & reproducible as CT

Free fluid in the pelvis can be missed without a full bladder

Important organ injuries that will require surgery can be missed

Misses retroperitoneal hemorrhage

Misses perinephric & periaortic hemorrhage

Limited in obese pt or with subcutaneous emphysema

Nutritional Support for Trauma Patients

Early nutrition helps maintain host defenses & preserves lean body mass in trauma pt (Jacobs DG, et al. *J Trauma.* 2004;57(3):660)

There is no proven benefit of starting enteral feedings within 24 hrs of admission versus within 72 hrs of admission

In pt undergoing laparotomy for abd injuries, direct small bowel access should be obtained

A nasojejunal or gastrojejunal feeding tube, or feeding jejunostomy should be placed

Pt with blunt & penetrating abd injuries should be fed enterally when possible

Beneficial effects include prevention of sepsis, preservation of gut mucosa & prevention of bacterial translocation, prevention of pneumonia, & prevention of abscess formation

Total parenteral nutrition (TPN) should be considered by postinjury day 7 if enteral feeding is not feasible

Pt who cannot tolerate 50% of their goal enteral nutrition rate should be started on TPN by postinjury day 7 until >50% of the goal rate for enteral nutrition is achieved

Enteral nutrition is not advised in pt who are incompletely resuscitated

Intestinal necrosis & aspiration are possible

Early gastric feeding is feasible for trauma pt & outcomes are equivalent for pt fed into the duodenum

Pt at high risk for aspiration should receive feedings into the jejunum

Venous Thromboembolism (VTE) Prophylaxis in Trauma

Risk factors for VTE in trauma pt are:

Spinal cord injuries

Lower extremity fx

Severe head injuries

Injury Severity Score (ISS) >8

Shock at the time of admission (sBP <90 mm Hg)

Any surgical procedure lasting >30 min

Femoral venous line insertion

Prior deep vein thrombosis (DVT) or pulmonary embolism (PE)

In pt with risk factors, pharmacologic ppx is recommended (Rogers FB, et al. *J Trauma.* 2002;53(1):142)

Low-dose unfractionated heparin (5,000 units subcutaneously t.i.d.) is one recommended approach

The optimal dose of heparin has not been established

DVT risk may be decreased by up to 25% with this approach

The risk for PE may be reduced by >50%

There is little evidence to support a benefit of low-dose heparin as the *sole* agent for VTE ppx in trauma pt

The use of low–molecular-weight heparin (LMWH) has been shown to be more efficacious than low-dose unfractionated heparin

Some studies in the general surgery literature show a clear benefit of LMWH over unfractionated heparin

LMWH is recommended for trauma pt with:

Pelvic fx requiring operative fixation or prolonged bed rest (>5 days)

Complex lower extremity fx requiring operative intervention & prolonged (>5 days) bed rest

Spinal cord injury with complete or incomplete motor paralysis

These pt must not have other injuries that predispose them for a high risk of bleeding

Serial ultrasound (duplex) exams in high-risk asymptomatic trauma pt should be considered to screen for DVTs

If a pt is freely ambulatory, & has no risk factors, VTE pharmacologic VTE ppx is not required; thromboembolic deterrent (TED) stockings & sequential compression devices (SCDs) should be used

Relative contraindications to pharmacologic ppx:

High risk of bleeding

Pelvic or retroperitoneal hematoma

Ocular injury with hemorrhage

Some traumatic brain injuries (acute phase)

Solid organ injury

Systemic anticoagulation

International normalized ratio (INR) ≥1.5, or activated prothrombin time (aPTT) ratio ≥1.3

Platelet count <50,000

Allergy; h/o heparin-induced thrombocytopenia For pt with these contraindications, TEDs/SCDs should be used until the contraindication no longer exists

Serial duplex surveillance scans should be ordered

Contraindications for enoxaparin are renal failure, renal insufficiency (creatinine clearance <30 ml/min), indwelling epidural catheter

Vena caval filters (IVC filters) have been shown to be efficacious for preventing PE in trauma pt

Indications include:

Recurrent PE despite full anticoagulation

Proximal DVT & contraindications to full anticoagulation

Proximal DVT & major bleeding while on full anticoagulation

Progression of iliofemoral clot despite anticoagulation (rare)

“Extended” indications for prophylactic vena cava filter placement in a pt with established DVT or PE include:

Large free-floating thrombus in the iliac vein or IVC

Following massive PE in which recurrent emboli may prove fatal

During/after surgical embolectomy

Insertion of a “prophylactic” IVC filter is no longer recommended.

Training in Trauma

Intensive care providers should complete the American College of Surgeons ATLS course (http://www.facs.org/trauma/atls)

Evidence-based practice guidelines for the management of traumatically injured pt are maintained & updated by the Eastern Association for the Surgery of Trauma (EAST; http://www.east.org)

Scoring Systems in Trauma

See **Chapter 43** for the use of the Glasgow Coma Scale (GCS) & **Chapter 7** for the details of the scoring systems used to assess injury severity for trauma pt.

Triage and Surveillance

Triage: process of rapidly & accurately evaluating pt to determine the extent of injuries & the appropriate level of medical care required

Civilian triage: the pt with the most life-threatening, but survivable, injuries given priority, as resources permit

Military triage: pt who can survive with the smallest amount of resources given priority

Mass casualty triage: victims separated into critical, urgent, delayed, or expectant (dead or expected to die)

Undertriage: transporting to a facility that does not have appropriate resources for a given pt

May result in increased mortality or morbidity from delays in definitive care

5% undertriage rate considered acceptable (American College of Surgeons—Committee on Trauma 2006)

Overtriage: transporting to a higher level of care than necessary based on injuries

little impact to pt but strain on resources

in order to reduce risk of undertriage, an overtriage rate of 50% is acceptable (American College of Surgeons—Committee on Trauma 2006)

Trauma Center Classification

Classification and Capabilities of Trauma Centers	
Level I	Capable of providing total care for every aspect of injury. Maintains resources & personnel for pt care, education, & research
Level II	Provides comprehensive trauma care regardless of injury severity. May supplement the activity of a Level I trauma center
Level III	Offers prompt evaluation, resuscitation, emergency surgery, & stabilization & when needed transportation to higher level of care
Level IV	Rural facility that supplements care provided within the larger trauma system. Must have 24-hr emergency coverage

Criteria for transfer to trauma center (Sasser SM, et al. *MMWR Recomm Rep.* 2009;58(RR-1):1)

Physiologic criteria

GCS score of <14

sBP <90 mm Hg

Resp rate of <10 or >29 breaths/min or <20 in an infant <1 yr

Anatomic criteria

Penetrating injury of the head, neck, torso, & extremities proximal to the knee or the elbow

Flail chest

≥2 long bone fx

Crushed, degloved, or mangled extremity

Amputation proximal to the wrist & the ankle

Pelvic fx

Open or depressed skull fx

Paralysis

Mechanism of injury criteria

Fall >20 ft for adult, or >10 ft or 2–3 times child's ht for child <15 yrs

High-risk motor vehicle crash (MVC)

Intrusion >12 in into occupants side, or >18 in to any site

Partial or complete ejection from motor vehicle

Death in same passenger compartment

Vehicle telemetry data consistent with high risk for injury

Auto vs. pedestrian/bicyclist thrown, run over, or with impact at >20 mph

Motorcycle crash >20 mph

Special considerations: consider transfer to a trauma center if

Age >55 or <15 yrs

Anticoagulation or bleeding disorder

Burns

Time-sensitive extremity injury

End-stage renal dz requiring dialysis

Pregnancy of >20 wks

Emergency medical service (EMS) provider judgment

Immediately Life-Threatening Trauma Conditions

Tension Pneumothorax

One-way valve forms, air forced into thoracic cavity without means of escape

Clinical dx, do not delay treatment for x-ray confirmation

Needle thoracentesis: large caliber needle into the 2nd intercostal space, midclavicular line of the affected hemithorax

Massive hemothorax

Rapid accumulation of >1,500 ml of blood in the chest cavity

Cardiac tamponade

Pericardium fills with blood from heart, great vessels, or pericardial vessels, restricting cardiac activity

Pericardiocentesis: large gauge catheter 1–2 cm inferior & to the left of the xiphochondrial junction at 45° angle to skin, advance needle cephalad while aspirating, & aim toward the tip of the left scapula. Aspirate as much fluid as possible. If extreme ST-T wave changes or widened QRS complex, pull back needle until normal ECG reading returns. Leave catheter in place, place 3-way stopcock

Pelvic fx

Disruption of the posterior osseous–ligamentous complex, tearing of the pelvic venous plexus, & disruption of the internal iliac arterial system

Immediately Life-Threatening Trauma Conditions		
Problem	**Assessment**	**Management**
Tension pneumothorax	Tracheal deviation Distended neck veins Absent breath sounds Tympany on percussion	Needle decompression Tube thoracostomy
Massive hemothorax	Tracheal deviation Flat neck veins Absent breath sounds Dullness on percussion	Venous access Volume replacement surgical consultation Tube thoracostomy
Cardiac tamponade	Distended neck veins Muffled heart sounds Ultrasound findings	Pericardiocentesis Venous access Volume replacement Pericardiotomy Thoracotomy
Pelvic fx (open book or vertical shear)	Unstable pelvis	Volume replacement ↓ pelvic volume wrap pelvis in sheet Orthopedic consultation Angiography External fixation

Principles of Damage Control Surgery

Definition: the rapid surgical control of hemorrhage & contamination, temporary closure, resuscitation to normal physiology in the ICU, & subsequent reexploration & definitive repair

Goal: to restore normal physiology rather than normal anatomy

When to employ damage control surgery

Multiple life-threatening injuries

Acidosis, pH <7.3

Hypothermia, temp <35°C

Coagulopathy—nonmechanical bleeding

Massive transfusion

Hypotension & shock on presentation

Combined hollow viscous & vascular injuries

Mass casualty

Primary operation & hemorrhage control: control hemorrhage & contamination; explore to determine extent of injury, therapeutic packing, & temporary abd closure.

Critical Care Considerations in Damage Control Surgery	
Core rewarming	Warm pt, room, ventilation gases, & all fluids
Reversal of acidosis	Aggressive resuscitation with crystalloid, colloid, & blood product Generally avoid sodium bicarbonate unless pH <7.2
Reversal of coagulopathy	Aggressive replacement with blood products 1:1:1 ratio of PRBC to FFP to platelets in massive hemorrhage See Section F. Life-Threatening Hemorrhage, Hemorrhagic Shock
Avoidance of abd compartment syndrome (ACS)	Monitor intra-abd pressure See Section E. Abdominal Compartment Syndrome

Planned reoperation: typically 24–48 hrs after injury. Must coincide with reversal of hypotension, acidosis, hypothermia, & coagulopathy

Unplanned reoperation: ongoing bleeding, missed enteric injury resulting in systemic inflammatory response syndrome & shock, ACS

This may take place in the OR or at the ICU bedside if pt is not stable enough for travel

Rhabdomyolysis

Anterior compartment of the lower leg–deep peroneal nerve sensation in web space between 1st 2 toes

Compartment pressure measurement: not required for dx. Generally >30 mm Hg warrants intervention

Rhabdomyolysis	
Definition	Breakdown of skeletal muscle fibers, resulting in release of myoglobin into bloodstream
Causes	Trauma, crush injury, electrical shock, burn injury, cardiopulmonary resuscitation (CPR), ischemia/reperfusion, hypothermia, medications & illicit drugs, compartment syndrome
Signs/sx	Myalgias/pigmenturia ↑ Serum creatinine kinase (CK), myoglobin, potassium, urea, phosphorus arrhythmia
Consequence	Free myoglobin toxic to renal tubules → acute renal failure Hyperkalemia → arrhythmia
Course	CK levels peak 2–5 days postinjury Levels >16,000 units/l more likely to cause renal failure HypoCa^{+} from influx/deposition of calcium in damaged muscles
Therapy	Restore perfusion IV fluids: maintain urine output ~200 cc/hr until CK ↓ No evidence for mannitol/sodium bicarbonate/Lasix Treat hypoCa^{+} if tetany/severe hyperkalemia develops Treat compartment syndrome if it develops Dialysis if fluid resuscitation fails to correct intractable hyperkalemia and/or acidosis

Source: From Johnson D. Trauma, Burn, and Critical Care Management. Pocket Anesthesia. Philadelphia, PA: Lippincott, Williams and Wilkins, 2009.

Abdominal Compartment Syndrome

Compartment Syndrome	
Definition	Tissue pressure exceeds perfusion pressure in a closed anatomic space
Causes	Fx, crush injury, penetrating injury, hemorrhage, burn, any high-energy trauma, prolonged lying on a limb
Locations	Hand, forearm, upper arm, abdomen, buttocks, upper leg, lower leg, foot
Signs/sx	Pain out of proportion to exam, pain with passive stretching of muscle (early sign), paresthesia, pale and/or cool skin, pulselessness (very late finding), tense compartment
Consequence	Tissue damage, muscle necrosis, nerve injury, functional impairment, renal failure, death
Treatment	Surgical fasciotomy of all associated compartments. Permanent damage by 6 hrs

An increase in the volume of any abd or retroperitoneal contents causes an increase in intra-abd pressure (IAP)

IAP in normal hospitalized pt ranges from 0 to 13 mm Hg (Chionh JJ, et al. *ANZ J Surg.* 2006;76:1106)

Markedly increased IAP leads to intra-abd hypertension (IAH)

The clinical condition that results from the organ dysfunction that occurs with IAH is termed ACS

IAH = IAP >12 mm Hg

ACS = IAP >20 mm Hg with evidence of end organ dysfunction

Types of Abdominal Compartment Syndromes		
Primary ACS	**Secondary ACS**	**Recurrent ACS**
Injury or dz that originates inside the abdomen	Due to conditions outside the abdomen—sepsis, capillary leak, burns, massive fluid resuscitation	Development of ACS after successful surgical treatment of primary or secondary ACS

Source: Malbrain ML, et al. *Intensive Care Med.* 2006;32:1722–1732. PMID: 16967294.

Abdominal Compartment Syndrome	
Definition	IAP of >20 mm Hg with evidence of end organ dysfunction
Causes	Abd trauma, ruptured abdominal aortic aneurysm (AAA), hemorrhagic pancreatitis, burns, sepsis
Signs/sx	Tense distended abdomen, elevated intra-abdominal pressure (IAP), ↓ carbon dioxide (CO_2), inadequate ventilation with elevated peak airway pressure, hypoxia, & hypercarbia & renal dysfunction
Definitive treatment	Decompressive laparotomy

Bladder pressure—most common indirect measure of IAP.

50 cc of saline is instilled into the urinary bladder through the Foley catheter. The tubing of the collecting bag is then clamped, & a needle is inserted into the specimen-collecting port of the tubing proximal to the clamp & is attached to a manometer. The transducer is zeroed at the level of the symphysis pubis.

Bladder pressure inaccurate in setting of intraperitoneal adhesions, pelvic hematoma or fx, neurogenic bladder (Kron IL, et al. *Ann Surg.* 1984;199:28)

Effects of Intra-abdominal Hypertension		
System	**Cause**	**Consequence**
Cardiovascular	Compression of heart via diaphragm—↓ compliance, ↓ contractility, ↑ SVR, Compression of IVC—↓ venous return	↓ CO ↑ Central venous pressure (CVP), pulmonary capillary wedge pressure (PCWP) (not reflective of volume status)
Pulmonary	Compression of lungs via diaphragm, inflammatory cytokines	↓ Functional residual capacity (FRC) ↑ Peak inspiratory pressure (PIP) ↑ Shunt fraction, dead space Hypoxia, hypercarbia, atelectasis & edema
Renal	Compression of renal vein Arterial vasoconstriction from sympathetic nervous & renin—angiotensin systems	Oliguria to anuria
GI	Compression of portal & mesenteric veins	↑ Intestinal edema Lactic acidosis ↑ Bacterial translocation
CNS	Possible impaired venous drainage from cerebral outflow	↑ Intra-cranial pressure (ICP) ↓ Cerebral perfusion pressure

Treatment of ACS

The only definitive treatment is immediate decompressive laparotomy
Early surgical consult

Initial Management	
Evacuate intraluminal contents	Nasogastric decompression Rectal tube decompression Stop or reduce enteral nutrition
Evacuate intra-abd space occupying lesions	Surgical evacuation of clot In certain situations, consider catheter drainage
Improve abd wall compliance	Ensure adequate sedations/analgesia Consider paralytic Remove constrictive dressings/eschar Position reverse Trendelenburg
Optimize fluid administration	Avoid excess fluid resuscitation Aim for 0 to negative fluid balance by day 3 Fluid removal by judicious diuresis if stable Consider hemodialysis, ultrafiltration
Optimize systemic/regional perfusion	Goal-directed fluid therapy Hemodynamic monitoring to guide resuscitation Consider pressors to maintain perfusion pressure

Life-Threatening Hemorrhage, Hemorrhagic Shock

Hemodynamically unstable trauma pt are bleeding until proven otherwise
Trauma pt should receive NO MORE than 2 l crystalloid (ATLS)
Common traumatic causes of hemorrhagic shock: solid abd organ injury, myocardial or major vessel laceration, pelvic & femoral fx, & scalp lacerations
Lethal triad: hypothermia, coagulopathy, acidosis
Do not delay surgical control of hemorrhage

Classification of Shock Based on a 70-kg Adult Male				
	Class I	**Class II**	**Class III**	**Class IV**
Blood loss (ml)	<750	750–1,500	1500–2,000	>2,000
Blood loss (% blood volume)	<15%	15–30%	30–40%	>40%
HR	<100	100–120	120–140	>140
BP	Normal	Normal	↓	↓
Pulse pressure	Normal/↓	↓	↓	↓
Resp rate	14–20	20–30	30–40	>40
Urine output (ml/kg)	>30	20–30	5–15	<5
Mental status	Slightly anxious	Mildly anxious	Confused	Lethargic/ obtunded
Fluid replacement	Crystalloid	Crystalloid	Crystalloid & blood	Crystalloid & blood

Source: The ATLS Subcommittee, et al. *J Trauma Acute Care Surg.* 2013;74(5):1363.

Transfusion

1:1:1 ratio of PRBC to FFP to platelets is associated with improved survival compared to previous transfusion strategies (Borgman MA, et al. *J Trauma.* 2007;63:805).
Use uncrossmatched blood products in unstable pt if necessary.
Type-specific blood products when immediately avail.
Revert to standard restrictive transfusion practice after bleeding is controlled

Agents That Decrease Coagulopathic Bleeding

Recombinant factor VIIa reduced blood product use in refractory traumatic hemorrhage but did not affect mortality compared with placebo (Hauser CJ, et al. *J Trauma.* 2010;69:489)

No established effective factor VIIa dose in trauma (17–400 μg/kg reported)

Tranexamic acid (TXA) has been shown to reduce mortality in the setting of traumatic coagulopathy if dosed within 3 hrs of injury (CRASH-2 Trial Collaborators. *Lancet.* 2010;376:263)

Recommended TXA dose for fibrinolysis in major trauma of 1 g per IV infusion over 10 min, followed by 1 g infused over 8 hrs.

Complications of Hemorrhage/Massive Transfusion

Hypothermia

Leads to decreased citrate metabolism, decreased hepatic metabolism, decreased drug clearance, decreased synthesis of acute phase proteins, decreased production of clotting factors

10% decrease in coagulation factor activity for each 1°C drop in temp

Warm the pt, fluids, room

Coagulopathy

Dilutional & consumptive coagulopathy & thrombocytopenia

1:1:1 transfusion ratio PRBC to FFP to platelets

Recombinant factor VIIa: binds to exposed tissue factor, increased conversion of factor X to Xa. Can reduce PRBC requirement in bleeding trauma pt, unclear if it improved survival

Electrolyte abnormalities

Hypokalemia, hyperkalemia: KCl concentration in PRBC from 7 to 77 mEq/l

HypoCa+, hypomagnesemia: each unit of PRBC contains 3-g citrate, which binds Ca++ & Mg++, must measure ionized Ca++ (not total serum)

Monitor closely & correct as needed

Acidosis/alkalosis: average pH in PRBC 7.0. Citrate metabolized to bicarbonate—leads to metabolic alkalosis after massive transfusion

Metabolic acidosis, therefore, indicates tissue hypoperfusion, not the result of transfusion

Sodium bicarbonate for severe metabolic acidosis with hemodynamic instability or renal failure

Transfusion reaction: cumulative risk of all transfused products

Transfusion-associated ALI

Occurs 1 in 5,000 units PRBC, 1 in 2,000 units FFP, & 1 in 400 units platelets (Wallis JP, et al. *Transfusion.* 2003;43(8):1053)

Care is supportive

GENERAL TRAUMA II

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Airway Trauma

Initial management focuses on airway control, testing to define extent of airway injury, & identification of associated injuries.

Investigations for Airway Trauma

Clinical Examination

Unstable face & malocclusion are signs of facial fx that may compromise the supraglottic airway

Stridor, impaired phonation (including "breathy" voice), cervical tenderness, or ecchymosis suggest cervical laryngotracheal injury

Subcutaneous emphysema & hemoptysis

Pneumomediastinum or pneumothorax with its associated physical findings can occur with intrathoracic airway injury

Chest X-ray (Figure 42-1)

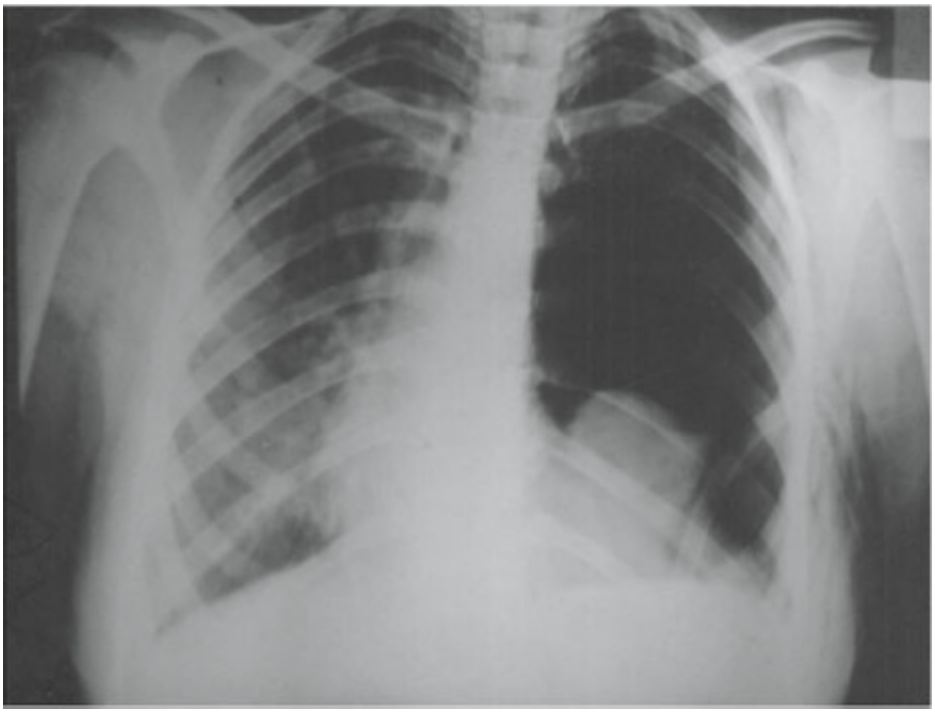
Can often be obtained before any other diagnostic test

Look for pneumothorax & subcutaneous or mediastinal air

If pneumothorax persists after chest tube placement with ongoing air leak, this suggests major bronchial injury. Lungs collapse away from the hilum (Fallen Lung sign) toward the diaphragm, suggesting complete main stem bronchial transection

Disruption of the tracheal air column or overdistension of the endotracheal tube (ETT) balloon may be seen with tracheal disruption

Figure 42-1. "Fallen Lung" Collapsing Away from the Hilum Toward the Diaphragm After Left Main Bronchus Disruption



Fiberoptic Laryngoscopy and Bronchoscopy

Mainstay of laryngeal evaluation in the awake patient (pt) protecting their airway

ETT (small, 6.5–7.5 for adults) should be loaded over bronchoscope in case findings mandate immediate intubation

Most sensitive method to evaluate for distal airway injury

Computed Tomography (CT)

Should not be undertaken until airway is secured, either by tracheal intubation or when examination & prior tests indicate that pt can protect their own airway

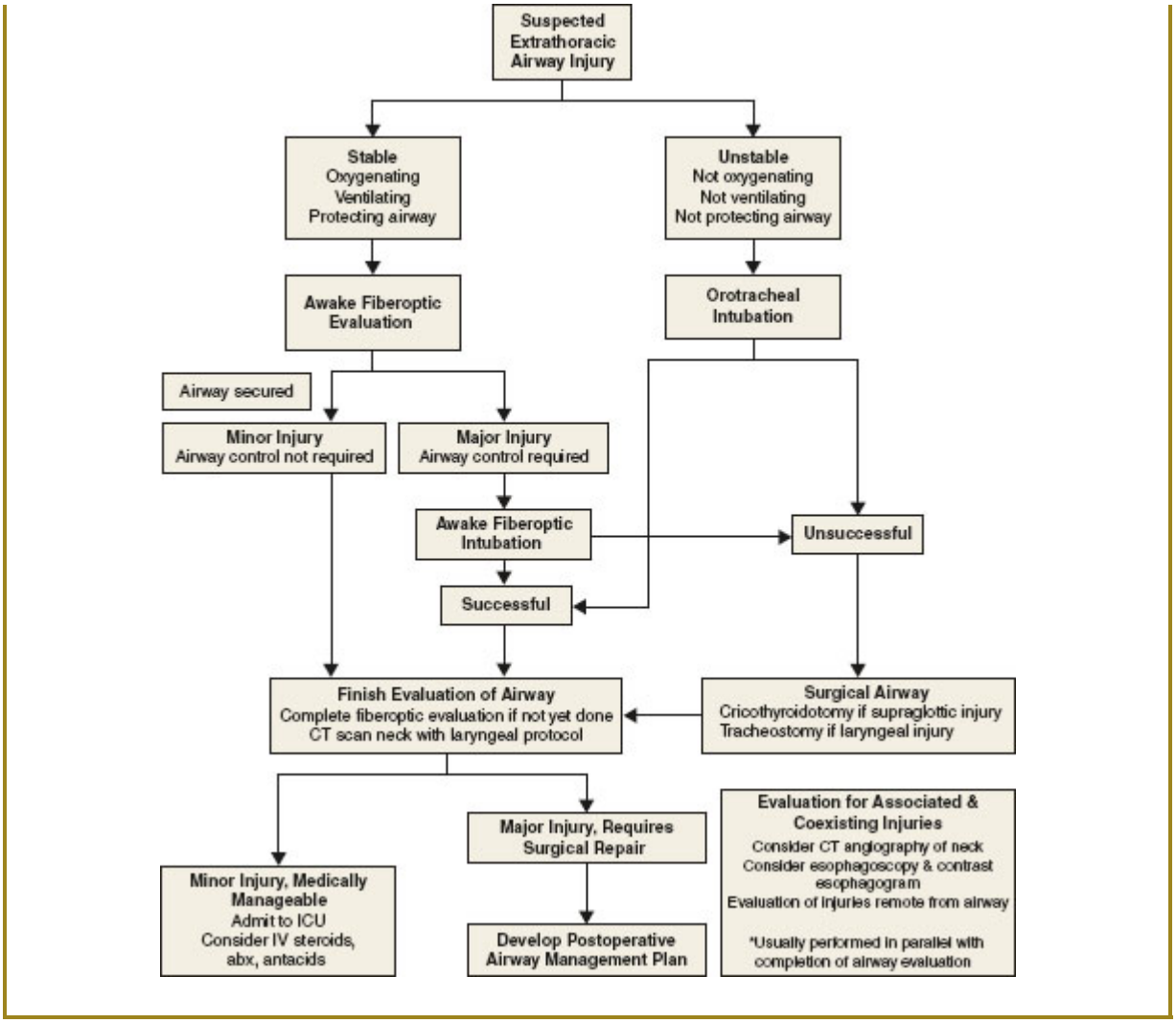
Neck CT is vital to identify presence of & alignment of laryngeal fx. CT can also identify associated cervical injuries (e.g., cervical, vascular, or spinal injury)

Facial & chest CT can help define associated injuries but are less important than bronchoscopy for evaluating the airway itself

Initial Management of Airway Trauma

Sections 1 & 2 are summarized by this algorithm in Figure 42-2.

Figure 42-2. Algorithm for Management of Suspected Extrathoracic Airway Injury



Supraglottic Injury

Injury to the midface, mandible, or soft tissues of the oropharynx or nasopharynx can compromise the pt's ability to maintain an adequate airway

When anatomy is distorted by injury & the pt is maintaining their own airway, rapid sequence intubation can turn a stable situation into an unstable situation. If intubation is required, use awake fiberoptic technique or proceed directly to a surgical airway

If pt is in extremis & not protecting their airway → attempt orotracheal intubation. If orotracheal intubation fails → place a surgical airway

If pt is oxygenating, ventilating, & protecting their airway → perform awake fiberoptic examination & intubation if necessary. If awake fiberoptic intubation fails & intubation is required, proceed directly to surgical airway

Cervical Laryngotracheal Injury

In suspected laryngotracheal trauma, if the pt is oxygenating, ventilating, & protecting their airway → perform fiberoptic laryngoscopy/bronchoscopy. If significant injury is identified, intubate over bronchoscope. If there is only minor or no injury, do not intubate & obtain a CT scan

In suspected laryngotracheal trauma, if the pt is not oxygenating & ventilating → attempt orotracheal intubation while simultaneously preparing for surgical airway. If orotracheal intubation is successful, perform bronchoscopy to evaluate distal airway. If unsuccessful, or resistance is met, abort → perform surgical airway

Avoid supralaryngeal devices such as laryngeal mask airway or esophageal obturator airway, as they may distort anatomy, worsen subcutaneous edema, or convert partial airway disruption to complete disruption

In penetrating injuries, if the open end of the disrupted trachea is visible in the wound, it can be directly intubated

Intrathoracic Airway Injury

Most distal airway injuries are from blunt trauma, often near the origin of the main stem bronchus

Distal injuries often present with pneumothorax. If pneumothorax after blunt trauma is treated with tube thoracostomy & a large air leak is present, airway injury must be considered

Early detection and treatment are important to avoid late stricture formation

Bronchoscopy is the best method to evaluate for distal airway injury

Definitive Therapy for Airway Trauma

Supraglottic Pharyngeal Injury

Repair of facial/pharyngeal injuries should precede removal of any artificial airway

Steroids often used if edema contributes significantly to airway compromise

Tracheostomy can provide a definitive airway

Cervical Laryngotracheal Injury

All cervical airway trauma should be monitored in the ICU, with the possible exception of an isolated, nondisplaced hyoid bone fx in an otherwise stable pt

Grade I & most grade II laryngeal injuries can be managed nonoperatively. Surgical repair is standard for grades III–V

Grading of Laryngeal Injury	
Grade I	Minor endolaryngeal hematoma; minimal airway compromise, if any; no detectable fx
Grade II	Endolaryngeal hematoma or edema associated with compromised airway; minor mucosal lacerations without exposed cartilage; nondisplaced fx shown on CT scan
Grade III	Massive endolaryngeal edema with airway obstruction; mucosal tears with exposed cartilage; immobile vocal cord(s)
Grade IV	Same as III with >2 fx lines on imaging studies; massive derangement of endolarynx
Grade V	Laryngotracheal separation

All pt should have head of bed elevation, voice rest, humidified air, antacids (H_2 blockers or proton pump inhibitors), & initially be kept NPO

If mucosal tears or cartilaginous fx of the larynx are identified, abx are recommended, usually broad spectrum for at least 5 days

Steroid use is controversial, though it is often used to decrease swelling after laryngeal injury

If surgical repair is indicated (grade III–V injury), it should be performed immediately

Tracheostomy is commonly performed after laryngeal repair

Immediate postoperative extubation is preferred after cervical tracheal repair

Intrathoracic Airway Injury

Intrathoracic injury is repaired by thoracotomy

In cases of iatrogenic trauma to the membranous posterior tracheal wall (from ET intubation with bougie or during percutaneous tracheostomy), small injuries may be manageable nonoperatively

Immediate postoperative extubation is preferred whenever feasible after airway repair

Investigations in Thoracic Trauma

Clinical Examination

External signs of trauma including chest wall ecchymosis, bony deformity, paradoxical respiratory motion, & subcutaneous emphysema

Neck examination should focus on tracheal position, & presence of subcutaneous air or jugular venous distension

Note location of entry & exit wounds in penetrating trauma

Absent or decreased breath sounds suggest pneumo- or hemothorax

Chest X-ray

Rapidly avail.

Identifies large hemothorax, pneumothorax, or pneumomediastinum. Can suggest aortic injury if mediastinum is widened

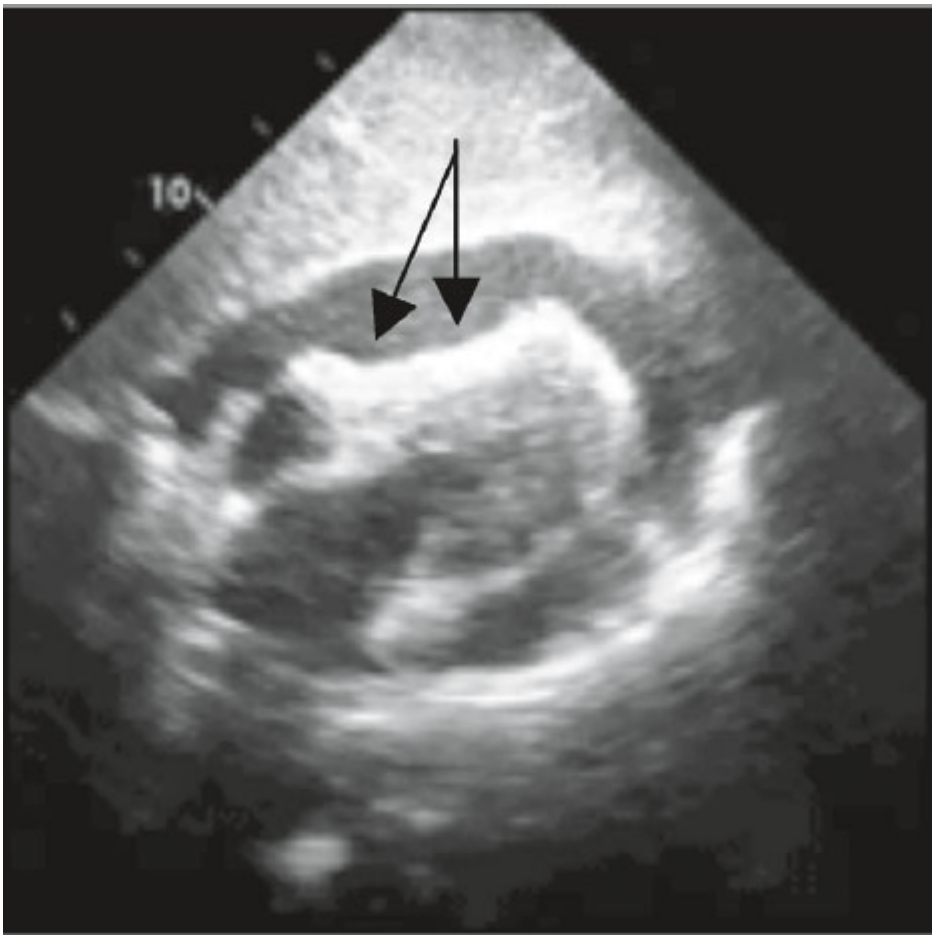
Can assess position of central venous catheters or tubes (ETT, CVC, chest tubes)

Ultrasound

Allows early identification of pericardial tamponade (see Fig. 42-3)

Can also identify hemothorax & pneumothorax as part of extended focused abdominal sonography for trauma (E-FAST)

Figure 42-3. Ultrasound Image of Pericardial Effusion Causing Tamponade. Arrowheads Are in the Pericardial Effusion.



Chest CT

Most sensitive test for hemothorax, pneumothorax
Can identify intrathoracic vascular injuries
Can assess chest wall injury & pulmonary contusion
Identifies associated spine injuries

Other

Angiography may better define vascular injury if CT is equivocal
Barium swallow & esophagoscopy can further evaluate suspected esophageal injury
Subxiphoid pericardial window has essentially been replaced by US. Can diagnose pericardial effusion if US equivocal or unavailable

Specific Injuries

Cardiac Trauma

Blunt

Must be suspected in all pt with blunt precordial trauma

Spectrum of injury is wide including cardiac rupture, pericardial rupture with cardiac herniation, valve injury, papillary or chordae tendineae rupture, septal injury, & blunt coronary injury.

EKG & troponin I are useful for screening—blunt cardiac injury can manifest as any type of arrhythmia (e.g., premature complexes, fibrillation, bigeminy); a completely normal EKG in a hemodynamically stable pt eliminates the need for any further testing (Velmahos GC, et al. *J Trauma.* 2003;54:45–50)

In hemodynamically unstable pt, or pt with an abnormal ECG, a focused abdominal sonography for trauma (FAST) is performed 1st; if there is no tamponade, an echocardiogram should be obtained next. Any injuries requiring repair (e.g., tamponade, valvular) can then be addressed.

Penetrating

Should be actively investigated in all pt with penetrating precordial or transmediastinal wounds. FAST/echocardiogram is the 1st test of choice

Usually presents with tamponade

Thoracotomy or sternotomy required for repair. Repair is performed without cardiopulmonary bypass

Postoperative echocardiogram should be performed to evaluate for valvular lesions, septal defect, or other endocardial injuries

Great Vessel Injury

Includes injury to the aorta & its brachiocephalic branches, pulmonary vessels, superior or intrathoracic inferior vena cava, & innominate & azygos veins

Penetrating injuries typically present with massive hemorrhage, which must be immediately surgically addressed

In stable pt, CT angiography is the single most useful diagnostic modality

Blunt injuries are often contained & are increasingly amenable to endovascular stenting

Chest Wall and Lung Injury

Chest wall

CXR & CT are the diagnostic cornerstones

Age, number of rib fx, & bilaterality are risk factors for respiratory failure after chest wall injury

Analgesia is critical to avoiding respiratory failure in pt with chest wall injury. If moderate pain does not respond to enteral or parenteral NSAIDs & opioids, or severe pain is present at presentation, proceed to regional analgesia. Epidural or paravertebral blocks are appropriate, depending on pt status (coagulopathy, hemodynamics) & local expertise

Surgical fixation of rib fx in selected pt may improve short-term (pneumonia, time spent on ventilator) & long-term (chronic pain) outcomes

Pneumothorax

Pneumothorax results from injury to the lung (e.g., laceration by projectile or fractured rib, tear from deceleration) or entrainment of air from the outside, as in open pneumothorax ("sucking chest wound")

Small pneumothoraces can be observed without intervention, even in pt on positive pressure ventilation. Large pneumothoraces or those causing respiratory or cardiovascular compromise are treated with tube thoracostomy. The chest tube can be removed after the air leak resolves

Percutaneously inserted small caliber tubes (8F–14F) are appropriate for drainage

Hemothorax

Hemothorax can originate from intrathoracic great vessels, lacerated chest wall blood vessels, or lung parenchyma

Initial treatment is with tube thoracostomy (percutaneously inserted small caliber tubes 8F–14F are appropriate in stable pt). If chest tube drains >1,500 ml blood initially or >200 ml/hr × 4 hrs, bleeding is unlikely to stop without thoracotomy

Retained hemothorax after trauma can be treated with thrombolytics instilled via a chest tube or with video-assisted thoracoscopic surgery (VATS) & evacuation.

VATS should be performed within the 1st week after injury, if possible.

If a large retained hemothorax is not drained, it can result in empyema, recurrent effusions, or fibrothorax with impaired pulmonary function

Esophageal Injury

Esophageal injury is rare. More than 80% of esophageal injuries are from penetrating neck trauma & involve the cervical esophagus

Signs & sx are nonspecific (hoarseness, hematemesis, subcutaneous air, dysphagia) & delayed treatment is associated with poor outcome, so index of suspicion must be high

Esophagoscopy & a contrast esophagogram together are highly sensitive for ruling out esophageal injury—neither modality alone is adequate. Neck & chest CT scan can show secondary signs such as pleural effusion, pneumomediastinum, or abscess

Injuries are usually repaired primarily. Broad-spectrum abx, gastric decompression, & antacids are standard. In severe injuries, distal enteral access (such as tube jejunostomy) should be considered early

Abdominal Trauma

Investigations for Abdominal Trauma

Clinical Examination

Still the most important diagnostic tool in the awake, cooperative pt.

Intubation, use of sedatives, & pain killers may hamper a reliable examination

Rigidity, involuntary guarding, & rebound tenderness (worsening pain upon release of pressure) are clinical signs of peritonitis

Seat belt marks are associated with intra-abd injuries in >20%

Pain referred to the left (Kehr's sign) or right shoulder is suggestive of splenic or hepatic injury, respectively, from irritation of the diaphragm

Chest X-ray

CXR is part of abd evaluation because thoracic trauma is commonly associated

Look for lower rib fx (consider associated splenic, hepatic, renal injuries), an elevated diaphragm or hollow viscus in the chest (diaphragmatic rupture)

Focused Abdominal Sonography for Trauma

US of the pericardium, hepatorenal recess, splenorenal recess, & retrovesicular pelvis

May reveal free fluid in these areas (potentially the source of bleeding in the hemodynamically unstable polytrauma victim)

Disadvantages: no visualization of the retroperitoneum, operator dependent.

Has largely replaced DPA & DPL (Diagnostic peritoneal aspiration & lavage) as the optimal method for ruling out intraperitoneal bleeding

Abdominal and Pelvic CT

Among the most reliable studies to evaluate abd trauma

Delineates the bullet trajectory in gunshot wounds, demonstrates free air or fluid in the peritoneal cavity

Rather insensitive in diagnosing hollow viscus injuries (free fluid in the absence of solid organ trauma, free air, bowel wall thickening, mesenteric stranding) & penetrating diaphragmatic trauma

Addition of IV contrast with appropriate timing of scanning helps identify arterial or venous injuries; delayed contrasted images can identify urinary tract injuries (delayed contrast extravasation from the kidneys or the bladder)

Specific Abdominal Injuries

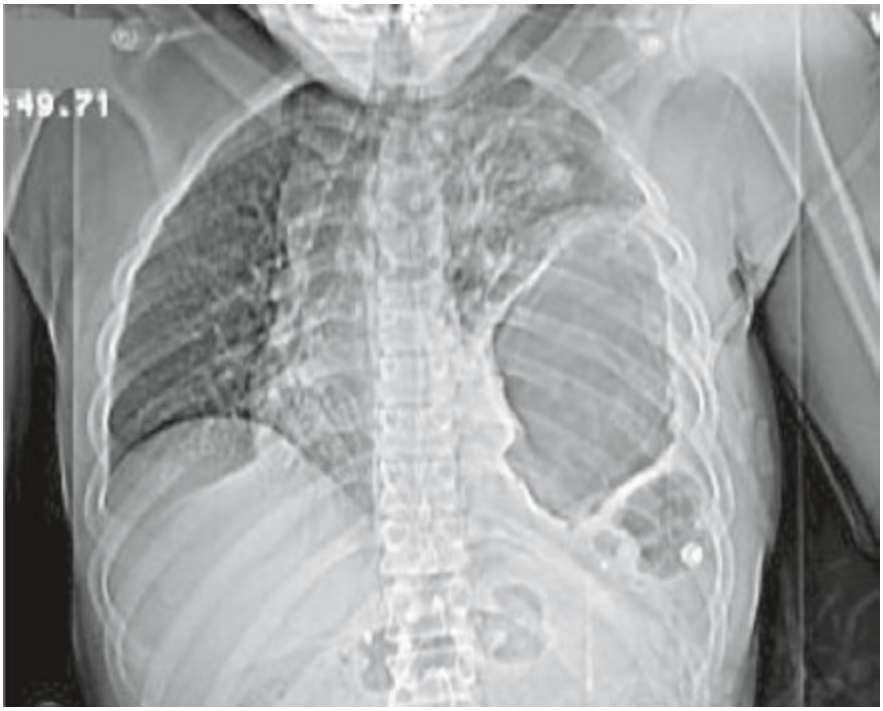
Diaphragmatic Injuries

Diaphragmatic rupture can occasionally be seen on plain CXR films with herniation of abd contents to the chest

Fine-cut CT or selective use of diagnostic laparoscopy aids dx

The left side is far more commonly involved than the right (Fig. 42-4)

Figure 42-4. Traumatic Diaphragmatic Rupture with Intrathoracic Stomach



Liver Injuries

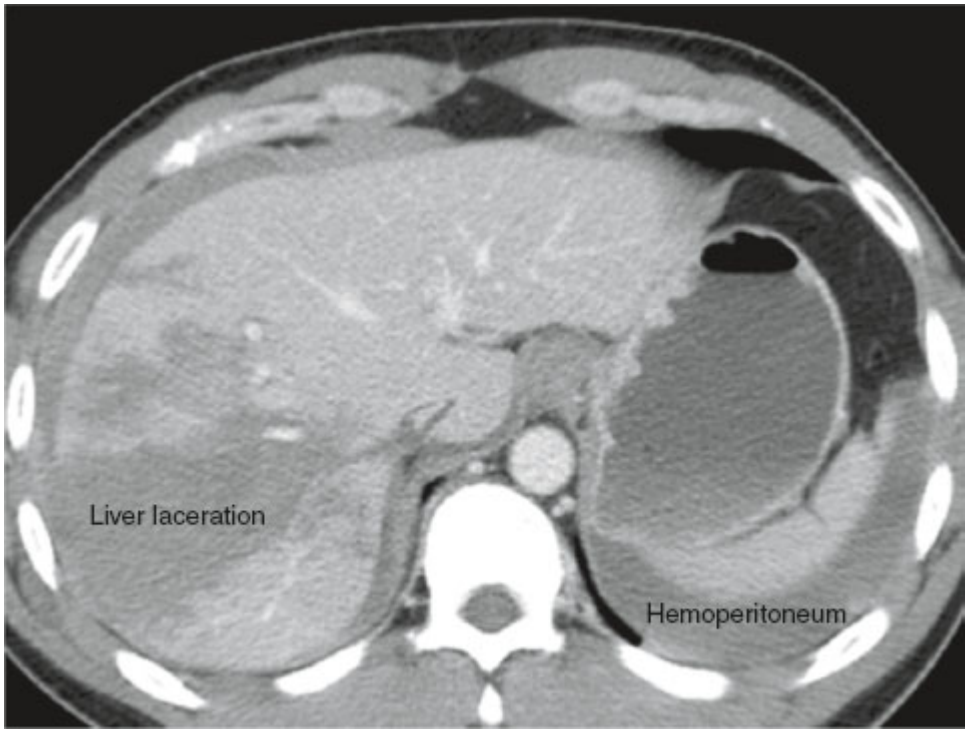
Most commonly injured abd organ in blunt abd trauma (Fig. 42-5)

Follow pt with serial Hb levels. Almost all liver injuries not needing emergent exploration because of hemodynamic instability can be successfully managed nonoperatively (Melloul E, et al. *J Trauma Acute Care Surg.* 2015;79:468–474)

Angiographic embolization is a useful adjunct of nonoperative management

Complications, such as bilomas or biliary ascites, hemobilia (connection between an artery & the biliary tree), & intrahepatic collections occur mostly in high-grade injuries & can also be managed nonoperatively (Green CS, et al. *J Trauma Acute Care Surg.* 2016;80:529–537)

Figure 42-5. Liver Laceration with Associated Hemoperitoneum on CT Scan



Splenic Injuries

Commonly associated with left lower rib fx

In contrast to the liver, nonoperative management of splenic trauma fails in up to 15%. High-grade injuries fail more frequently (Freitas G, et al. *Am J Surg.* 2016;211:744–749)

Rebleeding may occur late & can be catastrophic (Zarzaur BL, et al. *J Trauma Acute Care Surg.* 2015;79:335–342)

Angioembolization has a role in the absence of associated intra-abd injuries in the hemodynamically stable pt with persistent transfusion requirements

Vaccination against *Streptococcus pneumonia, Haemophilus influenza, & Neisseria meningitidis* is recommended in pt with splenectomy or splenic artery embolization; however, the timing remains controversial

Pancreatic Injuries

Typically seen in association with upper lumbar spine fx & duodenal (proximal) or splenic (distal) injuries

Dx: CT scan & elevated pancreatic enzymes (low sensitivity & specificity). A repeat CT scan 12–24 hrs later enhances diagnostic accuracy

Low-grade injuries can be managed nonoperatively

Assessment of integrity of the main pancreatic duct is essential: in the absence of ductal trauma, drainage is usually adequate; ductal injuries distal to the superior mesenteric vessels are managed with distal pancreatectomy, while head & proximal body injuries are treated with damage control principles in unstable pt (suturing, draining, packing) or with a pancreatoduodenectomy in stable pt

Hollow Viscus Injuries

The small bowel is the most commonly injured hollow viscus

High association with other intra-abd injuries

Small & large bowel injuries are typically repaired primarily. If >50% of the bowel circumference is involved, local resection & primary anastomosis can be performed. Proximal diversion if significant hemodynamic instability

Abx (ideally a 2nd generation cephalosporin with anaerobic coverage, i.e., cefotetan) do not need to be continued beyond 24 hrs perioperatively

Urologic Injuries

Macroscopic & persistent microscopic hematuria requires evaluation of the urinary tract typically with CT scanning, including delayed contrasted images & CT cystogram

Renal injuries are managed nonoperatively in the hemodynamically stable pt, while ureteral injuries are most commonly repaired primarily over stents

Bladder injuries are managed depending on their location: intraperitoneal injuries require operative repair, whereas extraperitoneal injuries are managed with prolonged catheterization & drainage

In the presence of blood at the meatus, a high riding prostate or perineal/scrotal hematoma, a retrograde urethrogram should be obtained. If injury is confirmed, long-term catheterization is indicated

Pelvic Fractures

Can lead to life-threatening bleeding from disruption of the extensive retroperitoneal venous plexus or less commonly from arterial trauma

Initial management requires decreasing the volume of the pelvis with a pelvic binder or external fixator

Angiographic embolization is effective in controlling arterial bleeding.

Preperitoneal pelvic packing is an alternative technique reserved for hemodynamically unstable pt or settings without angiographic capabilities

(Tai DK, et al. *J Trauma.* 2011;71:E79–E86)

Vascular Injuries

Inferior vena cava injuries can be repaired or ligated, if below the renal veins

Temporary control of arterial injuries can be achieved by shunts

PTFE grafts or autologous venous grafts are appropriate for arteries that cannot be repaired primarily

Blunt injuries (if not bleeding) can be managed with percutaneous stents

Extremity injuries

Always obtain plain x-rays to r/o bony injuries

Bone fx require stabilization through splinting & operative fixation

Open fx mandate irrigation, debridement, & abx coverage until definitive tissue coverage

Associated neurovascular injuries have to be screened for: as soon as the clinical situation permits, a careful neurologic examination should be performed to assess for subtle signs of neurologic injury; any suspicion of vascular injury should be screened with measurement of the ankle–brachial (ABI) or brachial–brachial index (BBI). ABI <0.9 or BBI <1 should prompt CT angiography of the affected extremity

Soft tissue crush injuries are also a consideration: crushed muscle releases nephrotoxic substances & can cause rhabdomyolysis. Management includes trending of serum creatine phosphokinase (CPK) & adequate hydration (maintain urine output >0.5 ml/kg/hr). In severe cases (CPK >15,000), consider urine alkalinization with a $NaHCO_3$ infusion

Extremity Compartment Syndrome

Due to increased pressure in the extremity muscular compartments, >20–25 mm Hg

More common in the lower extremities (esp. anterior compartment)

Results primarily from crush injuries, extremity vascular trauma followed by ischemia & reperfusion injury, or secondarily due to massive resuscitation

Pain out of proportion to injury & paresthesias. Swollen extremity, & the compartments are tense. Loss of pulses & sensorimotor function (late findings). Maintain higher index of suspicion in sedated, intubated pt

Intracompartmental pressure is assessed with a needle-monitoring device

Treatment consists of emergent fasciotomies of all compartments of the affected extremity

Fat Embolism Syndrome

Release of fat globules from the bone marrow. May lead to multiple organ failure from a direct embolic effect or from the release of inflammatory mediators

Most commonly associated with long bone fx. Related to the fx itself or reaming & manipulation during repair

Respiratory failure (from a worsening ventilation–perfusion mismatch), altered mental status and/or seizures (from fat emboli-induced cerebrovascular accidents), upper body petechial rash, & subconjunctival or retinal hemorrhages

Dx is difficult & typically made on clinical grounds. Sudan stain may identify fat particles in the urine, & bronchoalveolar lavage (BAL) washings may demonstrate >5% of cells staining positive for fat. However, neither of the 2 tests is sensitive or specific

Treatment is supportive

HEAD TRAUMA AND SPINAL CORD INJURY

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Traumatic Brain Injury

Traumatic brain injury (TBI) requires early dx, management of primary injury, & prevention of secondary injury. Morbidity & mortality from secondary injury may exceed that of primary injury.

Neurologic Assessment

Determine level of consciousness with Glasgow Coma Scale (GCS) score for stratification of injury severity, management strategies, & need for intervention (Teasdale G, et al. *Lancet.* 1974;2:81–84).

Glasgow Coma Scale					
Motor		Verbal		Eye Response	
6	Spontaneous, obeys command				
5	Localizes pain	5	Coherent, oriented		
4	Withdraws to pain	4	Confused	4	Spontaneous
3	Flexion to pain	3	Inappropriate	3	Opens to voice
2	Extension to pain	2	Incomprehensible	2	Opens to pain
1	None	1	None	1	None

Traumatic Head Injury Classification			
Injury Severity	GCS	Criteria	Management
Minimal	15	Neurologically intact No loss of consciousness No amnesia	No CT head required No hospitalization required
Mild	14	Brief loss of consciousness <5 min Mild memory impairment	CT head (abnormal in 16%)
Moderate	9–13	Loss of consciousness >5 min Neurologic deficit	CT head ± surgical intervention
Severe	3–8	Severe neurologic deficit	CT head ± surgical intervention

Focal injury results from restricted vector of force delivered to an intracranial region; includes: epidural hematomas, subdural hematomas, cerebral contusions, intraparenchymal hematomas, & subarachnoid hemorrhage

Diffuse injury results from wide force vectors & high acceleration/deceleration injuries; includes: concussion, diffuse axonal injury (DAI), posttraumatic coma

Surgical intervention is guided by a combination of radiographic findings as well as clinical exam

Prognosis

Severe TBI has ~30% mortality; 16% of the survivors have severe neurologic deficits; 3% remain in a persistent vegetative state. Risk factors for poor outcome include older age, low GCS score, poor pupil response or anisocoria, poor motor response, hypoxia, hypotension, coagulopathy, & significant CT characteristics (*J Neurotrauma.* 2007;24:329)

Intensive neurorehabilitation improves functional outcomes, with 85% of recovery occurring within the 1st 6 mo after injury (Maas AI, et al. *Lancet Neurol.* 2008;7:728).

Initial Management

Prehospital considerations: shorter transfer time to the hospital as well as management at Level 1 regional trauma centers improves outcome in TBI (Grotta J, et al. *Prehosp Emerg Care.* 2007:S12)

ABCs: secure airway, ensure adequate oxygenation, avoid hypotension

Provide adequate oxygenation & maintain normocapnia ($PaCO_2$ 35–40 mm Hg); hypoxia (PaO_2 <80%) & hypocapnia ($ETCO_2$ <27) from onset of trauma significantly increase mortality (Stocchetti N, et al. *J Trauma.* 1996;40:764–767; Davis DP, et al. *J Trauma.* 2004;57:1–8)

Maintain sBP >90 mm Hg; even a single episode of sBP <90 mm Hg can double mortality & worsen morbidity; hypotension is 1 of the strongest independent predictors of poor outcome in TBI (Chesnut RM, et al. *J Trauma.* 1993;34:216–222)

Resuscitation with hypertonic saline shown to improve survival compared to isotonic fluids (Vassar MJ, et al. *Arch Surg.* 1993;128:1003); use crystalloid & avoid albumin, which is associated with higher rates of mortality in severe TBI (*NEJM.* 2007;357:874–884)

Treat HTN (SBP >180) with β-blockers or agents that do not dilate cerebral vasculature (e.g., nitroprusside, hydralazine) given potential contribution to increased ICP.

Minimize deleterious effects of brain swelling by avoiding hyponatremia

Perform trauma survey: TBI is associated with extracranial injury in 35% of cases (Gennarelli TA, et al. *J Trauma.* 1989;29:1193). Immobilize C-spine, assess for fx. R/o internal bleeding & other associated injuries

Minimize risk for ongoing bleeding by discontinuing & reversing any anticoagulants with goal INR ≤1.3 & PTT ≤40; maintain platelet count >100,000/μl

In patients (pts) with GCS ≤8, place ICP monitor & consider intubation

Seizure prophylaxis in the 1st 7 days following injury reduces risk of posttraumatic seizures in pts with supratentorial hemorrhages

Neuroimaging

Obtain a noncontrast CT scan of head promptly to assess for operative lesions. CT is the initial imaging of choice due to speed, accessibility, & sensitivity for hemorrhage & fx.

Consider CT or MR venogram if a displaced skull fx is adjacent to venous sinus to assess for potential sinus thrombosis

MRI is more sensitive than CT for microhemorrhages & DAI but should be delayed until the patient (pt) is clinically stable & intracranial HTN has been ruled out, given risk for elevated ICP with prolonged supine position

CT findings of concern include midline shift of >5 mm, extra-axial hematoma thickness of >1 cm, effacement of basal cisterns, & pneumocephalus

Types of Primary TBIs and Their Initial Management

Skull Fractures

Skull fx may occur independently of or be associated with underlying epidural hematomas or contusions

Anterior skull fx may manifest with periorbital bruising, or Raccoon eye sign, & CSF rhinorrhea (damage of the cribriform plate)

Temporal skull fx may result in postauricular bruising, known as Battle's sign, CSF otorrhea, & hemotympanum; dedicated temporal bone imaging & possible ENT consult should be considered with the latter signs

CSF leak poses risk for CSF infxn & meningitis; confirm CSF leak by ring test (assess for halo effect of leakage on filter paper), glucose level (mucus usually does not contain significant glucose as opposed to CSF), & quantifying β-2-transferrin level (may take several days before confirmatory results return); initiate abx if suspicious for CSF leak; placement of lumbar drain offers CSF diversion to encourage spontaneous closure of leak site

Pneumocephalus in the setting of skull fx also raises concern for CSF leak

CN palsies may be associated with base of skull fx, resulting in anosmia (CN I from cribriform plate fx), diplopia or dysconjugate gaze (CN III, IV, VI from orbital fx or cavernous sinus injury), facial palsy, or hearing loss (CN VII–VIII from petrous temporal bone fx)

Significant scleral injection, pulsating exophthalmos, & retro-orbital bruit may suggest a direct or indirect carotid–cavernous fistula, which should be further evaluated by cerebral angiogram

Epidural Hematomas

Result from injury to the middle meningeal artery (most commonly), middle meningeal vein, diploic veins, or dural sinuses; may be associated with overlying skull fx

May present with headache, loss of consciousness with or without lucid interval for several hrs, hemiparesis, dilated pupils, or seizure

CT scan shows extra-axial, hyperdense, biconvex lesion confined by cranial sutures

Epidural hematomas should be evacuated if larger than 30 cm^3, in comatose pt with anisocoria, or in the posterior fossa with compression of the 4th ventricle

Pt with epidural hematomas smaller than 30 cm^3, & less than <15 mm in maximal thickness, with, midline shift <5 mm, GCS >8, & no focal neurologic deficit may be monitored with frequent neurologic exam & serial CT scans (*Neurosurgery.* 2006;58:S7)

Poor prognosis has been associated with low GCS score on presentation, older age, absence of a lucid interval, bilateral pupil dilatation, associated subarachnoid or intracerebral hemorrhage, & postoperative intracranial HTN.

Subdural Hematomas (Chapter 48)

Result from tearing of bridging veins or extension of large parenchymal hematoma

May be preceded by minor or no trauma in elderly pt, esp. if the pt is anticoagulated

CT scan shows extra-axial crescentic lesion that can cross cranial suture lines; density on CT depends on acute (<3 days, hyperdense), subacute (<2–3 wks, isodense), or chronic (3 wks to 3 mo, hypodense) state

Acute subdural hematoma >10 mm in thickness or >5 mm in midline shift should be surgically evacuated regardless of GCS (*Neurosurgery.* 2006;58:S16)

Acute subdural hematomas in pt with GCS score of ≤8 should be evacuated if GCS score drops by 2 points from time of injury to admission, finding of anisocoria or fixed & dilated pupils, or ICP >20 mm Hg (*Neurosurgery.* 2006;58:S16)

Emergent craniectomy or craniotomy for evacuation of acute subdural hematoma within 4 hrs of injury significantly improves mortality rate (Seelig JM, et al. *JAMA.* 1981;304:1511)

ICP control following evacuation of hematoma significantly improves functional recovery (Wilberger JE Jr, et al. *J Neurosurg.* 1991;74:212–218)

Subdural collections liquefy after 2 wks & may be drained by burr holes instead of craniotomy at that point; burr hole drainage may be limited by membranes compartmentalizing clot but may lead to better functional status than craniotomy (Svien HJ, et al. *J Neurosurg.* 1964;21:172–177)

Poor prognosis is associated with age >65 yrs, low GCS on presentation, delay in surgical intervention if acute, & postoperative intracranial HTN

Cerebral Contusions and Intraparenchymal Hematomas

Occur at sites where the brain strikes prominent bony margins, most commonly, the inferior anterior frontal lobe & anterior temporal lobe

May occur on contralateral aspects of cerebral hemispheres from direct impact, followed by rebound against cranium, or coup & contracoup injury; found in 25–35% of severe TBI cases, with significant risk for expansion & mass effect

Repeat CT scan of head within 6 hrs after initial scan to assess for evolution of contusion, or sooner if signs of clinical deterioration or significant coagulopathy; may blossom over the course of days, mandating close serial monitoring.

Risk factors for enlarging contusions include: large size of initial lesion, subdural hematoma, epidural hematoma, older age, & elevated PTT.

Mechanisms include shearing of intraparenchymal vessels at the time of injury or subsequent coagulopathy (from traumatic release of thromboplastin following brain injury), vascular necrosis, hyperperfusion injury from impaired cerebrovascular autoregulation, & release of tamponade effect after evacuation of extra-axial hematoma

Consider surgical evacuation for hematomas >50 cm^3 or temporal hematomas >20 cm^3 with compression of basal cisterns & impending uncal herniation (*Neurosurgery.* 2006;58:S25)

Early evacuation of traumatic intraparenchymal hematomas did not improve outcomes over medical management but may be offered to young pt with small & superficially located lobar clots (*STICH:* Mendelow AD, et al. *Lancet.* 2005;365:387)

Decompressive craniectomy may be indicated in pt <60 yrs with medically refractory intracranial HTN & malignant edema, with diligent monitoring for & control of potential associated complications, including postoperative subdural & epidural hematomas, infxn, & hydrocephalus. A recent trial suggested that bifrontotemporoparietal decompressive craniectomy compared to maximal medical management for diffuse traumatic brain injury decreased ICP & ICU stay but was associated with worse functional outcome & no diffuse in mortality (*DECRA:* Cooper DJ, et al. *NEJM.* 2011;364:1493); however, the study population excluded pt with mass lesions & dilated unreactive pupils, which comprise a significant portion of potential candidates, & also used a surgical approach that differs from the unilateral hemicraniectomy utilized at many institutions. Overall, systematic evidence

for benefits of decompressive craniectomy in adults with severe head trauma remains lacking

Diffuse Axonal Injury

Associated with poor prognosis

Manifests as small hyperdensities on noncontrast CT scan if hemorrhagic, or hyperintensity on DWI or T2-weighted MRI if nonhemorrhagic

Vulnerable regions include corpus callosum (esp. splenium), corona radiata (esp. gray–white junction), internal capsule, midbrain, & dorsolateral pons

Subarachnoid Hemorrhage (Chapter 48)

Occurs typically within cortical sulci, in the cerebral convexities rather than in basal cisterns

Low risk of subsequent vasospasm & cerebral salt wasting, in contrast to subarachnoid hemorrhage from aneurysm rupture

Duret Hemorrhage

Occurs in ventral or paramedian brain stem due to shearing of perforating arteries with transtentorial herniation; may occur in delayed fashion

Secondary Brain Injury

Results from evolution of primary injury processes, hypotension, hypoxia, intracranial HTN, & inadequate cerebral perfusion pressure (CPP)

Mechanisms include expansion of contusion or hematoma, excitotoxic neurotransmitter release, altered mitochondrial metabolism, free radical & calcium-mediated injury, blood–brain barrier disruption from mechanical injury & inflammatory cytokine release, increased extracellular potassium, & alterations in gene expression with increased production of proapoptotic factors

Intracranial Pressure

Monro–Kellie doctrine: the cranial vault comprises brain parenchyma, cerebrospinal fluid, & arterial & venous blood. Any single compartment can increase only at the expense of compression of the remainder compartments

Increased ICP → decreased cerebral perfusion or herniation

Normal ICP is ≤20 mm Hg in adults; sustained ICP ≥25 mm Hg correlates with worse outcome & higher mortality risk

Cushing's response to intracranial HTN: HTN, bradycardia, irregular respirations

Increased ICP → increased sympathetic response → increased SVR → increased MAP (HTN) → reflex compensatory response (bradycardia) → cerebral vasodilation → further increased ICP (Cheyne–Stokes respiration)

Cerebral Perfusion

Cerebral blood flow (CBF) & oxygenation are critical for brain viability but are difficult to measure; CPP is often used as an indirect surrogate for CBF.

CBF = CPP/CVR (CVR = cerebral vascular resistance)

CPP = MAP – ICP (Normal CPP >50 mm Hg)

Normal CBF = 50–55 cc/100-g brain tissue/min; CBF ischemic threshold = 18–20 cc/100 g/min; CBF <10 cc/100-g brain tissue/min leads to irreversible neuronal injury

CBF remains constant between CPP 50 & 150 mm Hg (or MAP 60 & 160 mm Hg if ICP normal) due to autoregulatory mechanisms; beyond this range, CBF becomes pressure-dependent

Decreased CPP → arteriole dilatation, decreased CVR → increased CBF → potentially increased ICP → decreased CPP

Increased CPP (>150 mm Hg) → maximal arteriole dilation → increased CBP → increased ICP

In TBI, autoregulation may be impaired with CPP <50 mm Hg, lowering the threshold for ischemic injury. Maintaining CPP between 50 & 70 mm Hg can reduces mortality by 50% in severe TBI, while driving CPP >70 mm Hg increases the risk of ARDS by 5-fold (Robertson CS, et al. *Crit Care Med.* 1999;27:2086–2095)

CBF correlates with $PaCO_2$ but not PaO_2: every 1 mm Hg change in $PaCO_2$ → 3–4% change in cerebral vascular lumen; increased $PaCO_2$ vasodilates, decreased $PaCO_2$ vasoconstricts

Cerebral oxygenation is optimized by PaO_2 >60 mm Hg & sBP >90 mm Hg

Intracranial Pressure Monitoring

ICP monitor should be placed in TBI pt with GCS score of ≤8 & an abnormal head CT (*J Neurotrauma.* 2007;24:S37)

Types of ICP monitors:

External ventricular drain (EVD): Effectively monitors as well as controls ICP through CSF drainage; most commonly placed into frontal horn of lateral ventricle with distal tip at the foramen of Monroe

Intraparenchymal monitor: Measures but does not reduce ICP; should be considered when CSF drainage considered unnecessary or compressed ventricular space prevents insertion of EVD; increased infxn risk & decreased accuracy after 3 days.

Subarachnoid bolt: Measures but does not reduce ICP; less accurate than intraventricular & intraparenchymal monitors but may be a good option in coagulopathic pt; decreased accuracy with high ICP & increased infxn risk after 3 days.

Duration of monitoring: Onset of intracranial HTN peaks at days 2–3 & days 9–11; continue monitoring until ICP therapy is weaned

Reverse coagulopathy & thrombocytopenia prior to placement; common practice is to give prophylactic abx although no definitive evidence this reduces infxns

ICP interpretation: Normal ICP waveform varies with respiration & blood flow but may be distorted in TBI due to intracranial HTN or craniectomy skull defect

Cessation of CSF drainage from EVD may be due to:

Low ICP

Malposition of EVD

Catheter occlusion: Assess patency by lowering the external collection system; if no CSF flow is visualized, the EVD tubing may be flushed with a small volume of sterile saline

Filter paper on top of external collection system may become wet when the system is moved for pt transport; the external system can be replaced in sterile fashion without replacement of intraventricular catheter

Management of Intracranial Hypertension

Elevated ICP, whether sustained or reversible, predicts poor neurologic outcome. If increased ICP is suspected, obtain initial noncontrast CT scan

of head immediately. Multiple measures exist to maintain ICP < 20 mm Hg & optimize CBF

CSF drainage: EVD effectively monitors as well as reduces ICP with instantaneous effect. Recommended in all possible cases in addition to hyperosmolar therapy

Hyperosmolar therapy: Mannitol & hypertonic saline are mainstays of ICP reduction & are associated with improved clinical outcome in select populations of TBI pt

Mannitol: 1–1.5 g/kg bolus over 30–60 min, followed by 0.25–0.5 g/kg q6h for increased ICP. Scheduled empiric mannitol dosing shown to decrease ICP more than reactive administration of mannitol in response to increased ICP (Smith HP, et al. *J Neurosurg.* 1986;65:820–824)

Monitor serum Na, Osm, BUN, Cr; consider holding if serum osmolarity >320 mOsm/l or osmolar gap >11

Risks: Rebound intracranial HTN, renal failure, hypotension, or HTN with prolonged use

Mechanisms of action: Osmotic diuresis, plasma expansion, decrease blood viscosity, free radical scavenging

Hypertonic saline: 30–60 ml of 23.4% over 20 min is effective alternative to mannitol; 3% & 7.5% NaCl also candidates to decreased ICP

Recommend: Bolus 23.4% NaCl through central venous line, then maintain hypernatremia with 3% infusion at 20–60 ml/hr through peripheral IV

Monitor serum Na, Osm, BUN, Cr; consider holding if Na >160 mEq/l or serum osmolarity >320 mosm/l

Risks: Central pontine myelinosis, seizures, hypernatremia, CHF, coagulopathy; lower risk of rebound intracranial HTN & renal failure compared to mannitol

Mechanisms of action: Osmotic diuresis, anti-inflammatory effect

Sedation & paralysis: Propofol & short-acting narcotics may decrease ICP by controlling sympathetic stimuli; neuromuscular blockage is a further adjunct for refractory severe ICP elevations

Monitor for hypertriglyceridemia & pancreatitis with prolonged use

Barbiturates: consider in pt with persistent increased ICP refractory to all preceding medical management & surgical compression; unclear impact on outcome (Eisenberg HM, et al. *J Neurosurg.* 1988;69:15–23)

Consider pentobarbital 10 mg/kg IV over 30 min, then 5 mg/kg q1h × 3 doses, then 1 mg/kg/hr

Monitor burst suppression with continuous EEG

Risks: Hypotension, oligemic hypoxemia, hypokalemia, respiratory depression, paralytic ileus, hepatic injury, renal injury, loss of neurologic exam, confounds brain death exam

Normocapnia: Goal $PaCO_2$ ~35 mm Hg; decreased CO_2 → decreased CBF → decreased ICP within 30 sec, sustained effect for <1 hr. Risk of rebound increased ICP when CO_2 normalizes

Prolonged prophylactic hyperventilation ($PaCO_2$ 24–28) is associated with worse outcome than normoventilation ($PaCO_2$ 30–35) in severe TBI pt (Muizelaar JP, et al. *J Neurosurg.* 1991;75:731–739)

Consider brief hyperventilation to $PaCO_2$ 30–35 as temporizing measure in pt with acute neurologic deterioration & impending herniation until other treatments can be implemented

Consider monitoring jugular bulb venous saturation ($SjVO_2$), brain tissue oxygen tension ($PBtO_2$), or CBF during hyperventilation for potential cerebral ischemia

Positive pressure support may exacerbate ICP, although the relationship between PEEP & ICP is unpredictable

Maximize venous drainage: Elevate head to 30°; further elevation risks compromising CPP & CBF; prevent constriction of neck veins from any cervical collar or ETT straps

Decompressive craniectomy: removal of cranial vault & expansion of dura over affected hemisphere, with possible resection of contused brain parenchyma, may augment ICP control in those pt with intracranial HTN refractory to aggressive medical management; impact on functional outcome remains unclear, possibly due to complications associated with surgery (*DECRA:* Cooper DJ, et al. *NEJM.* 2011;364:1493–1502)

Hypothermia: Controversial whether prophylactic cooling to 32–35°C improves outcome in severe TBI; does not improve mortality rate (Clifton GL, et al. *NEJM.* 2001;344:556–563; Brain Trauma Foundation; et al. *J Neurotrauma.* 2007;24:S21–s25)

Steroids: *Not recommended* for cytotoxic cerebral edema in TBI; increased risk of death within 2 wks (Roberts I, et al. *Lancet.* 2004;364:1321–1328)

Consequences of Intracranial Hypertension

Cerebral ischemia

Herniation:

Uncal herniation: Medial displacement of the temporal lobe causing midbrain compression & consequent ipsilateral fixed & dilated pupil (CN3 palsy), contralateral hemiparesis, & decreased state of arousal

Ipsilateral hemiparesis can result from compressing the contralateral cerebral peduncle against the tentorial incisura (Kernohan's notch)

Imaging demonstrates: Effacement of suprasellar & perimesencephalic cisterns, medial dislocation of the temporal horn of lateral ventricle, & unilateral compression of cerebral peduncle

Central diencephalic herniation: Caudal displacement of diencephalon from bilateral supratentorial HTN, causing altered consciousness, decreased motor response, abnormal eye movements, & eventual bilateral fixed & dilated pupils

Lethargy or agitation is the 1st sign of central herniation, while pupillary changes are a late finding, in contrast to uncal herniation

Impingement of posterior cerebral arteries can lead to occipital infarcts

Stretch of the pituitary infundibulum may result in diabetes insipidus

Imaging demonstrates: Effacement of perimesencephalic cisterns, Duret hemorrhages

Tonsillar herniation: Caudal displacement of cerebellum by increased pressure in the posterior fossa, leading to medullary compromise & coma

Classically associated with Cushing's triad (HTN, bradycardia, respiratory irregularity)

Imaging demonstrates: Tonsillar descent through the foramen magnum, hydrocephalus

Subfalcine herniation: Lateral displacement of cingulate gyrus under falx cerebri, which may compress the anterior cerebral arteries & lead to lower extremity paresis; may precede central herniation

Mortality

Sympathetic Storms

Episodic HTN, tachycardia, tachypnea, hyperthermia, diaphoresis, pupillary dilation, & flexor–extensor posturing observed in severe TBI pt.

Onset can occur hrs to wks after injury; periodicity of minutes to hours.

May be precipitated by discontinuation of sedatives, such as following extubation of critically ill pt, & tactile stimuli.

May be confused for infectious state (given persistent fever) or catecholamine-secreting mass.

Dx of exclusion: r/o underlying etiologies with pan-cx, lab workup, & imaging; clinical hx & periodic nature of syndrome strongly suggest autonomic dysregulation.

Treatment: Narcotic analgesia, bromocriptine, clonidine, propranolol, labetalol

Recommend: Morphine sulfate q4h & bromocriptine 2.5–5 mg q4h–q8h, followed by trial of clonidine 0.1–0.2 mg b.i.d.

Spinal Cord Injury

Neurologic Assessment

Physical exam should include assessment of key muscle groups, sensory levels, deep tendon reflexes, rectal exam, & the bulbocavernosus reflex, as well as palpation of the spine.

Key Muscle Groups to Assess in Spinal Cord Injury (SCI)			
C5	Elbow flexors	L2	Hip flexors
C6	Wrist extensors	L3	Knee extensors
C7	Elbow extensors	L4	Ankle dorsiflexors
C8	Finger flexors	L5	Long toe extensors
T1	Finger abductors	S1	Ankle plantar flexors

Adapted from: American Spinal Injury Association classification of spinal cord injury.

Neurologic deficit, even if transient, in the setting of a high-energy mechanism suggests an unstable spine.

Complete SCI refers to absence of any motor or sensory function below the level of injury, including in S4–S5. This should be distinguished from incomplete SCI to guide management & prognosis, as long as the pt is not in spinal shock.

Incomplete injury requires perianal sensation or voluntary rectal tone, as opposed to involuntary tone, which may be partially preserved in complete SCI.

Presume SCI in trauma pt until proven otherwise.

Spinal shock:

Suppression of spinal cord reflex activity in the early phase of acute SCI.

Confounds distinction between complete & incomplete SCI during period of spinal shock, most common within the 1st 24 hrs.

May be distinguish by assessing the bulbocavernosus reflex, presence of which excludes spinal shock.

Neurogenic shock:

Triad of hypotension, normal to bradycardia, & hypothermia

Results from a temporary loss of sympathetic tone & inability to mount reflex response; unopposed parasympathetics lead to vasodilation, decreased CO, & hypotension

Usually seen in cervical or upper thoracic cord injury

Avoid aggressive fluid resuscitation to prevent fluid overload

Manage with β-agonists, α-agonists, or anticholinergics to improve CO

Spinal Cord Injury Classification	
ASIA Impairment Scale	
ASIA A	Complete injury. No motor or sensory function below the level of injury, including in the sacral segments S4–S5.
ASIA B	Incomplete injury. Sensory but not motor function is preserved below the level of injury, including the sacral segments S4–S5.
ASIA C	Incomplete injury. Motor function is preserved below the level of injury, with more than half of the muscles below the level of injury with grade <3 in strength.
ASIA D	Incomplete injury. Motor function is preserved below the level of injury, with at least half of the muscles below the level of injury with grade 3 or more in strength.
ASIA E	Normal. Intact motor & sensory function.

Adapted from: American Spinal Injury Association (ASIA) classification of spinal cord injury.

Incomplete SCI Syndromes

Central cord syndrome:

Mechanism: Hyperextension injury, esp. in elderly pt with preexisting spinal stenosis

Presentation: Bilateral weakness with upper extremities affected more than lower extremities, bilateral sensory deficits, upper extremity hyporeflexia, lower extremity hyperreflexia, urinary retention

Prognosis: Partial recovery may be expected, esp. of the lower extremities & bowel & bladder; half of the pt with cord contusion without hematomyelia regain ambulatory capacity; recovery of fine motor hand function is less frequently observed

Brown–Sequard syndrome:

Mechanism: Hemisection of the spinal cord; may result from penetrating trauma, lateralized disc herniation, epidural hematoma, tumors, & arteriovenous malformations.

Presentation: Ipsilateral paralysis & loss of proprioception with contralateral loss of pain & temp sensation below the level of injury; preserved sensation of light touch

Prognosis: Favorable, 90% of pt recover ambulation & bowel & bladder function

Anterior cord syndrome:

Mechanism: Anterior spinal artery compromise, retropulsion of fractured vertebral body

Presentation: Bilateral weakness & loss of pain & temp sensation below the level of injury

Prognosis: Poor, few regain motor function

Posterior cord syndrome:

Mechanism: B_{12} deficiency, tertiary syphilis

Presentation: Loss of deep pressure sensation & proprioception, intact motor function, intact pain & temp sensation, foot slapping gait

Prognosis: Favorable, treat the underlying dz

Cauda equina syndrome:

Mechanism: Compression of cauda equina by lumbar disc herniation, tumor, hematoma, abscess, or fx
Presentation: Saddle anesthesia, weakness involving multiple nerve roots, paraplegia, urinary retention or incontinence, sciatica
Prognosis: Dependent on timing before decompression

Radiographic Evaluation

Imaging of the cervical spine should be obtained in pt who are awake & symptomatic or obtunded & cannot be evaluated

In an awake, asymptomatic pt with a normal neurologic evaluation, no neck pain/tenderness, & no distracting injuries or intoxication, imaging is not required

In symptomatic or obtunded pt, CT C-spine is the imaging study of choice; if CT is not avail., 3-view (anteroposterior, lateral, & open-mouth) x-rays may be performed

CTA should be performed in pt with suspected vertebral artery injury (assess with modified Denver Screening Criteria)

MRI may be performed for pt with neurologic deterioration, neurologic deficits not accounted for by degree of bony injury, to assess for ligamentous injury, or prior to closed reduction

CT is also the imaging study of choice for pt with suspected trauma to the thoracic & lumbar spine

CT of the thoracic & lumbar spines should be obtained in blunt trauma pt with back pain/tenderness, neurologic deficits, altered mental status, intoxication, other injuries, or high-energy mechanisms

CT should also be performed in pt with known/suspected cervical injuries due to the high incidence of multilevel injuries

Cervical spine may be clinically cleared without imaging if pt with minor trauma fulfills NEXUS criteria (Hoffman JR, et al. *NEJM.* 2000;343:94–99):

Alert & oriented pt

Intact neurologic status

Absence of midline posterior cervical spine tenderness on palpation

Absence of other painful injuries, which may distract the pt from neck injury

Clearance of the cervical spine in unresponsive pt may be made if imaging (CT alone or CT + MRI) of the cervical spine is negative for injury; some may choose to continue immobilization until pt is awake & asymptomatic

Be cautious for SCI without radiographic abnormality (SCIWORA), esp. in children. In these pt, MRI C-spine & flexion–extension x-ray films are recommended along with CT screening of the remaining spinal column.

Initial Management of SCI

Early open or closed reduction is recommended, particularly in the setting of ongoing spinal cord compression

Maintain MAP 85–90 in the 1st 7 days following injury; avoid hypotension (sBP <90 mm Hg)

Consider neurogenic shock if hypotension with bradycardia; use vasopressors rather than aggressive hydration

Dopamine is vasopressor of choice to minimize risk of reflex bradycardia

Closely monitor respiratory status; assess VC when stable

High risk for aspiration & respiratory failure in cervical SCI

Intubate if signs of hypoxia, hypercarbia, decreasing VC, or poor mental status

Perform early tracheostomy in pt likely to remain ventilator dependent

Stress ulcer ppx should be given if pt is intubated

Treat retained secretions due to expiratory muscle weakness with manually assisted coughing, mechanical insufflation–exsufflation, or other expiratory aids in addition to suctioning

Early venous thromboembolism ppx is recommended

Pharmacologic Therapy

Methylprednisolone is not recommended due to lack of class I or class II evidence, demonstrating clinical benefit & presence of class I, II, & III evidence that steroids might result in numerous complications including death (Hurlbert RJ, et al. *Neurosurgery.* 2013;72[suppl 2]:93–107)

Complications and Long-term Management of SCI

Autonomic dysreflexia

Pulmonary infxn

Urinary training: Scheduled straight catheter regimen to increase detrusor tone

Spasticity

Skin breakdown: Monitor for pressure ulcers vigilantly

Turn or reposition every 2 hrs for pressure relief, while maintaining spinal precautions

Provide air mattress bed for quadriplegics

Avoid spinal orthosis when pt is resting in bed

BURN MANAGEMENT

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Introduction

Advances in initial resuscitation, critical care, & surgical management of burns have led to dramatic improvements in the overall survival & quality of life of the burn patient (pt). Initial evaluation of the burn pt follows the same systematic assessment of all trauma pt with additional attention to critical areas of airway management, fluid management, & wound care.

Anatomy and General Principles

The skin is composed of 2 distinct layers.

Epidermis: outer layer, acts as barrier, provides thermal regulation, protects against infxn, UV light, & evaporation of fluids

Dermis: inner layer, provides durability & elasticity

Epidermis & dermis separated by basement membrane zone: BMZ plays significant role in burn wound healing, anchoring structures, & protecting epithelialized wounds from shear injury

Epidermis will recover if viable dermis present → 1 goal of burn wound care is to maintain dermal viability

A burn is tissue injury resulting from exposure to thermal, electrical, chemical, or radioactive agents

Zones of injury

Zone of coagulation: central, most severely damaged, cells here are coagulated or necrotic

Zone of stasis: area characterized by vasoconstriction & ischemia, cells initially viable but may convert to coagulation as a consequence of development of edema, infxn, decreased perfusion

Zone of hyperemia: characterized by vasodilatation resulting from release of inflammatory mediators, typically viable

Evaluation of the Burn Patient

Always begins with initial systematic primary & secondary survey to evaluate for any traumatic injuries, as in Chapter 41.

Type of injury, heat source, circumstances of injury:

Thermal: most common type of burn, from contact with extreme heat

Electrical injuries: may present with little injury to skin but significant injuries to muscle, vasculature, & bone; cardiac standstill or arrhythmia complications; myonecrosis common, monitor for signs & sx of rhabdomyolysis

Chemical:

Acids → coagulation necrosis, hydrofluoric acid burns cause calcium/magnesium chelation, risk of cardiac arrest

Alkali → liquefaction necrosis, vascular thrombosis, dermal ischemia

Scalds: burn from hot water or steam, may be seen in child/elder abuse

Clean burn wound with soap & water, remove debris

Assess extent of wounds & total body surface area (TBSA) involved: "Rule of nines." (Figure 44-1)

Estimates surface area in adult pt

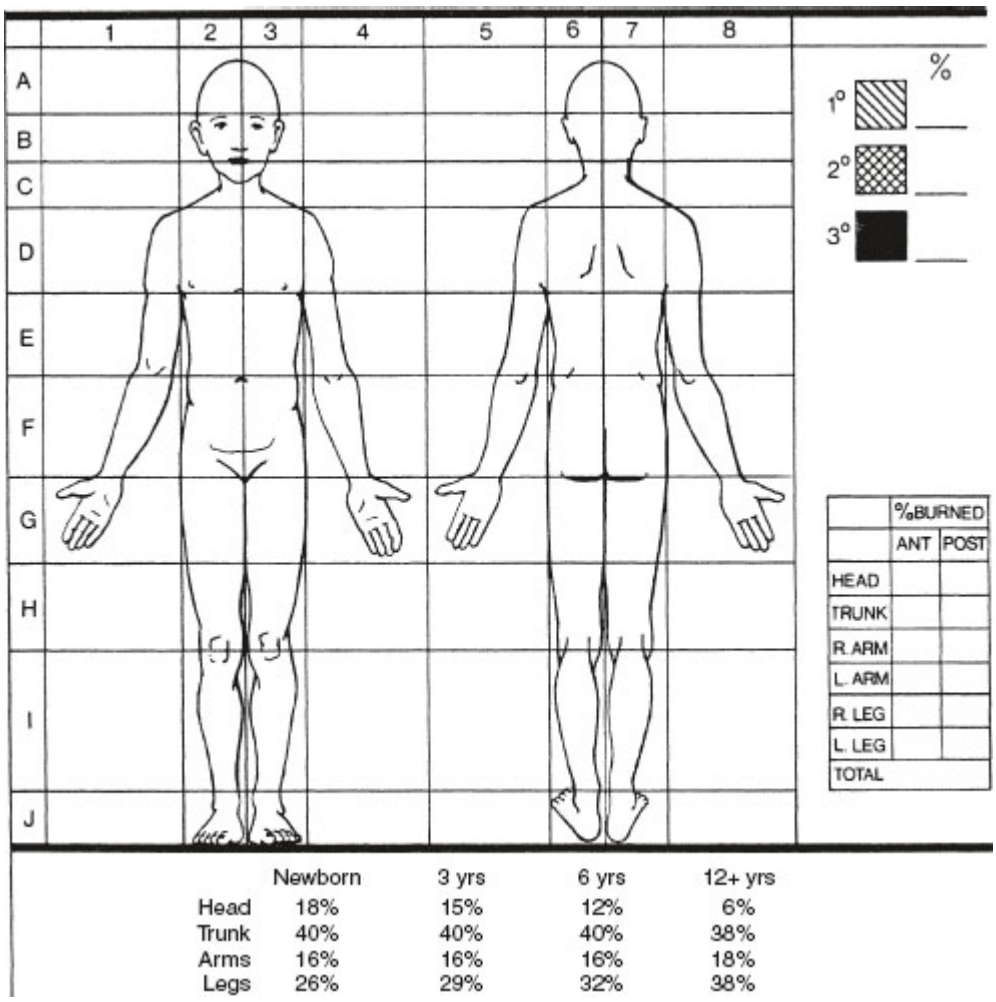
Head & each upper extremity represent 9% TBSA each

Anterior trunk, posterior trunk, & each lower extremity represent 18% TBSA each

Less accurate in children due to different body proportions

Assess depth of burns

Figure 44-1. Example of One of a Number of Age-Specific Burn Diagrams Available to Facilitate Accurate Estimation of the Extent of a Burn, Compensating for Anthropometric Differences Between Age Groups



(From *Critical Care Handbook of the Massachusetts General Hospital.* 2010:556.)

Overview of Burn Wound Management		
Depth of Burn	**Clinical Features**	**Management**
Superficial/1st degree	Dry, erythematous, blanches with pressure, painful	Soothing, moisturizing lotions
Partial thickness/2nd degree	Blisters, pink, moist, blanches with pressure, painful	Greasy gauze
Deep partial thickness/ 2nd degree	Blisters, wet or waxy, patchy color, less painful	Silver sulfadiazine, surgical excision & grafting if not going to heal within 3 wks
Full thickness/3rd degree	Dry, leathery, black or white, does not blanch, painless	Silver sulfadiazine, early excision & skin grafting
4th degree	Extends into fascia and/or muscle	

Airway and Respiratory Management in Burns

Deliver maximal FiO_2 during initial resuscitation.

Inhalation injuries: inhalation of hot gases may cause direct injury to airway without obvious signs to head/neck, associated with increase in mortality & morbidity.

Risk of inhalation injury increased if voice change, carbonaceous sputum, singed nasal hairs, swelling of nose/mouth/lips/throat, h/o being in enclosed space

Low threshold for intubation: perform before progression of airway edema prevents safe intubation, should be considered for pt presenting with stridor

Carboxyhemoglobin level taken within 1 hr after injury indicative of smoke inhalation if >10%

Fluid Management in Burns (Latenser BA. *Crit Care Med*. 2009;37:2819–2826; Pham TN, et al. *J Burn Care & Research*. 2008;29(1):257–266)

CO is reduced immediately postburn (decreased circulating volume & myocardial depression). 3–5 days postburn → hypermetabolic state (increased CO, decreased SVR).

Resuscitation goal is to anticipate & prevent burn shock. Delay in fluid resuscitation increases mortality; however, excessive resuscitation ("fluid creep") & volume overload also deleterious → can lead to pulmonary edema, conversion of superficial burns to deeper burns, compartment syndrome (extremities, abd), & need for fasciotomies

Factors that influence fluid requirement during resuscitation include: age, TBSA, burn depth, inhalation injury, associated injuries, delay in resuscitation, fasciotomies

Lactated Ringer's solution most closely resembles normal body fluids

Resuscitation should be titrated to hemodynamics & urine output (goal 0.5 ml/kg/hr in adults, 0.5–1.0 ml/kg/hr in children <30 kg)

Pt with TBSA <20% can undergo standard fluid resuscitation titrated to urine output, & oral rehydration can be considered in these pt

Pt with TBSA >20% should be resuscitated intravenously using a formula accounting for body wt & TBSA

Parkland formula: 4 ml of lactated Ringer × kg × % TBSA burn in the 1st 24 hrs, with half of calculated fluid given in 1st 8 hrs postburn, remainder over the next 16 hrs (e.g., 70 kg man with 50% TBSA burns needs 4 × 70 × 50 = 14,000 ml; give 7,000 ml during 0–8 hrs after burn, then 7,000 ml over the next 8–24 hrs after burn)

Modified Brooke formula: 2 ml of lactated Ringer × kg × % TBSA burn in 1st 24 hrs, with half of calculated fluid given in 1st 8 hrs postburn, remainder over next 16 hrs (e.g., 70 kg man with 50% TBSA burns needs 2 × 70 × 50 = 7,000 ml; give 3,500 ml during 0–8 hrs after burn, then 3,500 ml over the next 8–24 hrs after burn)

No clinical advantage with colloids or hypertonic saline; some studies show increased mortality & complications with these

Dressings and Topical Antimicrobial Agents Used in Burn Care

Burn dressings include silver-containing dressings, biologics, & skin substitutes

Dressings containing nanocrystalline silver embedded provide some broad-spectrum antibacterial activity: Acticoat (polyethylene mesh), Aquacel AG (hydrofibers), Mepilex AG (soft silicone dressing)

Biologic dressings for temporary wound coverage: allograft, xenograft

Skin substitutes: integra (outer layer of Silastic film protective barrier, which is removed after dermal inner layer has become incorporated into wound over time)

Topical Agents Used in Burn Care

Agent	Antimicrobial Coverage	Advantages	Disadvantages
Bacitracin, Xeroform	Gram positive	Soothes, moisturizes, good for facial care & epithelializing wounds	Not appropriate for deeper wounds
Mafenide	Broad-spectrum antibacterial, anticlostridial	Penetrates eschar well	Painful on application, carbonic anhydrase inhibition → met acidosis
Mupirocin	Anti-MRSA	MRSA coverage	Narrow antimicrobial coverage
Silver nitrate	Broad-spectrum antibacterial	Effective for ppx & treatment of wound infxn	Poor eschar penetration, hyponatremia, methemoglobinemia
Silver sulfadiazine	Broad-spectrum antibacterial, antipseudomonal	Soothes on application, not painful	Poor eschar penetration, leucopenia

Source: ACS Surgery: Principles and Practice. 2007:1425.

Surgical Burn Wound Management

Early excision & skin grafting: decrease risk of burn wound sepsis, attenuates SIRS.

Full-thickness skin grafts: less contraction but will leave greater dermal deficit at donor site, increasing length of time needed for healing & increased risk of hypertrophic scarring

Split-thickness skin grafts: these will contract

Escharotomy: may be required for circumferential full-thickness extremity burn wounds in which distal perfusion is compromised or chest burns in which eschar poses external mechanical barrier to respiration.

Metabolism and Nutrition

Hypermetabolic response to burns can result in life-threatening protein-calorie malnutrition. Increase in normal resting energy expenditure is compounded by insensible losses through wound bed & protein loss/leaking into interstitial space

Enteral nutrition (nasogastric, gastric, or intestinal tube) is preferred as this maintains intestinal integrity & associated immunity & limits complications of TPN

Indirect calorimetry considered "gold standard," however, results affected by oxygen therapy, hemodynamic instability, fever

Many formulas exist for estimating basal energy expenditure → adjust by stress factor of 1.2–2

Harris–Benedict equation: estimates basal energy rate

Male: kcal/d = 66.5 + (13.8 × wt in kg) + (5 × ht in cm) – (6.76 × age in yrs)

Female: kcal/d = 655 + (9.6 × wt in kg) + (1.85 × ht in cm) – (4.68 × age in yrs)

Macronutrients	
Protein	1.5–2.0 g protein/kg/d
Carbohydrate	5–7 mg/kg/min of glucose representing 50% of total cal/d
Fat	Fewer than 15% of nonprotein calories from fat

Vitamin A, C, D in standard multivitamin formulations, trace minerals (selenium, zinc, copper)

Glutamine (0.35 gm/kg/d) may decrease infectious complications, decrease hospital length of stay, decrease mortality

Anticatabolic/anabolic agents:

Oxandrolone: promotes protein synthesis, nitrogen retention (Demling RH, et al. *Burns.* 2003;29:793)

Beta-blockade/propranolol: decrease HR, reduce cardiac index (*N Engl J Med.* 2001;25:1223)

Complications

Burn wound sepsis: risk decreased by early excision, confirm dx by biopsy

Abd compartment syndrome: suggested by urinary bladder pressure >20 mm Hg, can contribute to respiratory & renal failure & bowel ischemia, may require celiotomy & leaving abd compartment open (see Chapter 41)

Extremity compartment syndrome: may require escharotomy, fasciotomy (see Chapter 41)

Pneumonia: avoid prophylactic abx as they increase risk of wound infxns with resistant organisms

DVT: increased risk for DVT, ppx as with trauma pt unfractionated heparin or low-molecular-wt heparin, but pay attention to renal function (as they are renally cleared)

Stress ulcer: prophylactic H_2 receptor blocker or proton pump inhibitor

Hypothermia: dramatic loss of the thermal regulation properties of skin, can contribute to coagulopathy & hemodynamic instability, institute warming measure, warm room, forced air heating, fluid warmer

COMMON ICU PROCEDURES

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Endotracheal Tube Exchange

Indications:

Replacement for obstructed ETT or tube with malfunctioning cuff

Special considerations:

DNR/DNI, difficult airway

Materials:

Intubating instrument (laryngoscope, videolaryngoscope, intubating LMA, tube changer)

ETT

Stylet (optional)

Sedatives/muscle relaxants (optional)

Topical anesthetic (optional)

10-cc syringe

Assistant

Technique (depends on intubation strategy):

Position patient (pt) supine

Prepare rescue medications & suction. Verify working IV if possible

If nonemergent, consider holding tube feeds

Adjust sedation as necessary; may need muscle relaxant once adequate sedation achieved

Increase inspired oxygen fraction on ventilator to 100%

Intubate

Many successful ETT exchange strategies exist. None are successful all the time. Some sample techniques follow:

Direct or videolaryngoscopy

This technique is the quickest way to perform tube exchange

With the original ETT in place, perform direct laryngoscopy & visualize the vocal cords

The laryngoscopist should insert the new ETT into the mouth & position it parallel to the old tube

The assistant should then unfasten the old ETT, deflate the cuff, & remove it. This way, the pt spends the least time without a secure ETT & the entire procedure is performed under direct vision

Alternatively, a blind tube changer–assisted exchange can be performed

An access elbow connector is placed at the end of the ETT in the circuit to allow placement of the tube changer while the pt is still being ventilated

A tube changer is then placed into the old ETT to a depth sufficient to ensure location in the trachea

The old ETT is then removed & a new tube placed over the tube changer If the new tube does not readily pass through the cords, rotate ETT 180°, apply jaw thrust, or adjust the position of the tube changer

Clinicians are increasingly using combinations of the aforementioned techniques for ICU tube exchange. Performing direct or video laryngoscopy simultaneously with tube changer-assisted exchange allows continuous direct visualization of the exchange & decreases chance of upper airway obstruction, preventing passage of the new ETT over the tube changer

Verify $ETCO_2$ & bilateral breath sounds

Monitor BP & O_2 saturation

Secure ETT

Obtain CXR or perform fiberoptic bronchoscopy to verify tube placement & r/o postintubation complications

Complications/keys to success:

Hypoxemia; cardiopulmonary instability; death; esophageal intubation; aspiration; pharyngeal, esophageal, & tracheal perforation; dental/oral injury

Most important key to success is anticipatory & contingency planning. When elective, should be performed under optimal conditions & with optimal personnel: consider time of day, nursing/staffing patterns, feeding status, family availability, etc.

Recognize strengths & weaknesses of different visualization strategies

Central Venous Catheter Placement (also see Chapters 8, 47)

Indications:

Venous access in pt with severe vascular dz

Rapid volume resuscitation

Central venous pressure monitoring

Swan Ganz catheter placement

Administration of vasoactive agents or caustic chemotherapy drugs

Parental nutrition

Contraindications:

Vascular anomaly

Infxn at the site of catheter insertion

Coagulopathy (more for subclavian placement as compression is not possible)

Complications:

Arterial puncture, bleeding, hematoma, infxn

Pneumo- or hemothorax (higher incidence with IJ or subclavian cannulation)

Tamponade (with right subclavian approach)

Air embolism, VT

Technique:

Discuss the procedure with the pt (if awake)

Choose the site of catheter insertion—IJ vs. subclavian vs. femoral

Positioning:

If IJ approach: most institutions recommend or mandate the use of ultrasound guidance; position pt in supine, Trendelenburg position, & turn head 30–45° contralateral to the side of catheter insertion. IJ landmarks include the triangle formed by the 2 heads of the sternocleidomastoid muscle & the medial part of the clavicle. The IJ vein is usually located lateral to the carotid artery but may move underneath the carotid, as head rotation increases

If subclavian approach—lay pt supine (Trendelenburg position is not needed) with small towel placed between shoulder blades. The ipsilateral arm should be positioned at the pt's side

If femoral approach: lay pt supine & slightly abduct the ipsilateral leg. Palpate the femoral artery (lateral to femoral vein). Needle insertion point: 1–2 cm caudal to inguinal ligament. Leg abduction such as the "frog leg" position (place ipsilateral foot on the contralateral knee) may facilitate exposure of the femoral anatomy

Prep the site. Apply an antiseptic per your institutional guidelines. The antiseptic usually should be administered in a back & forth, scrubbing motion rather than a concentric "inside out" motion

Note that for the femoral site, care should be taken to not track bacteria from the groin to the line insertion site

Drape the pt with the sterile sheet in the kit with the opening over the site of line insertion & place a 2nd sterile full body drape on the pt over any other exposed areas

US is recommended by most insertion guidelines for central venous catheter insertion (see Chapter 47 for US-guided placement):

If using US guidance, place the sterile sheath over the US probe & identify the vein. The vein can be distinguished from the artery by Doppler flow pattern, compressibility, position (the vein is superior & lateral to the artery in the IJ view), & pulsatility

If not using US guidance, identify the IJ using a 16-gauge finder needle attached to a 5-cc syringe

Anesthetize the site with subcutaneous local anesthetic

Using a thin-walled hollow needle or catheter-over-needle "modified Seldinger" assembly, cannulate the IJ vein & insert the guide wire. If using US, the needle should be introduced so that its contact with the vein can be captured visually by the US beam. If not using US, the needle should be aligned with the finder needle so that it contacts the vein in approx. the same location

The "J" end of the wire should enter the pt as the "straight" end of the wire may puncture through a vessel during insertion

For the subclavian site:

Consider US for identification of the subclavian cite

After palpation of the lateral clavicle, the 16-gauge introducer needle should be inserted 1 cm below & ~3 cm lateral to the midpoint of the clavicle

Deeper infiltration anesthesia is needed than for IJ or femoral sites. Infiltrate the skin & the periosteum of the lateral clavicle with lidocaine

Make contact with the clavicle & then "walk" the needle along the clavicle until it passes underneath. Aim needle at the sternal notch, keeping it as parallel to the skin as possible. Once under the clavicle, advance the needle attached to a 5-cc syringe (in many pt, the needle may need to be inserted nearly to the hub) while applying continuous negative pressure on the syringe until venous return is achieved

Be alert for anatomic complications of subclavian line insertion that occur with a higher frequency than with IJ insertion

The "J" end of the wire should enter the pt as the "straight" end of the wire may puncture through a vessel during insertion

For the femoral site (see Chapter 47 for ultrasound guided placement):

Palpate the femoral artery with the nondominant hand & anesthetize the site with subcutaneous local anesthetic

Keeping the nondominant hand on the femoral artery, advance introducer needle attached to a 5-cc syringe at a 60° angle to the skin (cephalad) & advance the needle while aspirating until venous return is achieved

For all the sites, once the vessel is cannulated, the guide wire should be advanced through the needle to a depth that clearly exceeds the anticipated depth of the cannula. The "J" end of the wire should enter the pt as the "straight" end of the wire may puncture through a vessel during insertion

Once the guide wire is placed, its location within the vein should be verified either via US or via manometry. If manometry is used, a catheter should be placed over the wire & into the vessel. The wire should then be removed & the catheter attached to an open piece of IV tubing. Allow the tubing to fill with blood & then raise the free end to evaluate the pressure inside the vessel. If US is used, the wire should be visualized in the vein as far as is possible

TEE may also be used & is closest to a "gold standard"

When the wire location is verified, the insertion site should be dilated & the appropriate catheter inserted. For the subclavian site, care should be taken to verify that the dilator & catheter pass with the wire under the clavicle

Be sure to remove and account for the guide wire! This complication occurs with a measurable frequency in published literature

Fasten the catheter to the skin, apply the Biopatch, & dress with transparent adhesive dressing

Order a CXR to verify catheter position. The tip of the catheter should be on the right side of the pt & should not protrude below the lower border of the right main stem to avoid erosion into the distal SVC or right atrium & consequent tamponade

Keys to success:

Many successful techniques exist

Passing the guide wire can often be as difficult as cannulating the vessel with the needle. If a sufficient length of the guide wire does not pass freely, be extremely careful passing the catheter

If the dilator or catheter becomes difficult to pass at any point, verify that the guide wire moves freely to r/o the possibility of a kink in the wire

Keep track of the wire at all times to verify that the guide wire does not slip completely into the pt. Be sure to remove at the end!

Pulmonary Artery Catheter Insertion (also see Chapter 2)

Indications:

Direct access to the pulmonary circulation (for delivery of vasodilators or anticoagulants)

Dx of complex hemodynamic states including tamponade, & increased pulmonary vascular resistance

PA pressure monitoring

CO monitoring

Titration of fluid therapy

Little evidence supports the benefits of PA catheter placement on outcome

Contraindications:

Lack of vascular access

Presence of right-sided ventricular assist device (VAD)

VSD/ASD

Tricuspid regurgitation, presence of right ventricular pacing hardware, & pulmonary stenosis are not contraindications but may complicate placement

Keys to success:

Many different successful techniques exist for advancing the PA catheter. This section will outline some general principles

Do not withdraw the catheter while the balloon is inflated as chordal rupture or valve damage may result

Do not leave the catheter tip in the RV for any prolonged period. It may cause dysrhythmias & even perforation

If the catheter must be inserted excessively far (70+ cm) before a PA tracing is observed, looping may have occurred. The catheter should be withdrawn & readvanced to avoid knotting the catheter

Do not leave the balloon inflated for prolonged periods as PA rupture may occur

No evidence exists to favor either continuous advancement or intermittent advancement steps. Both approaches may be successful in specific pt

Flat or reverse Trendelenburg position, & tilting the pt left side up may facilitate advancing the catheter to the PA position

Be extremely careful “wedging” the catheter. Balloon inflation always involves a risk of PA rupture, which is often fatal

Arterial Catheter (Line) Placement (also see Chapter 2)

Indications:

Beat-to-beat monitoring of BP

Assessment of pulse pressure variation

Contraindications:

Vascular insufficiency of the arm or hand

Keys to success:

A common challenge in arterial line placement is threading of the catheter into the artery that has smaller & thicker muscular walls than a vein; although the needle may easily penetrate the arterial wall, the catheter may not easily pass through the wall

If identifying the artery using palpation is difficult (ECMO or LVAD), US is an effective alternative

THORACENTESIS

Indications:

Diagnostic (obtain sample for cx, cell count, protein, glucose, triglycerides/cholesterol, cytology/pathology)

Therapeutic (remove air or liquid from the pleural space to improve lung mechanics & work of breathing. Note that therapeutic thoracocentesis may be followed by placement of a drainage catheter)

Contraindications

Coagulopathy, noncooperative pt

Bullous lung dz (emphysema)

Materials:

Sterile gloves, gown, & drapes. A cap & mask should also be worn

Prep the site. Apply an antiseptic per your institutional guidelines. The antiseptic usually should be administered in a back & forth, scrubbing motion rather than a concentric "inside out" motion. Drape the area to exclude nonsterile areas

Local anesthetic, suture, US machine

Assistant (required to stabilize the pt in the sitting position, collect specimens, & hand equipment to the operator)

A hollow needle for puncturing the skin & accessing the thoracic cavity & a syringe to identify when the catheter has entered the thoracic cavity. For both diagnostic & therapeutic thoracentesis, a plastic catheter is often mounted over the needle & threaded into the pleural space to reduce damage to the lung from the presence of the sharp needle in the pleural space

Specimen containers to capture the pleural fluid for lab analysis

Technique:

Discuss with pt (if awake) & describe procedure

Because CXR may not always determine whether sufficient fluid exists to allow successful thoracentesis, US examination of the thorax may allow an estimate of fluid volume & identify an appropriate insertion site

Position the pt. Usually the pt is positioned sitting up with or without the legs dangling off the side of the bed. This position allows pleural fluid to drain to the lowest part of the thoracic cavity so that it can be more easily removed. An assistant may be needed to stabilize the pt in this position

Identify landmarks for needle placement. To avoid the neurovascular bundle on the underside of each rib, the needle should be "walked off" the superior border of the appropriate rib. If the procedure is performed without US-guided localization of the fluid collection, or for a needle thoracotomy, the operator should identify the 9th interspace at the midaxillary line & position the needle to enter just over the superior border of the 9th rib

Alternatively, US may be used to identify the best interspace for loculated or otherwise difficult effusions

Prep the site. Apply an antiseptic per your institutional guidelines. The antiseptic usually should be administered in a back & forth, scrubbing motion rather than a concentric "inside out" motion. Drape the area to exclude nonsterile areas

Anesthetize the insertion site with subcutaneous local anesthetic. Because the needle will contact the rib surface during the "walking off" process, be sure to anesthetize the rib surface as well

Attach the empty syringe to the thoracentesis needle. Insert the needle perpendicular to the skin until it contacts the surface of the rib below the desired interspace. This step identifies the location of the rib. Then, withdraw the needle slightly, reposition it to still be perpendicular to the skin but more cephalad, & advance again until the rib is contacted. Repeat until the needle slips over the superior border of the rib

Advance the needle while aspirating with the syringe. Entry into the pleural space should be identified by sudden loss of resistance to aspiration & appearance of fluid in the syringe

When pleural fluid is aspirated into the syringe, stop advancing the needle. Thread the plastic catheter into the pleural space, remove the needle, & reattach the syringe to the catheter. Remove pleural fluid and/or send for diagnostic studies

When the procedure is complete, remove the catheter during a period of intrathoracic positive pressure. If the pt is receiving positive pressure ventilation, intrathoracic pressure would be highest during end-inspiration. If the pt is breathing spontaneously, he or she should be instructed to perform a Valsalva maneuver before removing the catheter

Complications:

Infxn, hemothorax, pneumothorax, hypotension, reexpansion of pulmonary edema

Needle Thoracostomy

Indications:

Pneumothorax (whether suspected or confirmed) with associated pulmonary or hemodynamic compromise (hypotension, shock, severe dyspnea)

Contraindications:

No absolute contraindications exist

Materials:

14-gauge or 16-gauge 2–2½ inch needle with cannula
5-cc syringe attached to needle
Chlorhexidine skin preps
Sterile gauze 4 × 4 inch, tape

Procedure:

On the side of the pneumothorax, proceed with sterile prep using chlorhexidine skin preps at the 2nd intercostal space, midclavicular line

Insert the needle with attached syringe perpendicular to the chest wall at the superior border of the 3rd rib

Once the needle makes contact with the 3rd rib, maintain negative pressure on the syringe & walk the needle & catheter over the superior border of the 3rd rib & advance the needle & catheter into the pleural space

Entry into the pleural space becomes apparent by a "pop" sound, air aspirate into the syringe, or change in resistance

Once the pleural space is accessed, remove the needle while leaving the cannula in the pleural space

Secure the cannula with gauze dressing & tape

Keys to success:

Do not reinsert the needle into the cannula since the cannula may be damaged/sheared

The procedure should be effective immediately, demonstrated by relief of dyspnea, hypotension, or shock. Air sounds should be audible over side of previous pneumothorax

Careful attention to landmarks helps prevent iatrogenic injury

PARACENTESIS

Indications:

To obtain fluid for diagnostic analysis

To drain fluid from the abd cavity

Contraindications:

Pt refusal, coagulopathy

Loculated or difficult to access fluid

Materials:

Sterile gloves, gown, & drapes. A cap & a mask should also be worn

Topical sterilizing solution (per individual institutional guidelines)

Local anesthetic, suture

US machine

Assistant (optional) to collect specimens & hand equipment to the operator

Paracentesis kit. All kits should have specimen containers to capture the peritoneal fluid for lab analysis

Technique:

Verify presence of abd fluid. Physical examination is often sufficient, although CT, abd x-ray & US may be useful for complex anatomy

Supine position or head/back slightly elevated to allow intra-abd fluid to collect in 1 place. Occasionally, a lateral position may be used

If large volume paracentesis is planned, BP and pulse oximetry monitoring are necessary

Identify landmarks for needle placement. Avoid the liver & any visible blood vessels. If the procedure is performed without US-guided localization of the fluid collection, the periumbilical area is usually chosen. Alternatively, US may be used to identify the best entry site for loculated or otherwise difficult effusions

Prep the site. Apply an antiseptic per your institutional guidelines. The antiseptic usually should be administered in a back & forth, scrubbing motion rather than a concentric "inside out" motion. Drape the area to exclude nonsterile areas

Anesthetize the insertion site with subcutaneous local anesthetic. Aspirate during needle movement. If ascites fluid is withdrawn during local anesthetic infiltration, withdraw the needle until fluid drainage stops

When the needle enters the peritoneal cavity, thread the plastic catheter & remove the needle. Peritoneal fluid may be withdrawn using either a syringe or by attaching the catheter to a vacuum bottle

Nasogastric and Duodenal Feeding Tube Placement

Indications:

Administration of feeds & oral medications

NGTs:

Decompression of GI tract when ileus or bowel obstruction present

Suction & removal of gastric contents (i.e., overdose ingestion)

Lavage & suction for evaluation of GI bleeding, or for active internal warming or cooling of a pt

Administration of activated charcoal

Duodenal feeding (including Dobhoff) tubes:

Safer administration of feeds & oral medications during OR procedures—potentially lowering the risk of aspiration since the tube can be placed distal to the pyloric sphincter in the proximal duodenum

Contraindications:

Maxillofacial trauma

Nosebleeds

Esophageal abnormalities such as stricture

Abnormal anatomy (esophagectomy, gastric bypass)

Caustic ingestion

NGT: inability to protect the airway (if the pt has high residuals from gastric feeds, these feeds may be aspirated)

Materials:

Nasogastric or duodenal feeding (including Dobhoff) tube, lubricant, 60-cc syringe, stethoscope, tape, glass of water, 10-cc saline

Procedure:

Sitting position if awake & not intubated with the neck flexed; if intubated & sedated, lay the pt flat in the bed & place 1 hand under the pt's head to flex the neck (when flexing the neck, be careful that the ETT does not migrate into the right main stem bronchus)

Measure the tube from the ear to the nose to the xiphoid; this is how far the tube should be inserted; the duodenal feeding tubes have markings & they are usually inserted to ~65 cm

Generously lubricate the tip of the tube

If inserting a duodenal feeding (including Dobhoff) tube, flush the tube 1st with 10 cc of saline, keeping the wire in place

Insert the tube through the nares (for the Dobhoff, keeping the wire in the tube during insertion) parallel to the floor of the nares, not angled cephalad or caudad

If resistance is met & if the pt is not intubated & gags, ask them to start drinking water & with each swallow slowly advance the tube until the proper length of the tube is inserted

Resistance is often met at the gastroesophageal junction & at the pylorus as the Dobhoff is supposed to pass the pylorus into the proximal duodenum

Secure the tube to the nose with tape

Note: many institutions now require direct visualization of the passing of the duodenal feeding (including Dobhoff) tubes into the esophagus (& not the trachea as it can cause severe lung damage if it passes to the lung). These visualization techniques can use x-ray, direct laryngoscopy, or fiberoptic bronchoscopy

NGT confirmation

Confirm placement by injecting the tube with the 60-cc syringe filled with air while listening over the stomach with the stethoscope—hear a rush of air/bubbles

When connected to suction, gastric contents should return

Confirm placement with CXR

Confirmation of correct placement of duodenal feeding (including Dobhoff) tube

It is prudent that the operators use direct visualization techniques during placement & ensure that the duodenal feeding tube is NOT placed into the trachea or the lungs

The tip of the correctly placed duodenal feeding (including Dobhoff) tube should be below the diaphragm & should cross the midline to be properly placed in the duodenum

Once the correct placement is confirmed, the wire may be removed

The feeding tube may be used whether it is intragastric or in the proximal duodenum

The risk of aspiration with the feeding tube is potentially lower when it is placed past the pylorus in the duodenum

Complications (acute & chronic)

ET placement (pt will have difficulty speaking, or lower tidal volumes on ventilator)

Intracerebral placement (leakage of cerebrospinal fluid from perforated cribriform plate)

Pneumothorax (PTX), aspiration

Bleeding (epistaxis), esophageal perforation

Sinusitis, pressure ulcers

Keys to success

Insert tube parallel to the floor of the nares

Do not force tube placement when resistance is met

Removing the tube a few centimeters & twisting the tube gently may help with the placement; use generous lubrication

Always flush a duodenal feeding tubes with the wire in place before inserting them

Only remove the wire from the Dobhoff once the positioning is confirmed on an abd film or by fluoroscopy

Never reinsert the duodenal feeding tube wire after it has been pulled

Lumbar Puncture

Indications:

Obtain opening pressure.

CSF drainage for high ICP (if risk of herniation is low)

CSF sampling for diagnostic

Contraindications:

High ICP & risk of cerebral herniation

Coagulopathy/thrombocytopenia (controversial)

Local infxn at the site of lumbar puncture

Anticoagulated pt

Fused lumbar vertebrae

Pt refusal

Materials:

Lumbar puncture kit, sterile gloves & drape, mask/cap

Technique:

Discuss procedure with pt (if awake)

Position pt either sitting or lateral. If sitting, place chin to chest, with arms resting on a table to maximally flex the back. If lateral, bring chin to chest & knees to chest (fetal position)

Prep the site. Apply an antiseptic per your institutional guidelines. The antiseptic usually should be administered in a back & forth, scrubbing motion rather than a concentric "inside out" motion. Drape the area to exclude nonsterile areas

Identify interspaces. The interspace associated with the top of the iliac crest is usually L4–L5 interspace. Choose this interspace or 1 interspace up (L3–L4) for the lumbar puncture, whichever feels more open, more space between the spinous processes

Anesthetize the skin via subcutaneous infiltration with local anesthetic. Infiltration below the subcutaneous layer may be needed as the dura is 3–5 cm below the skin in most pt. Reidentify the space between the spinous processes & insert both the spinal needle & the introducer as a unit, with bevel facing cephalad. The spinal needle & the introducer will pass through the skin, subcutaneous tissue, supraspinous ligament, & interspinous ligament. A greater resistance will be felt by the operator as the needle & the introducer move through the ligamentum flavum. The needle should be directed perpendicular to the skin or aimed slightly cephalad in alignment with the spinous processes

Although not universal, a change in resistance may occur when the introducer/spinal needle passes through the dura & into the spinal canal. Remove the spinal needle while holding the introducer steady

Measure the opening pressure. This is usually done by attaching the introducer to a column manometer & marking the ht of the CSF after it reaches equilibrium

Collect CSF for diagnostics. The amount of the CSF collection can vary depending on the tests being ordered

When CSF collection is complete, place the introducer into the spinal needle & remove as 1 unit

Wipe off back with gauze & water, place gauze dressing over the site of lumbar puncture, remove drape, reposition pt comfortably in bed

The pt should be ordered a brief, 30-min bed rest following the procedure

Complications:

Bleeding/hematoma, infxn/abscess/meningitis, headache, paralysis

Urinary Catheter (Foley) Placement

Urinary catheters are a recognized source of nosocomial infxns. Their removal should be considered as soon as possible & clinically acceptable (for management and complications also see Chapters 8 and 23).

Indications:

Drain bladder contents/decompress the bladder, obtain urine specimen, identify GU bleeding, monitor volume status/renal perfusion by evaluating urine output, treat bladder outlet obstruction, treat urinary retention, bladder irrigation

Obtain urine specimen

Identify GU bleeding

Monitor volume status/renal perfusion by evaluating urine output

Treat bladder outlet obstruction

Treat urinary retention

Bladder irrigation

Contraindications:

Urethral trauma, blood present at the urethral meatus, pelvic fx, scrotal hematoma, high riding prostate, inadvertent vaginal insertion

Procedure:

Discuss the procedure with the pt (if awake)

Place the pt in supine position, legs abducted, feet together

Open the Foley catheter kit

Put on mask/sterile gloves

Coat cotton swabs with sterile Betadine solution

For the female pt: use nondominant hand to separate labia

For the male pt: use the nondominant hand to hold the penis

With the dominant hand use forceps to hold sterile coated cotton swabs & cleanse the periurethral space (inner to outer, anterior to posterior) with 1 swipe per swab

Discard swabs away from sterile field; apply sterile drape

Check the catheter balloon for patency by injecting 10 cc of saline into the balloon & then aspirating back the 10-cc saline into the syringe to the balloon is deflated for Foley placement

Place generous lubrication over distal ~3 cm of Foley catheter

For the female pt: continue to spread the labia with the nondominant hand—with the dominant hand hold Foley catheter & gently insert 1–2 in. beyond the point where urine is returned

For the male pt: hold the penis perpendicular to the pt's body with the nondominant hand using upward traction—with the dominant hand insert the Foley 1–2 in. beyond the point urine is returned

Inflate the balloon using a set amount of sterile water (usually ~10 cc)

With a gentle tug, pull the catheter back until the inflated balloon sits against the bladder neck

Connect the drainage system to the catheter

Secure the catheter to the thigh, making sure to prevent tension on the tubing

The drainage bag should be below the level of the bladder

Complications/keys to success:

If prostatic hypertrophy present, or urethral stricture, the insertion of the catheter may be difficult & a urology consult is indicated

Tissue trauma, bleeding, & infxn are possible complications

If unable to pass the catheter, a smaller size may be needed

BEDSIDE SURGICAL PROCEDURES IN THE ICU OR ED

OVEYS MANSURI, MD, MBA, FACS • SELWYN O. ROGERS, JR., MD, MPH

Introduction

These bedside surgical procedures should be performed only by qualified, competent personnel. This is an evolving area that is transforming care in ICU, & thus 1 should work collaboratively & with best practices in mind to ensure the safest & highest quality of care for our patients (pt). Please note that each ICU may have specific protocols in place when performing these procedures.

Bedside Tracheostomy (*World J Surg.* 2013;37:1633; *J Intensive Care Med.* 2014;29:110)

Indications

Respiratory failure & need for prolonged intubation

Airway protection

Access for pulmonary toilet

Inability to secure the airway by oro- or nasotracheal intubation (often an emergent procedure)

Contraindications/considerations

Age <16 yrs

Infxn at site

Coagulopathy

Cervical spine instability

Anatomic variation (e.g., short neck, dz, previous surgery/radiation)

High ventilatory requirement (e.g., FiO_2 ≥80%, PEEP ≥15)

Materials

Bronchoscope

Percutaneous tracheostomy kit (including: scalpel, needle, guidewire, dilator(s), & tracheostomy)

Technique (described here for elective bedside tracheostomy using single dilator)

Position pt supine with neck extended

Administer appropriate sedation

Bronchoscopy through ETT with identification of tracheal rings

Apply local anesthetic

Carefully withdraw ETT to the level of the vocal cords while maintaining bronchoscopic visualization

Insert needle along midline into trachea (~3rd tracheal ring) under direct visualization by bronchoscopy

Advance guidewire through needle down toward carina & then remove needle

Perform single dilation over guidewire, maintaining bronchoscopic visualization

Load tracheostomy tube onto cannula & carefully insert, confirm position, & secure tube

Obtain CXR to verify placement & r/o postprocedure complications

Complications/keys to success

Bleeding: apply pressure if uncontrolled, then proceed to OR for exploration

Pneumothorax: possible need for tube thoracostomy

Loss of airway: abandon procedure & regain airway by reintubation

Tracheal wall injury or tracheal ring fx

Tracheoarterial/esophageal fistula: rare complication that requires appropriate surgical consultation

Bedside Peg (Percutaneous Endoscopic Gastrostomy) (Rahnemai-Azar AA, et al. *World J Surg.* 2014;20:7739–7751; *World J Surg.* 2016;2:618)

Indications

Need for long-term enteral access

Contraindications/considerations

Infxn on abd wall

Coagulopathy

Prior abd surgery

Anatomic variation and/or dz (interposed organs, tumor, varices, ulcer, or ascites)

Materials

Endoscope

Percutaneous gastrostomy kit (including: scalpel, needle, guidewire, dilators, & gastrostomy tube)

Technique

Endoscope stomach & insufflate stomach

Use endoscope to transilluminate abd wall

Apply local anesthetic to the site of maximal illumination

Introduce needle under endoscopic visualization

Pull technique

Guidewire placed through introducer

Pulled out through mouth using endoscope

Attach to PEG tube

PEG tube then pulled into stomach & through abd wall

PEG tube secured noting position

Repeat endoscopy to confirm appropriate placement & r/o complications

Complications/keys to success

Do not proceed with PEG tube placement if inadequate transillumination

Bleeding: fluid support & appropriate surgical evaluation if hemodynamic instability

Infxn: tube site infxn most common complication

Bowel perforation: requires prompt surgical evaluation & intervention

Device malposition: be mindful of buried bumper syndrome & tube dislodgement

Pneumoperitoneum: common after PEG placement, but potential for bowel injury evaluated when present after 72 hrs postprocedure

Bedside Diagnostic Laparoscopy (Peris A, et al. *Crit Care.* 2009;13:R25; Jaramillo EJ, et al. *J Soc Laparoend Surg.* 2006;10:155–159)

Indications

Sepsis of unknown origin or multiorgan failure with suspicion of intra-abd pathology when other diagnostic modalities (CT, US) are not possible or accurate or the pt is not suitable for transfer to the OR

Contraindications/considerations

Indication for formal exploratory laparotomy (bedside laparoscopy is not a substitute for pt requiring formal exploration)

Coagulopathy

Abd compartment syndrome (ACS)

Extensive prior abd surgery

Abd wall infxn

Morbid obesity (relative contraindication)

Physiology refractory to treatment of intra-abd process

Materials

Personnel: surgeon, assistant surgeon, anesthesiologist, scrub nurse, circulator, & critical care nurse

Standard laparoscopy tower

Sterile drapes, gowns, gloves, set of sterile surgical instruments for diagnostic laparoscopy

Technique

Strict adherence to universal precautions & routine OR sterile protocols

General anesthesia administered by anesthesiologist

Peritoneal access can be achieved by various methods including Veress needle, Visiport, or open technique

Pneumoperitoneum should be achieved by inflating the abd cavity with carbon dioxide to a pressure of 8–15 mm Hg

Laparoscopic exploration of the abdomen should be performed with careful attention to standard safe practices

Port sites should be appropriately closed

Complications/keys to success

Veress needle and/or trocar injury to solid organ, hollow viscous, or vascular structure

Hemodynamic instability secondary to carbon dioxide insufflation

Recognize limitations of laparoscopy & be prepared for complications requiring conversion to open procedures in the ICU setting and/or aborting the procedure

Bedside Decompressive Laparotomies (*Trauma.* 2012;6:91; *Trauma.* 2012;38:725; Schreiber J, et al. *Crit Care.* 2014;18:R123)

Indications

Acute & life-threatening intra-abd conditions with need for laparotomy where the clinical condition of the pt makes it prohibitive to transport to the OR suite (i.e., hemodynamic instability, complex ventilator needs)

Examples: ACS or washout/pack removal

Contraindications/considerations

Complex surgeries requiring resources more readily avail. in the OR suite

Intestinal anastomoses, stoma creation

Coagulopathy

Given the emergent nature of this procedure, the surgeon must be prepared for any of the aforementioned scenarios

Materials

Personnel: surgeon, assistant surgeon, anesthesiologist, scrub nurse, circulator, & critical care nurse

Sterile drapes, gowns, gloves, set of sterile surgical instruments for laparotomy, variety of suture material

Technique

Prior to incision:

Strict adherence to universal precautions & routine OR protocols

General anesthesia administered by anesthesiologist

Pt should be adequately resuscitated with reliable access to ensure large volume replacement if necessary

Prep & drape in usual sterile fashion

Enter the abdomen:

Make an incision from the xiphoid process to the symphysis pubis

Incision should be taken down to the level of the fascia, & the fascia then carefully opened

Careful attention should be paid to the pt's respiratory & hemodynamic parameters at the time of release of the fascia

Routine exploration of the abdomen should be performed at this time

Temporary abd closure:

Multiple methods: use which 1 surgeon is most experienced & comfortable with. Below is 1 that uses materials most readily avail.

Insert large sterile towel & cover on both sides with Ioban (3M) sterile adhesive drape

Tuck below the fascia & overlying the bowel & the omentum

Two JP drains should be placed over the Ioban & cover with laparotomy pads

Cover with an additional large piece of Ioban (3M) drape

Apply suction to the system

Complications/keys to success

Plan to return for reexploration & washout in 24–48 hrs

Recurrent ACS

Infxn (abscess or other infected fluid collection)

CV collapse at the time of decompression that will require aggressive volume resuscitation

DEBRIDEMENT (*Acute Care Surg.* 2012;43:589)

Indications

Infected or necrotic wounds

Chronic nonhealing wounds in the absence of ischemia

Contraindications/considerations

Underlying vascular dz with associated gangrene

Coagulopathy

Materials

Local anesthetic

Scalpel blades

Hemostat, clamp, forceps, curved Mayo scissors, electrocautery (if avail.)

Gauze, dressing supplies, & tape

Sterile saline

Technique

Place disposable, absorbable drapes under & around area of procedure to minimize contamination of linens

Prep & drape area in usual fashion

Apply local anesthetic to the area or provide parenteral sedation (if needed)

Make incision in the area most inflamed, tender, or indurated

Incise & assess for necrotizing soft tissue infxn

Excise all necrotic tissues using scalpel or curved Mayo scissors

Evaluate wound for hemostasis & any remaining devitalized tissue

Wounds should be dressed in sterile gauze or bandages moistened with sterile saline

Complications/keys to success

Do not proceed with any debridement no matter how minor unless you understand & appreciate the anatomy

Do not hesitate to perform any extensive debridement procedure in the OR if the pt is stable & there is concern for safety

Return to wound within 24 hrs to reassess need for additional debridement

Be careful not to miss areas of infected or necrotic tissue and/or fluid collections

Be concerned about bleeding, vascular, and/or nerve injury

When infxn is documented or suspected, it is imperative to start immediate treatment with broad-spectrum abx, esp. in cases of necrotizing fasciitis

Obtain appropriate wound care & nutritional consult to optimize wound healing & recovery

Emergent Thoracotomy (Emergency Department Thoracotomy) (*J Trauma.* 2015;1:159; *J Trauma.* 2012;14:236)

Indications

Penetrating thoracic injury: (+) signs of life & pulseless → strongly recommended

Penetrating thoracic injury: (−) signs of life & pulseless → conditionally recommended

Penetrating extrathoracic injury: (+) signs of life & pulseless → conditionally recommended

Penetrating extrathoracic injury: (−) signs of life & pulseless → conditionally recommended

Blunt injury: (+) signs of life & pulseless → conditionally recommended

Contraindications/considerations

Blunt injury: (−) signs of life & pulseless → conditionally NOT recommended

Be mindful of blood-borne pathogen exposure

Materials

Sterile prep: chlorhexidine/Betadine

Sterile gloves & towels

#10 blade & scalpel

Functional suction apparatus

Resuscitative thoracotomy kit: chest wall retractor, Mayo scissors, Metzenbaum scissors, smooth forceps, toothed forceps, aortic/vascular clamp

Technique (anterolateral thoracotomy | leave options open for changing approach depending on injury/findings)

Intubated with ETT/orogastric tube & appropriate IV access

Supine position with both arms extended & wide prep

Thoracotomy, pericardiotomy, & cardiac repair

Identify LEFT 4th/5th intercostal space (in females, displace breast cranially & use inframammary fold)

Incision from lateral edge of sternum to latissimus dorsi with #10 scalpel

Divide intercostal muscles & parietal pleura along superior margin of rib using heavy scissors (take care not to injure the underlying heart/lung)

Pay special attention to identifying & ligating the transected ends of the internal mammary artery

Place rib retractor with the handle directed inferiorly toward the axilla

For exposure optimization: mobilize lung by cutting inferior pulmonary ligament (be mindful of the inferior pulmonary vein)

Open the pericardium longitudinally paying attention to avoid the phrenic nerve

Any blood clots should be evacuated & bleeding sites controlled with digital pressure

Cardiac repair/cardiac function

Beating heart: delay repair until resuscitation complete

Nonbeating heart (see cardiac arrest later)

Repair done prior to defibrillation

Use 3-0 nonabsorbable horizontal mattress sutures or running (Teflon pledgets routinely on RIGHT heart, selectively on LEFT)

Balloon catheter occlusion: use selectively, may increase size of hole

Cardiac arrest: may occur during emergent thoracotomy

Bimanual internal massage should be performed (do not use 1 hand)

Internal defibrillation 1st at 20 J, followed by 30 J

Aortic occlusion via cross-clamp

Elevate the left lung anteriorly & superiorly

Incise the mediastinal pleura & bluntly separate aorta from the esophagus anteriorly & prevertebral fascia posteriorly

Cross-clamp inferior to left pulmonary hilum

If unable to visualize or place clamp safely, may digitally occlude aorta against spine

Complications/keys to success

Emergent thoracotomy pt must be eventually taken to OR for definitive evaluation of injuries & repair, & their advanced trauma life support workup completed as appropriate

Poor exposure: make incision as wide as possible

Be cognizant of the internal mammary artery

Esophageal injury (most likely to occur during aortic cross-clamp)

When performing ventricular repair, careful attention must be paid to coronary vessels (suggested: vertical mattress sutures)

Chest wall infxn, intrathoracic infxn

Recurrent bleeding

Risks to health care providers: be mindful of sharps & exposure to bodily fluids, universal precautions including eye protection are a must

Chest Tube/Tube Thoracostomy (*ATLS.* 2012:119; Dev SP, et al. *NEJM.* 2007;357:e15)

Indications

Pneumothorax (clinical correlation required: i.e., clinically unstable, large size, tension pneumothorax after needle decompression, recurrent/persistent)

Malignant pleural effusion, recurrent pleural effusion, empyema, postoperative

Contraindications/considerations

No absolute contraindications

Consider large adhesions

Coagulopathy

Materials

Local anesthetic (i.e., lidocaine)

Scalpel

Curved clamp

Needle driver, nonabsorbable suture, scissors

Appropriately sized chest tube

Pleural drainage system (i.e., Pleur-evac)

Dressing

Technique

Properly position the pt (supine & arm abducted out of way)

Determine insertion site (usually nipple level/4th to 5th intercostal space, anterior to the midaxillary line)

Proper prep & drape of the surgical field including full barrier precautions & sterile technique

Anesthetize at skin level & then proceed to subcutaneous tissues & intercostal muscles including periosteal surface & parietal pleura

Make a 2- to 3-cm transverse incision at the predetermined site

Use blunt dissection to go through the subcutaneous tissue & arrive at the rib, & use the clamp to dissect the intercostal muscles

Upon reaching the parietal pleura, gently push the clamp through it & can use a gloved finger to confirm that there are no adhesions to the lung & explore the tract

Clamp the proximal end of the chest tube & advance the distal end into the pleural space, directing it posteriorly & apically. Can aim the tube basally if it is for the purpose of evacuating fluid. Look for fogging of the chest tube

Connect proximal end of chest tube to pleural drainage system & unclamp

Secure chest tube using nonabsorbable suture, apply dressing, & make sure that chest tube is taped to chest to avoid unnecessary tension

Obtain confirmatory CXR for positioning & resolution of indication (pneumothorax, hemothorax, etc.)

Complications/keys to success

Bleeding

Hemothorax (intercostal artery injury)

Injury to intrathoracic or intra-abd structures (lung, diaphragm, spleen/liver, major vessels)

Subcutaneous emphysema (confirm that all chest tube holes are within the pleural cavity)

Recurrentpneumothorax, hemothorax, or ineffective evacuation/drainage

Infxn, empyema (never reuse prior chest tube site or wounds for new chest tube insertion site)

Tunneled Central Venous Catheter Removal (Kohli MD, et al. *Radiology.* 2001;219:651–654; Barnacle AM, et al. *Br J Radiol.* 2005;78:147–149)

Indications

Infected catheters or catheter no longer needed

Contraindications/considerations

Uncontrollable bleeding diathesis

Materials

Scalpel #10 or #15 blade

Hemostats

Forceps

Mayo scissors

Nonabsorbable suture

Local anesthetic

Surgical gauze

Sterile saline

Technique

Prep & drape the surgical field in the standard surgical fashion

If the pt is obese or edematous, the US machine may be used for localizing the cuff of the catheter

Anesthetize the skin & surrounding tissues overlying the cuff of the catheter

Make a skin incision overlying the cuff of the catheter

Dissect the cuff of the catheter free from the underlying skin & soft tissues

Once the cuff of the catheter is free, it should be removed as a single unit without any difficulty

Ensure that adequate hemostasis is present

Close the skin with interrupted nonabsorbable sutures

Complications/keys to success

Retention of the cuff of the catheter

Partial removal of the catheter

If the catheter does not remove easily after adequate dissection, abort the procedure

WOUND V.A.C. CHANGES

(http://www.kci1.com/KCI1/vacapplicationvideosandguides)

Indications

Skin grafts & local flaps

Diabetic ulcers

pressure ulcers

Acute and/or subacute wounds

Traumatic wounds

Contraindications

Excessive pain uncontrollable with IV medications

Coagulopathy

Wound with necrotic and/or nonviable tissue

Infected wound

Untreated osteomyelitis

Exposed arteries, veins, or nerves

Malignancy in wound

Materials

Appropriately sized V.A.C. sponge, drapes, & Sensa Trac Pad/Tubing

Sterile saline

Sterile gloves, surgical gown, & eyewear

Surgical gauze

Technique

Turn off the V.A.C. machine prior to removing the old dressing

Gently remove the old dressing

Irrigate the wound with NS

Cut & shape the foam dressing to fill the entire width & depth of the wound before placing it on the wound

Fill in any sinus tracts or cavities within the wound with the foam dressing

Size & trim the clear plastic dressing to cover the wound & ~2–3 cm of the surrounding skin circumferentially

Cut a small hole ~2 cm in size in the clear plastic dressing before it is applied to the foam sponge

Remove the backing from the Sensa T.R.A.C. pad & place it directly over the opening in the drape

Connect the Sensa T.R.A.C. tubing to the canister tubing

Set adequate pressure to 125 mm Hg of suction & check the system for any leaks

Complications/keys to success

Seal any leaks with the excess V.A.C. drapes

If the foam sponge does not remove easily, apply saline to the sponge prior to removal

Adjust suction pressure of system depending on wound location & anatomy

PERICARDIOCENTESIS (Gluer R, et al. *Heart Lung Circ.* 2015;24:621–625; *Adv Trauma Oper Manage.* 2004;6:323)

Indications

Pericardial tamponade

Large or recurrent effusion

Contraindications/considerations

Aortic dissection (absolute contraindication)

Uncorrected bleeding diatheses in nonemergent setting

Always have cardiac surgical backup

Materials

16-gauge Angiocath (preferred) or 18-gauge spinal needle

60-cc syringe

Image guidance such as US/ECHO (unless emergent)

Continuous ECG monitoring

Systemic arterial pressure monitoring

Personnel & equipment required for emergency intubation & cardiac resuscitation

1% lidocaine with epinephrine

Technique

Place the pt in supine or semirecumbent position

Sterile conditions including glove, gowns, & proper skin prep & drapes

Infiltrate local anesthesia to the left of the xiphoid tip

Attach the Angiocath or needle to the syringe

If image guidance is being used, obtain preprocedure views as well as skin to effusion depth & proceed with appropriate visualization

Introduce the tip of the needle between the xiphoid & left costal margin, aiming toward the left shoulder at a 30- to 45-degree angle to the skin

Carefully advance the needle while applying constant negative pressure until a return of fluid is visualized

If injury pattern is seen on the ECG such as ST or T wave changes, the needle should be withdrawn a few millimeters & readvanced more medially

Remove ~50 ml of bloody fluid

Place a soft catheter over guidewire through the needle for continuous drainage

Proceed to OR if indicated on the basis of findings in cases of trauma

Complications/keys to success

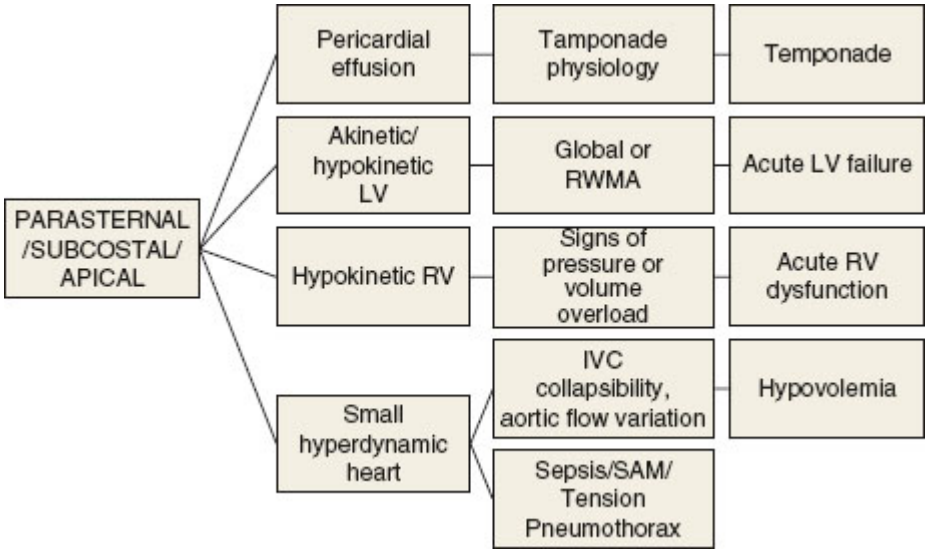
Rate of major complications under image guidance is 1.3–1.6%, this rises to a 20.9% rate of life-threatening complications when done unguided
Perforation or laceration of the myocardium or coronary vessels
Infxn
Pneumothorax
Cardiac arrhythmias
Vasovagal reaction
Abd peritoneal violation resulting in gastric or bowel perforation
Acute pulmonary edema

ULTRASOUND-GUIDED THERAPY AND PROCEDURES

SAJID SHAHUL, MD, MPH • GYORGY FRENDL, MD, PhD

Echocardiography in the Management of Shock (Figure 47-1)

Figure 47-1. Shock Algorithm for Echocardiography



Echocardiographic Approach to Tamponade

Demonstration of pericardial fluid (have to distinguish between pericardial fluid & pleural fluid)

Localized or circumferential echo-free space (echolucency) surrounding the heart

Limited by parietal pericardium

Demonstration of tamponade physiology

Right atrial systolic collapse (60% specificity & sensitivity)

Fluid accumulation in pericardial sac

RA thin walled RA with low intracavitary pressure

Collapse-lowest pressure in end diastole

Right ventricular diastolic collapse (intrapericardial pressure > RV pressure)

Fluid accumulation in the pericardium

RV lowest pressure in diastole

Collapse starting in the RV outflow tract

60% sensitive & 90% specific

Respiratory variation in transmitral flow (Intrathoracic pressure → intrapericardial pressure → PCWP–LADP)

Diastolic filling gradient

Tamponade-fluid isolates pericardium

Decrease in inspiratory filling

ΔMitral inflow

Decrease in transmitral flow

Ventricular interdependence

Inferior vena cava plethora

Increased RA pressure leads to the IVC being stented open by high distending pressure

Diameter >2 cm, 84% sensitive, 100% specific RAP >8 mm Hg

Respiratory variation in mitral & tricuspid diastolic velocities

Clinical Caveats for the Diagnosis and Management of Tamponade

Rapid accumulation of small amounts of fluid may lead to tamponade, severity is not merely a function of the volume of pericardial fluid

Chambers may not collapse because of high pressure

Tamponade postcardiac surgery is atypical

The etiology of pericardial tamponade (most common causes are pericarditis, iatrogenic pericardial fluid, malignancy, idiopathic, MI, ESRD, CHF, collagen vascular dz, TB, other infxn, & trauma) & the drainage procedure (pericardiocentesis) are described in more details in Chapter 46.

Echocardiographic Approach to Pump Failure

Large hypokinetic LV → LV systolic function → global or regional wall motion abnormalities → inotropy/IABP/cath lab

Echocardiographic Approach to LV Systolic Function

LV systolic function assessed by measuring EF: EDV-ESV/EDV

Normal > 55%, mild > 45 < 54%, moderate >30 < 44%, severe < 30%

Wall motion abnormalities:

Global or regional

Assess thickening & movement in coronary artery territories

Qualify by using the segmental model

Echocardiographic Approach to RV Dysfunction

RV function assessment mostly qualitative

RV free wall motion is toward the apex

Look for thickening of the RV free wall

Look at tricuspid annular motion

For RV dysfunction—assess the following:

Size of the RV-normally 2/3rds of the LV, when size of RV = LV moderate dysfunction, RV size > LV size severe dysfunction

Movement of the RV free wall is diminished toward the apex

Motion of the tricuspid annulus, normal >1.8 cm

Septal movement: barometer of relative pressure between the LV & the RV. In the case of RV pressure overload, the septum moves toward the LV in systole; in RV volume overload, the septum moves toward the LV in diastole.

Echocardiographic Approach to Hypovolemic Shock

Small hypercontractile LV

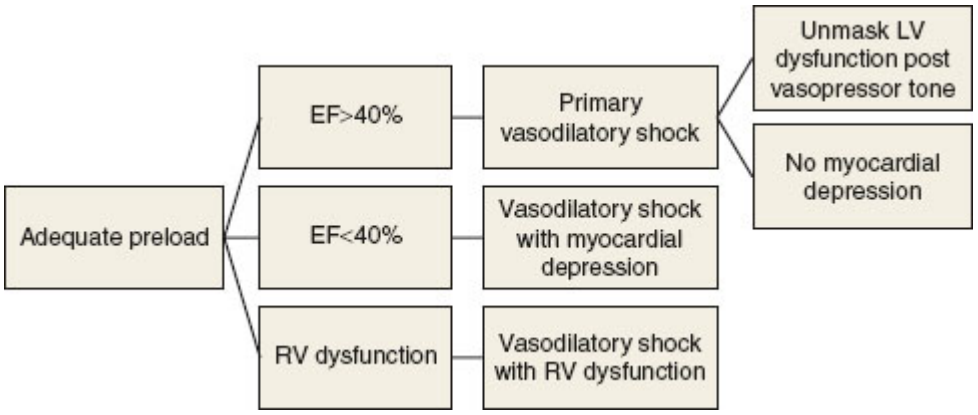
Small LVEDA <5.5 cm

Assess volume responsiveness → aortic flow variation index = 100×/V peakmax − Vpeakmin)/(Vpeakmax + V peakmin)/2: >12% indicates volume responsiveness (Feissel M, et al. *CHEST.* 2001;119:867–873)

→ Change in the diameter of IVC, DIVC = 100 × (IVCinsp − IVCexp)/IVCinsp: >18% indicated fluid responsiveness (*Intensive Care Med.* 2004;30:1740)

Echocardiographic Approach to Septic Shock

Figure 47-2. Echocardiographic Workup of Septic Shock



Septic Shock:

Establish adequate preload

Use echocardiography to establish—sepsis with normal EF; use echo postvasopressor administration to unmask LV dysfunction, & to identify sepsis with impaired EF or sepsis with RV dysfunction

Echocardiographic Approach to Tension Pneumothorax

Absence of lung sliding

Doppler evidence of pulsus paradoxus & respiratory variation in transmitral flow

Echocardiographic Approach to SAM (Systolic Anterior Motion)

Hypertrophic cardiomyopathy or severe flow acceleration through the LVOT → Anterior mitral valve leaflet sucked into the LVOT → SAM

Ultrasound-Guided Placement of Central Venous Catheters (CVC)

Variants of the typical anatomy are common

Arteries & veins are found in an atypical position 3–10% of the time & their size may be too small for cannulation (3–5%). Therefore, the "landmark" technique is associated with a relatively high incidence of mechanical complications (pneumothorax, hemothorax, arterial cannulation, injury to the arteries & veins)

US guidance can both expedite the placement of CVCs & reduce the related complications However, operators must be trained in a standardized program & use standardized US imaging techniques & safety steps

Procedural Standards for CVC Placement

Preprocedural checks:

Critically evaluate the need for CVC placement (risk vs. benefit assessment)

Obtain consent for the procedure

Check whether patient (pt) condition is appropriate for safe placement (stop heparin infusion, correct thrombocytopenia & coagulopathy, & other modifiable risk factors) if time & clinical condition allow

Recruit team (assistance, supervising operator if needed, nurse), secure equipment

Perform safety check (including site verification) for the procedure

Follow institutional & national safety standards & maintain sterile precautions

Standardized Imaging Required Before and During the Placement of Internal Jugular and Femoral CVC (All Images Are Archived) (Figure 47-3)

Visualize target (IJ or femoral) veins & the adjacent arteries; document compressibility of the veins. This step allows to diagnose whether the veins are too small for cannulation, are in an atypical anatomical location, or whether they have thrombus in them (thrombus can be seen & will lead to the loss of compressibility). Obtain side-by-side pre- & postcompression images

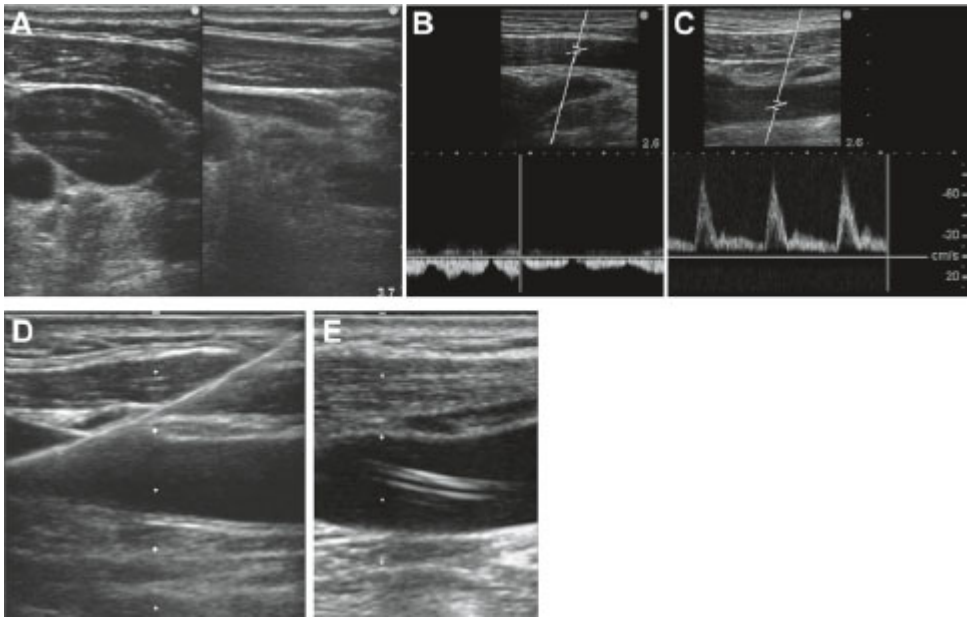
Document appropriate velocity flow in both artery & vein using pulse–wave Doppler imaging. Color Doppler may be used to visualize vessels, but Doppler evaluation is mandatory to confirm appropriate flow

Visualize the needle as it is approaching the vein

Visualize & confirm the presence of the guidewire in the vein before dilating the vessel (note: a longitudinal view is superior to cross-sectional view)

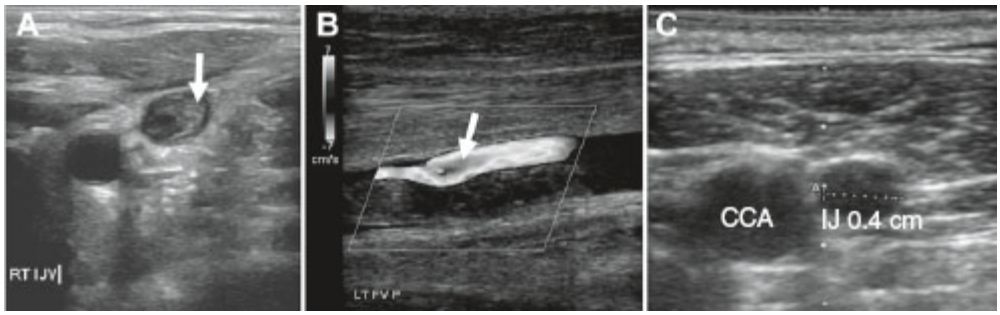
Visualize & confirm the presence of the catheter in the vein once the placement is completed (again, longitudinal view is superior to cross-sectional view)

Figure 47-3. Images of Standardized US Exam for US-Guided CVC Placement



A: Pre- & postcompression image of the internal jugular vein & the carotid artery (in dual image/side-by-side mode); **B:** Doppler mode image of the internal jugular vein; **C:** Doppler mode image of the carotid artery; **D:** Guidewire visualized in the vein; **E:** Catheter visualized in the vein.

Figure 47-4. Most Common Abnormal Findings During US Examination



A: Thrombus (arrow) developing in the internal jugular vein (cross-sectional view); **B:** Partial blood flow is seen (arrow) around the thrombus; **C:** Abnormally small internal jugular vein (CCA: Common carotid artery; IJ: internal jugular vein).

Standardized Training of Operators for US-Guided Placement of CVC

Web-based, self-directed learning programs:

Prevention of CVC-related bloodstream infxn, standardized sterile technique

The use of US imaging for the placement of CVC (instructional video & narrated slide show), followed by a multiple choice (pass/fail) test

Simulation-based practice & competency test (1 hr) at our simulation center (test based on the scores standardized in our study)

Less-experienced operators (interns) are offered additional practice sessions in the simulator & in the vascular US lab

Less-experienced operators are required to be supervised by experienced operators for their 1st 5 procedures (which have to be performed free of complications)

Steps for Enhancing the Safety of Subclavian Catheter Placement

Subclavian veins should only be dilated & CVC be placed once it is confirmed that the access needle (or small gauge angiocatheter) is placed into the vein & not into the artery. This reduces the incidence of inadvertent arterial placement

RADIOLOGIC IMAGING

YUKA OKAJIMA A, MD, MPH • HIROTO HATABU, MD, PhD

ICU Portable Chest X-Rays (CXR)

Guide to Interpretation

Check patient's (pt) identity & the date of the study: make sure the subject is correct (Fig. 48-1)

Evaluate the technical quality of the image

Check the position of the supporting tubes & lines

Check for abnormal air collections (pneumothorax, pneumomediastinum, pneumopericardium, or intra-abd free air)

Evaluate the cardiovascular status (the heart size & the width of the pulmonary vasculature) & the mediastinal width

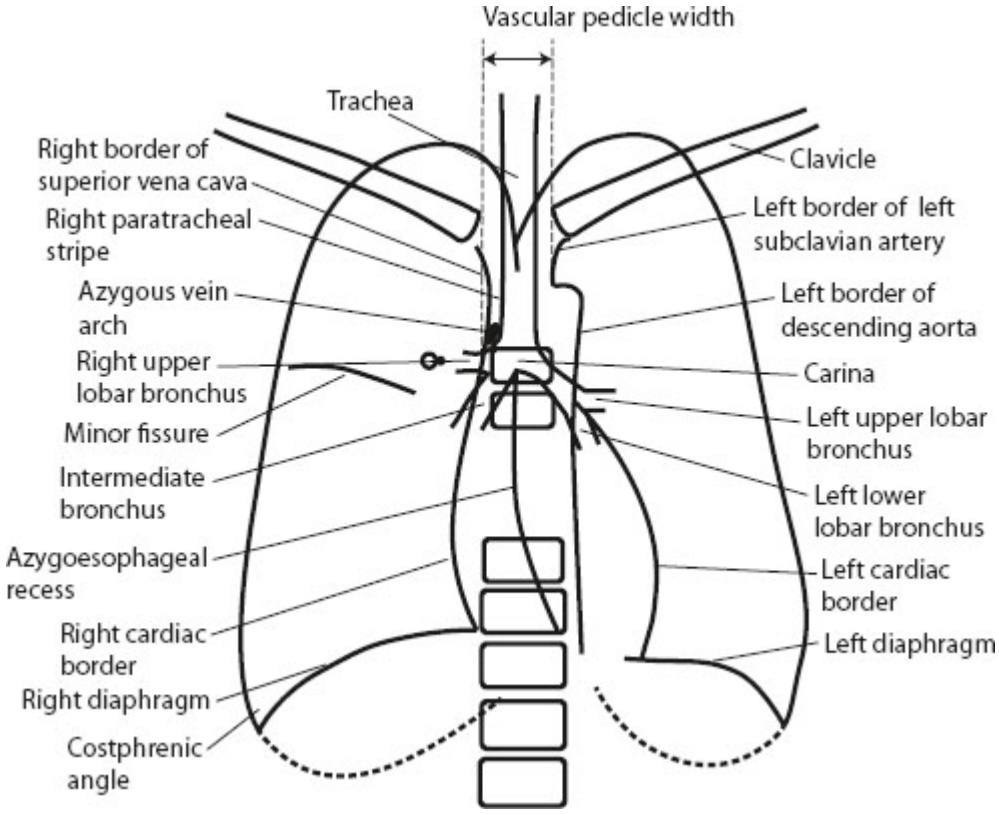
Note: The mediastinal lines are helpful to depict abnormal findings

Check for abnormal pulmonary opacities & pleural effusions

Check for bone & soft tissue abnormalities

Compare with the prior studies

Figure 48-1. Image Components of Chest X-Rays: Mediastinal Lines and Stripes



Characteristics of Portable CXR

The anterior–posterior supine position magnifies the mediastinal structures, compared to the posterior–anterior upright position (Fig. 48-2)

Cardium: magnified up to 14%, upper mediastinum: magnified up to 50%

The supine position may lead to vascular redistribution

Low lung volumes due to poor inspiration may make the heart, the superior mediastinum, & the pulmonary vasculature appear prominent

Supporting Tubes and Lines

Endotracheal Tube

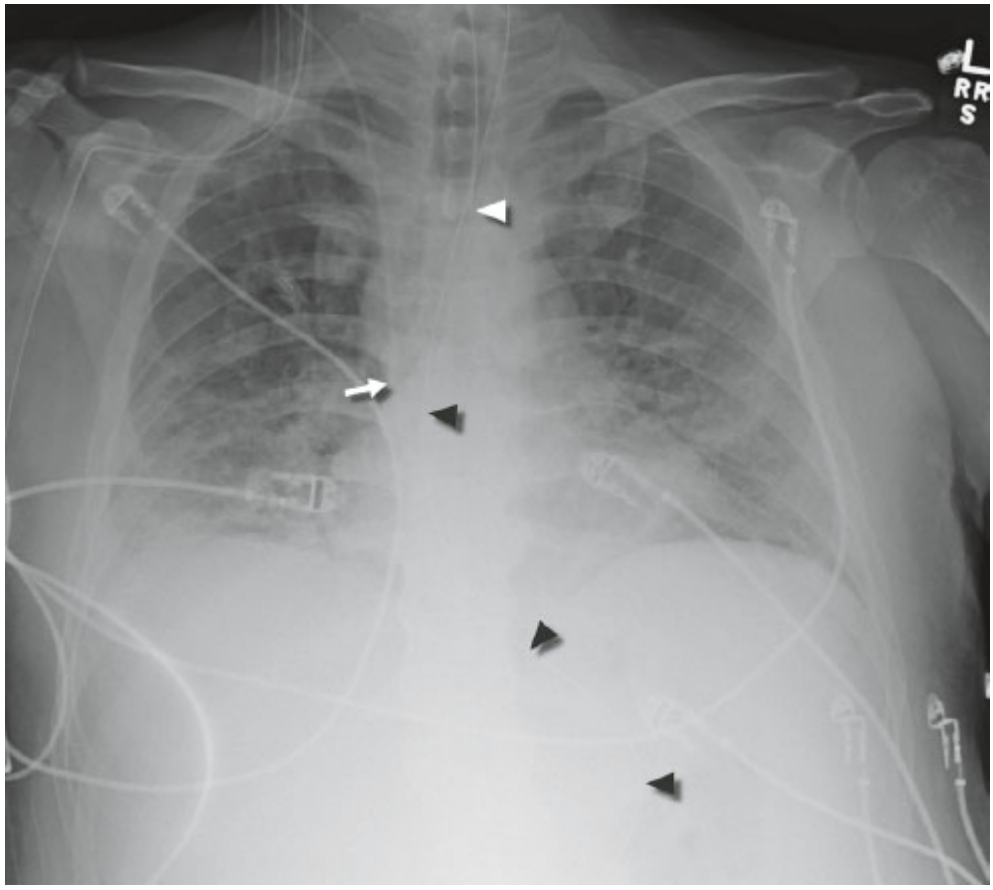
Ideal position of the distal tip: 5 cm above the lower edge of the carina to just below the clavicle, with the neck in the neutral position

The tip positioned at Th 3–4 level is considered safe when the carina is invisible (Carina: at Th 5–7 level, vocal code: at C5–6 level)

The position of the tip may change up to 2 cm, depending on the position of the head

Check for complications: intratracheal or intraesophageal foreign materials (e.g., dislodged teeth), tracheal injury, subcutaneous emphysema, pneumomediastinum

Figure 48-2. Portable Chest X-Ray



The Projection of Supporting Lines and Tubes Endotracheal Tube Tip (*White Arrowhead*); Right Internal Jugular Catheter Tip (*White Arrow*); Nasogastric Tube (*Black Arrowheads*).

Central Venous Catheter

Ideal position of the catheter tip: in the superior vena cava about slightly above the right atrium (landmark: 1st intercostal portion)

Check for procedure-related complications: pneumothorax, subcutaneous hematoma, & hemothorax

Delayed complications: venous obstruction, vessel perforation

Radiographic findings indicating vessel perforation: mediastinal widening, enlarged cardiac silhouette, pleural effusions

Radiographic findings suggesting impending vessel perforation: curving of the catheter tip, direct placement of the catheter tip against the wall of the superior vena cava

Nasogastric Tube

Ideal position of the distal tip: ≥10 cm beyond gastroesophageal junction

Check the proximal lateral hole (generally located within 10 cm proximal to the tip) located in the stomach

Chest Drainage Tube

Check the distal tip & side holes located in the thorax, & the way the tube runs

Ideal position of the tip: apical for pneumothorax, posteroinferior for pleural effusions

The tube generally runs outside lung fields in a gently curving course

The tube running in a straight course may often be interlobar positioning

Check for procedure-related complications: hemorrhage at insertion sites (e.g., intercostal arteriovenous injury), lung injury, diaphragmatic injury, intra-abd organ injury

Swan–Ganz Catheter

Ideal position of the tip: inside the right or left main PA, no further than proximal interlobar PA

Check for complications: displacement, injury of PA, pulmonary infarction

Intra-aortic Counterpulsion Balloon Catheter

Ideal position of the distal marker: in the proximal descending aorta 2 cm below the aortic arch

Chest CT

Indications for Contrast-Enhanced CT (CECT)

Evaluation of vascular dz such as aortic aneurysm, aortic dissection, PE, mediastinum (see Fig. 48-3 for cross-sectional anatomy), active bleeding (trauma, hemothorax), abscess & empyema, etc.

Evaluation of pulmonary parenchyma, usually does NOT require contrast medium

Evaluation before Contrast Injection

General status: hemodynamic & neurologic status

H/O significant allergies & asthma

Consider oral steroid premedication

H/O renal dz, diabetes mellitus, & CHF

Medications of concern: metformin, nephrotoxic drugs (nonsteroidal anti-inflammatory drugs, aminoglycosides, etc.)

Metformin should be stopped at the time of or before the exam & withheld for 48 hrs after contrast media injection in pt with acute kidney injury or severe chronic kidney dz (estimated glomerular filtration rate [eGFR] <30 ml/min/1.73 m^2) to reduce the risk of lactic acidosis

Other medications of concern: β-blocker, calcium channel blocker, etc.

Check renal function in all pt at risk for contrast-induced nephropathy (see risk factors listed below): serum creatinine w/ or w/o eGFR

Allergic-Like and Physiologic Reactions to Intravascular Iodinated Contrast Media

Mild (self-limiting): nausea, vomiting, cough, headache, dizziness, itching, flushing, rash, facial swelling, nasal stuffiness, chills, sweats

Moderate (frequently requiring prompt treatment): tachycardia, bradycardia, HTN, erythema, dyspnea, bronchospasm, wheezing, mild hypotension

Severe (often life-threatening, requiring aggressive treatment): laryngeal edema, profound hypotension, clinically manifest arrhythmias, convulsion, unresponsiveness, cardiopulmonary arrest

Delayed reaction: nausea, vomiting, headache, itching, skin reaction, fever, abd pain, diarrhea

Risk factors: prior allergic-like reaction to IV contrast media, atopic individuals, asthmatics

The efficacy of ppx, such as corticosteroid, is unknown

With H/O severe adverse reaction, consider alternative examinations

Postcontrast Acute Kidney Injury and Contrast-Induced Nephrotoxicity

(ACR Manual on Contrast Media version 10.1, 2015)

Dose-dependent (intra-arterial injection > intravenous injection)

Serum creatinine level peaks within 2–5 days

Usually transient; serum creatinine returns to the baseline within 7–10 days

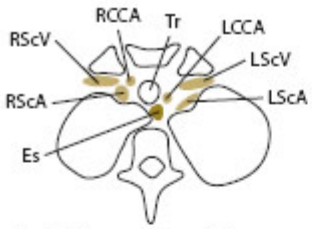
Risk factors: elderly (age >60 yo), renal dz, diabetes mellitus, CHF, HTN requiring medication, concurrent use of metformin

Significant risk factor: preexisting renal dysfunction (eGFR < 30 ml/min/1.73 m^2) → Consider alternative imaging strategies if possible

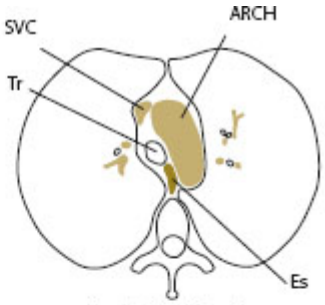
Prevention: IV volume expansion prior to contrast medium administration

Possible protocol: 0.9% saline at 100 ml/hr, beginning 6–12 hrs before the contrast media injection, continuing 4–12 hrs after contrast medium administration

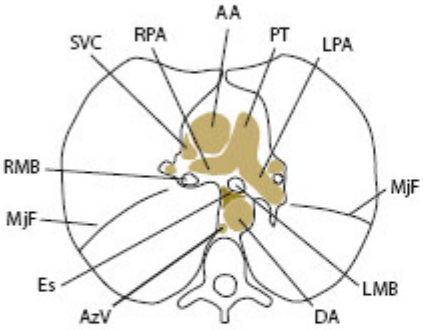
Figure 48-3. Cross-sectional Anatomy of the Thorax



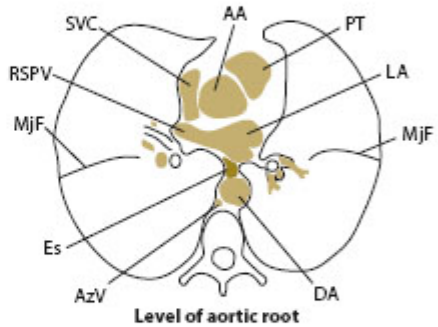
Level of manubrium of sternum



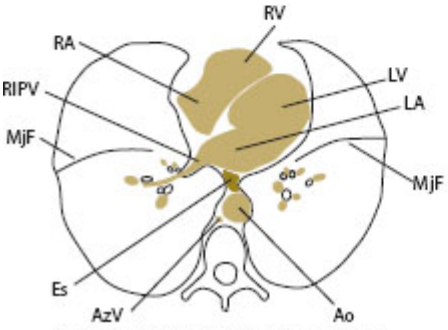
Level of aortic arch



Level of pulmonary trunk



Level of aortic root



Level of right inferior pulmonary vein

ARCH: aortic arch
AA: ascending aorta
AzV: azygous vein
DA: descending aorta
Es: esophagus
LA: left atrium
LCCA: left common carotid artery
LMB: left main bronchus
LPA: left pulmonary artery
LScA: left subclavian artery
LScV: left subclavian vein
LV: left ventricle
MjF: major fissure
PT: pulmonary trunk
RA: right atrium
RCCA: right common carotid artery
RIPV: right inferior pulmonary vein
RMB: right main bronchus,
RPA: right pulmonary artery
RScA: right subclavian artery
RScV: right subclavian vein
RSPV: right superior pulmonary vein
RV: right ventricle
Tr: Trachea

Pneumothorax

Pneumothorax in supine projection does not present typical findings in upright projection (Fig. 48-4)

In the supine position, intrathoracic air extends from basilar ventral to superior ventral & lateral portion

Check basilar & lateral portion in supine projection

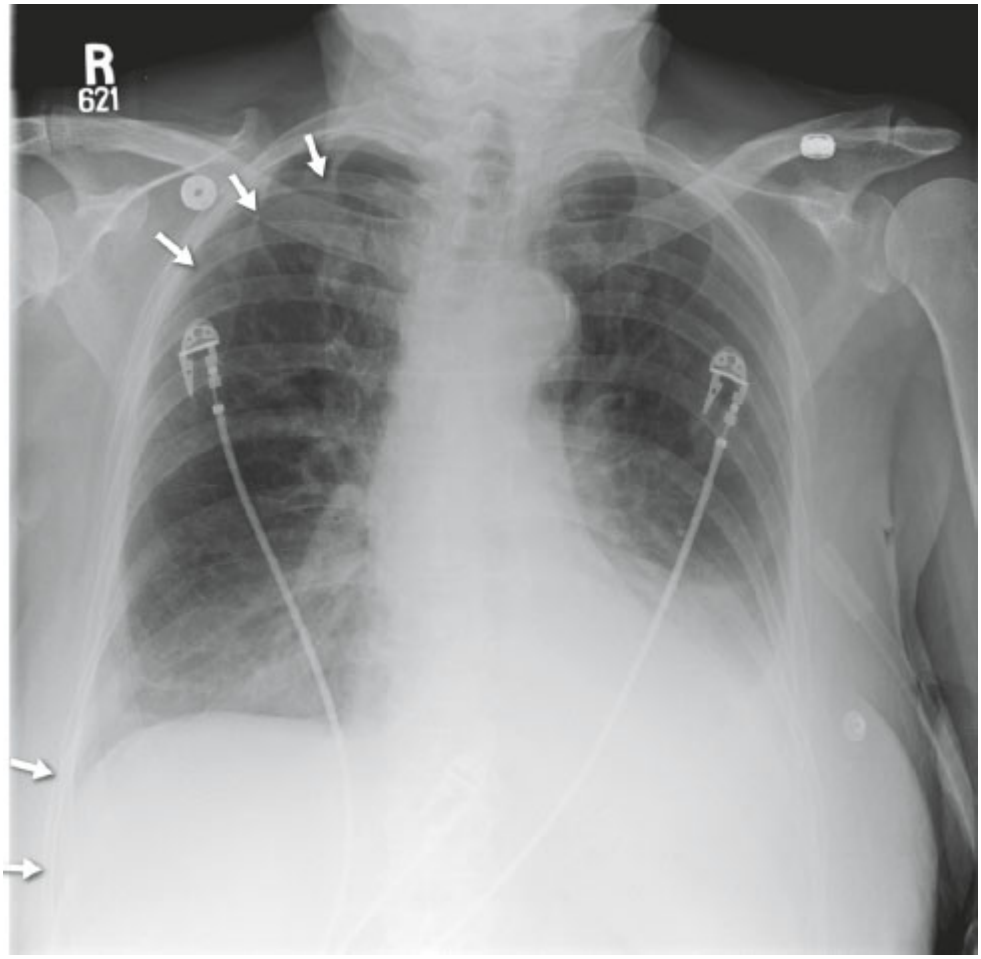
10–50% cannot be depicted in the supine position (occult pneumothoraces)

CXR (in the supine position): increased sharpness of the cardiac borders & aortic border, basilar hyperlucency, deep sulcus sign, relative lucency of the involved hemithorax, visualization of visceral pleural line

Check for findings suggesting tension pneumothorax: lower deviation of the diaphragm, flattening of the cardiac border, deviation of the mediastinum to the opposite side

Mimickers: skin folds, lateral aspects of the scapula

Figure 48-4. Right Pneumothorax and Bilateral Pleural Effusions



Right Pneumothorax Is Marked by Upper Arrows Outlining the Lining of the Lung.

Pneumomediastinum

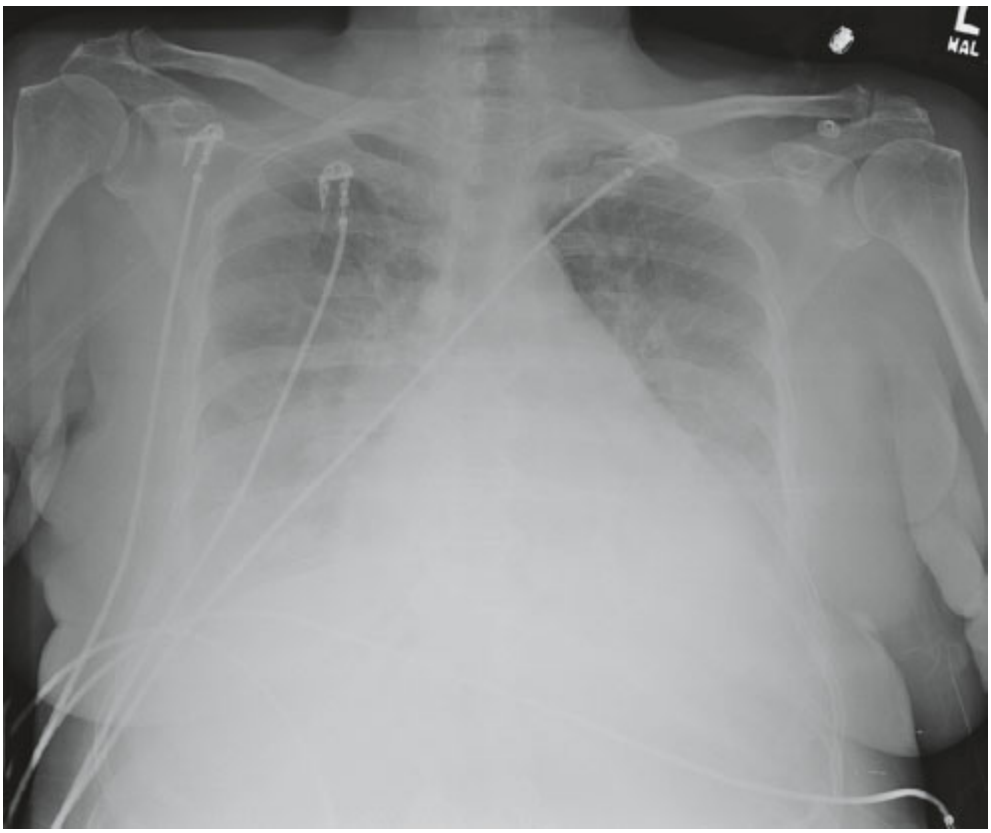
CXR: Streaky radiolucency in mediastinum, “continuous diaphragm” sign (air connecting both hemidiaphragmatic domes), “double bronchial wall” sign, “V sign of Naclerio” (mediastinal air extending laterally between mediastinal pleura & diaphragm), air in azygoesophageal recess, subcutaneous emphysema

In children: radiolucency outlining the thymus

Pleural Effusions

Small pleural effusions are difficult to depict on a supine CXR (Fig. 48-5)
Lateral decubitus views are more sensitive, may detect >25 ml
(Detectable amount of effusions: upright lateral views >75 ml; upright posteroanterior views >175 ml)
CXR: (small–intermediate amount) obscured paravertebral area (esp. basilar area), obscured vascular marks around the diaphragm (intermediate–large amount) obscured diaphragm, hypolucency of the ipsilateral lung field, thickened interlobar fissure, collapse of ipsilateral lung
Findings suggestive of specific conditions: rapid increase in pleural effusion (hemothorax), gas bubbles in pleural space (empyema due to gas-producing bacteria, bronchopleural fistula), unilateral effusion (malignant dz, infxn, congestive heart dz [right-sided], subdiaphragmatic dz, PE, trauma, chylothorax)

Figure 48-5. Congestive Heart Failure on Anteroposterior Chest X-Ray



Pulmonary Edema, Cardiomegaly, and Bilateral Pleural Effusions Are Seen

Hemothorax

CT: increased fluid density (fresh hematoma: 40–60 HU, simple fluid <20 HU)
CECT may help depict active bleeding & a bleeding point

Pulmonary Edema

Increased hydrostatic pressure: cardiogenic (most common), noncardiogenic (volume overload, renal failure)
Decreased colloid osmotic pressure: hypoproteinemia, rapid reexpansion of the lung
Increased capillary permeability: anaphylaxis, physical trauma aspiration, chemical inhalation, drug-induced injury, vessel occlusion

Hydrostatic Pulmonary Edema

Radiographic findings:

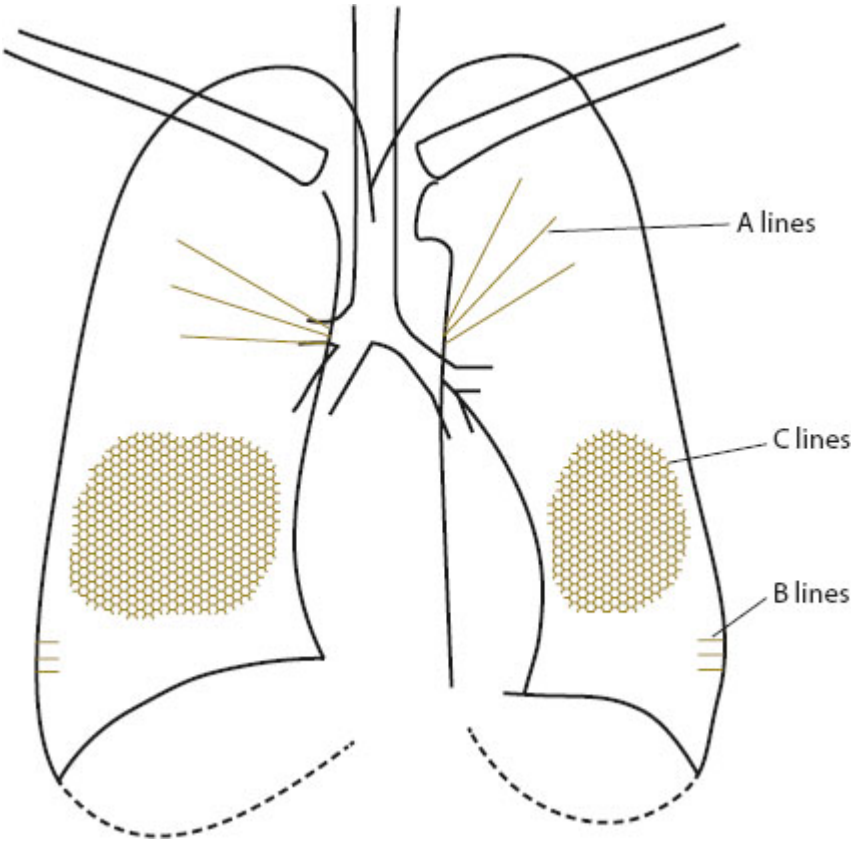
Type of Edema	CXR	CT
Engorgement of pulmonary vessels	Pulmonary vascular redistribution (cephalization), enlarged azygous vein, widened vascular pedicle	Enlargement of pulmonary vessels
Interstitial edema	Perihilar haziness, vascular haziness, peribronchial cuffing, septal lines (Kerley lines), thickened fissures, pleural effusion	Smooth interlobular septal thickening, peribronchovascular thickening
Alveolar flooding edema	Tiny nodular opacity, consolidation	Ground-glass opacities in a perihilar or dependent portion, centrilobular ground-glass nodules, consolidation

Vascular pedicle (Fig. 48-1): the distance between the point at which the superior vena cava crosses the right main bronchus & the point at which the left subclavian artery takes off
Kerley lines (Fig. 48-6):
A lines = Long fine lines radiating from hilum in the upper lungs
B lines = Short parallel lines perpendicular to pleura in peripheral lungs
C lines = “Lacelike” polygonal lines or reticular linear opacities (least common)

Acute Lung Injury/Acute Respiratory Distress Syndrome

The most severe permeability edema with diffuse alveolar damage
Abnormal radiographic findings may appear later than clinical onset of respiratory failure

Figure 48-6. Kerley Lines



No cardiomegaly or pleural effusion

CXR: 1st (exudative) stage: perihilar patchy opacities throughout bilateral lungs, widespread bilateral massive consolidation, air bronchogram, gravitational gradient

2nd (proliferative) stage: inhomogeneous consolidation and/or ground-glass opacities

3rd (fibrotic) stage: reticular opacity, subpleural & intrapulmonary cysts

CT: bilateral ground-glass opacities, bilateral homogeneous consolidation, traction bronchiectasis, interlobular septal thickening, intralobular reticulation

Note: differential findings of ARDS from hydrostatic edema: peripheral distribution, absence of pleural effusion, slow resolution, intubated (ARDS tends to cause severe hypoxemia)

Pneumonia

Radiographic findings are generally nonspecific

DDx: atelectasis, pulmonary hemorrhage, noninfectious lung inflammation, pulmonary edema, ARDS

Radiographic patterns: (i) lobar pneumonia, (ii) bronchopneumonia, (iii) interstitial pneumonia

Indications for CT: suspected pneumonia w/o apparent abnormal findings on CXR, with subtle finding compared with severe sx, & w/ poor response for treatment

Estimating pathogen is essentially difficult: some findings may strongly suggest a specific pathogen

Lobar pneumonia (Fig. 48-6): *Streptococcus pneumoniae, Legionnaires' bacillus, Klebsiella pneumonia, Hemophilus influenzae*

Cavitation: *Staphylococcus aureus* (abscess), *Haemophilus influenzae, S. pneumoniae,* fungal infxns, TB, septic emboli

*Lobar Pneumonia (Alveolar Pneumonia) (**Fig. 48-7**)*

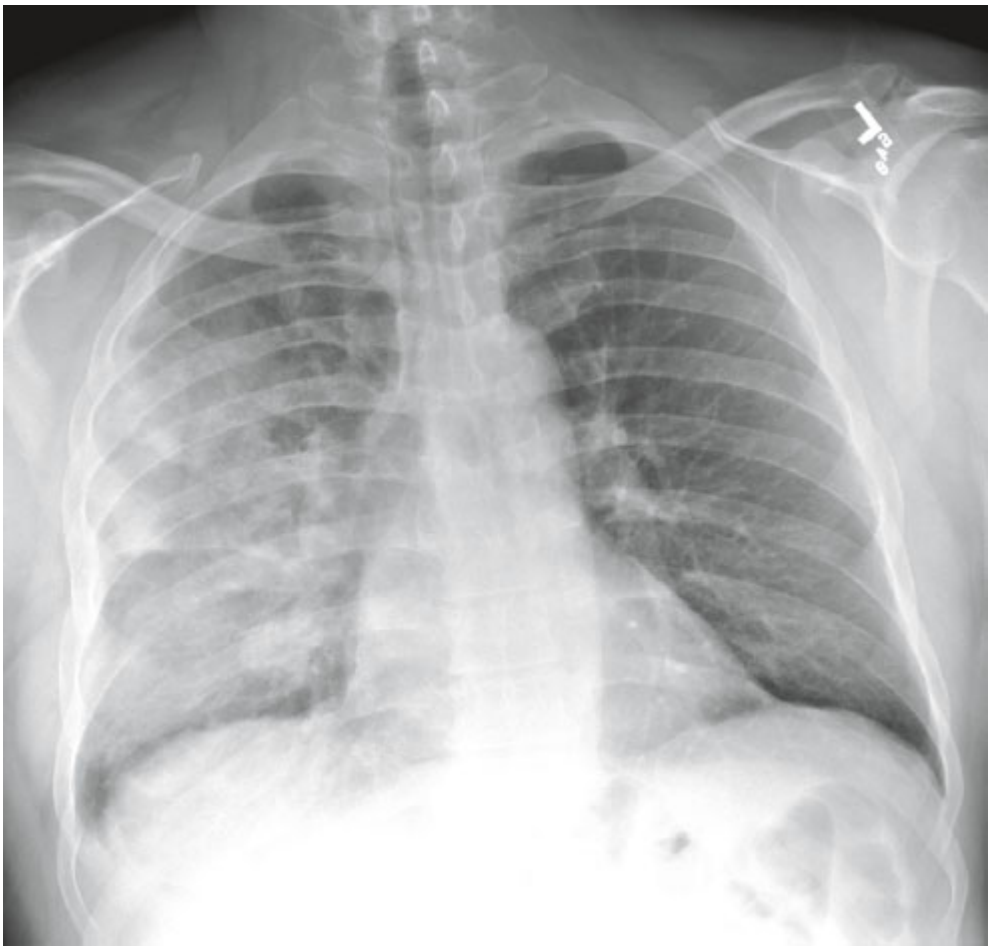
Dz progress: peripheral alveoli → surrounding alveoli through Kohn holes & Lambert holes

Lobar distribution, preserved or increased lung volume

CXR: consolidation w/ surrounding lobular opacities, air bronchogram, w/o volume loss

CT: sublobar consolidation w/ clear boundary, air bronchogram, bulging fissures

Figure 48-7. Legionella Pneumonia (Lobar Pneumonia) on Anteroposterior Chest X-Ray



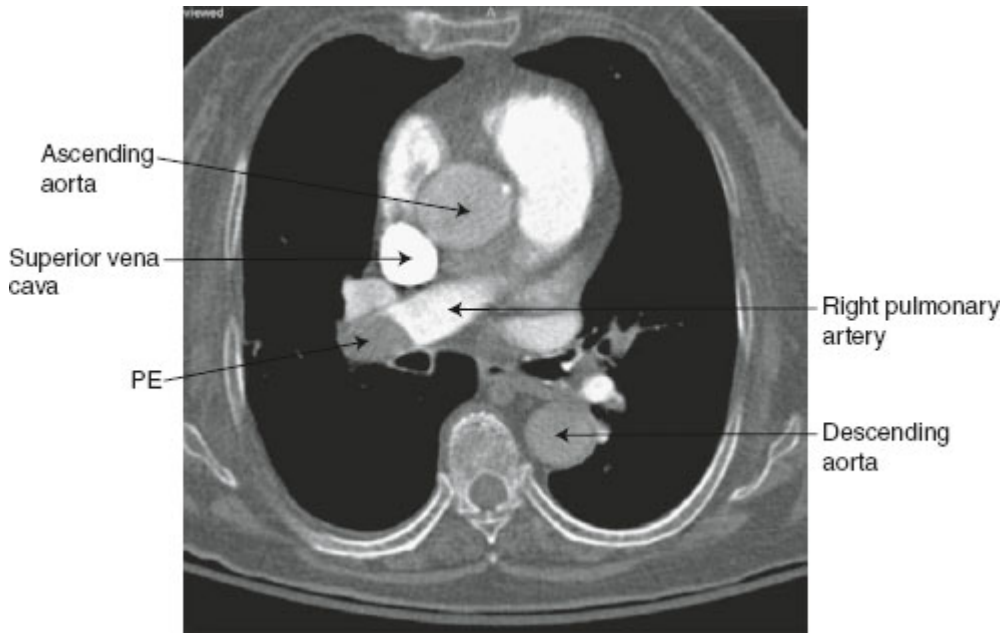
Bronchopneumonia (Lobular Pneumonia)

Dz starts as bronchitis or bronchiolitis, extending to the surrounding alveoli
Segmental & inhomogeneous distribution with volume loss due to mucus plug and/or narrowed airways
CXR: inhomogeneous opacity, lobular opacities, peripheral atelectasis
CT: small ill-defined centrilobular nodules, panlobular opacities, bronchovascular thickening, segmental opacities
Pathogen: various bacteria, such as *S. aureus, H. influenzae, Pseudomonas aeruginosa,* & anaerobes

Acute Pulmonary Embolism

CXR: low sensitivity & specificity; normal (most common); subsegmental atelectasis, pleural effusion, pleural opacities, elevated diaphragm, prominent PA, decreased vascularity
Suggestive CXR findings of PE: Westermark sign (reduced vascularity distal to a large embolus; "knuckle sign" (steep distal tapering of an occluded vessel); Hampton hump (a pleura-based, wedge-shaped consolidation with convex border, representing pulmonary infarction)
CT pulmonary angiography (CTPA): recommended as the 1st imaging modality (sensitivity: 83%, specificity: 96%) (Fig. 48-8)
In pt with renal dysfunction, or severe iodine allergies: venous US is recommended after D-dimer testing
Diagnostic CTPA findings for PE: complete filling defect; partial filling defect surrounded by a rim of contrast media ("railway track" sign); enlarged less-enhanced artery (occluded artery), compared to adjacent patent arteries; peripheral filling defect
Other CTPA findings: linear atelectasis (100%), pleural effusion (87%), consolidation, ground-glass opacity, Hampton's hump, dilated central PA
Predictors: Right heart strain (RV/LV ratio ≥1), reflux of contrast media into the inferior vena cava & hepatic veins, clot burden

Figure 48-8. Pulmonary Embolism (PE) in Right Pulmonary Artery



Aortic Dissection

Classifications: see Figures in Chapter 27

CXR: normal in 25%; irregular or obscured outline of aorta, different in size between ascending & descending aorta, left ventricular dilatation, left pleural effusion, medial lower lobe atelectasis, widened upper mediastinum

With calcified atherosclerotic plaque: displacement of calcified plaque from aortic outline

CECT: high sensitivity & specificity (>87%); crescentic hyperdense hematoma within false lumen, intimal flap separating 2 aortic lumens, intimal calcification displaced from aortic wall

Thoracic Aortic Aneurysm

>50% increase in diameter compared to the expected normal diameter (Normal average diameter of thoracic aorta: aortic root: 3.6 cm, ascending aorta: 3.0 cm, middescending aorta: 2.5 cm)

Location: arch > descending aorta

CXR: wide tortuous aorta, mediastinal mass adjacent to aorta

CT: wide tortuous aorta, circumferential mural thrombus

Ruptured aneurysm: extravasation of contrast media, hyperdense fluid collection or hematoma in the mediastinum, pericardium, pleural sac, or extrapleural space

Note: “Crescent sign” (peripheral hyperdense crescent hematoma in aneurysm) indicates impending rupture

Traumatic Rupture of the Thoracic Aorta

Location: aortic isthmus (most common) > ascending aorta > descending aorta (least common)

Brain CT

Check Points in Emergency Brain CT

Check pt's identity & the examination date: make sure the subject is correct

Check for emergency requiring immediate intervention: brain herniation, mass effect (midline shift, narrowed ventricles, loss or obscuration of cisterns & fissures)

Symmetricity

Localized or diffuse abnormal lesion

Hemorrhage (high density in acute phase, gradual decrease in density later), edema (low density)

Trace brain surface; check for cisterns & fissures

Size of ventricles

In trauma pt: fx, subcutaneous hematoma, foreign bodies (air, bone fragments, bullet); carefully evaluate the affected site & the opposite site (contrecoup injury)

Note: make sure that the very top & bottom slices are included!

Brain Herniation

Descending Transtentorial Herniation (Uncal Herniation)

CT: widening of ipsilateral ambient and/or prepontine cistern, widening of contralateral temporal horn, disruption of suprasellar cistern, displacement of uncus into suprasellar cistern (anterior herniation), parahippocampal gyrus herniation (posterior herniation), entire hippocampal herniation (total herniation)

Ascending Transtentorial Herniation

CT: compressed midbrain bilaterally on posterolateral aspect ("spinning top" appearance), narrowed ambient cistern and/or quadrigeminal cistern

Hyperacute Cerebral Infarction (<12 hrs)

CT: normal in 10–60%

Subtle hypodense gray matter, obscuration or loss of gray–white matter separation, hyperdense intraluminal thrombus within cerebral artery (e.g., "hyperdense middle cerebral artery (MCA) sign"), narrowed ipsilateral sulci, and/or sylvian fissure

Acute Cerebral Infarction (12 hrs–1 wk)

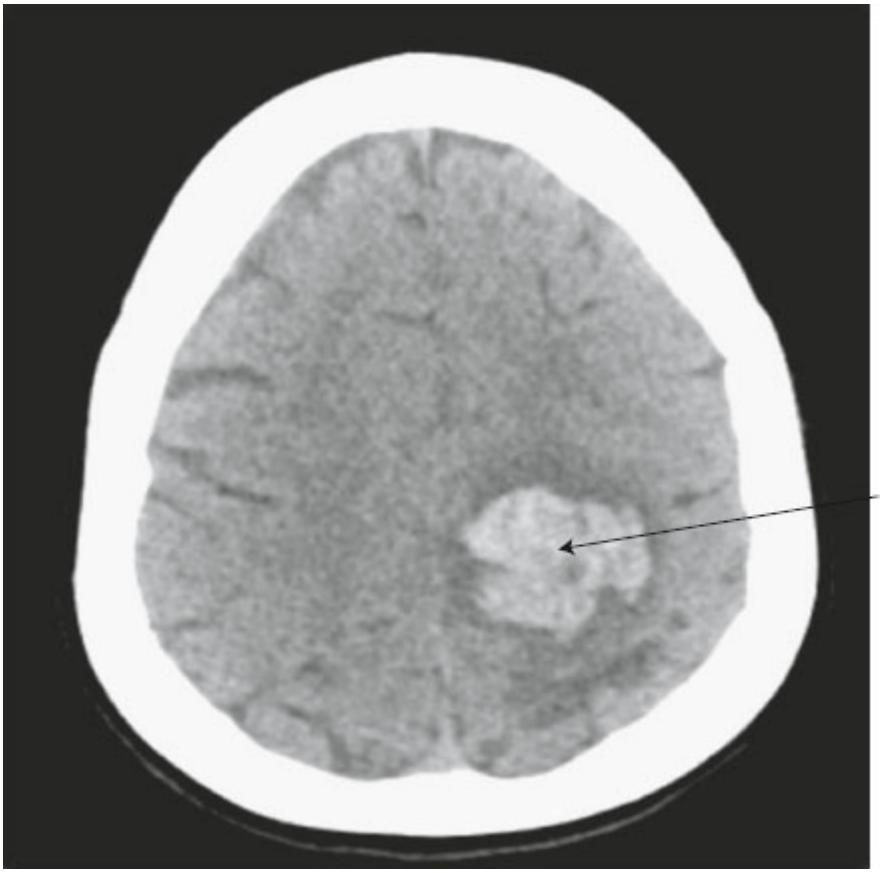
CT: low-density area (become more prominent than hyperacute phase), loss of gray–white matter separation, mass effect due to large infarction, hemorrhagic infarction after 2 days

Intracerebral Hemorrhage (Fig. 48-9)

CT:

Hyperacute (4–6 hrs)	Well-defined homogenous hyperdense lesion surrounded by low attenuation
Early subacute (3–7 days)	Hyperdense lesion
Late subacute (>1 wk)	Gradual ↓ in density (resorption starts from periphery toward the center)
Chronic (>1 mo)	Isodense lesion surrounded by hypodense area

Figure 48-9. Intracerebral Hematoma



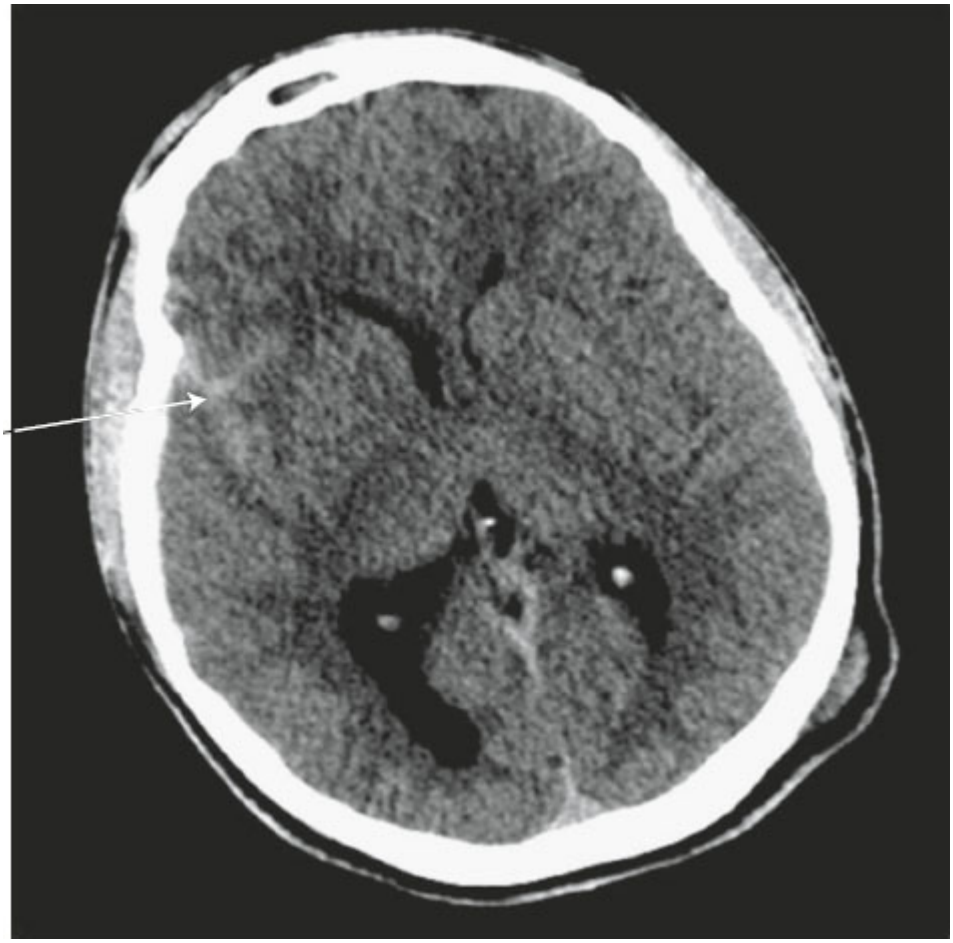
Subarachnoid Hemorrhage (Fig. 48-10)

CT: accuracy of depiction depending on amount of hemorrhage & timing of scan (highly accurate within 4–5 days from onset)

Increased density in cisterns and/or fissures, intraventricular hematoma due to reflux

Complications: hydrocephalus (acute, delayed), cerebral infarction due to vasospasm, transtentorial herniation

Figure 48-10. Subarachnoid Hemorrhage

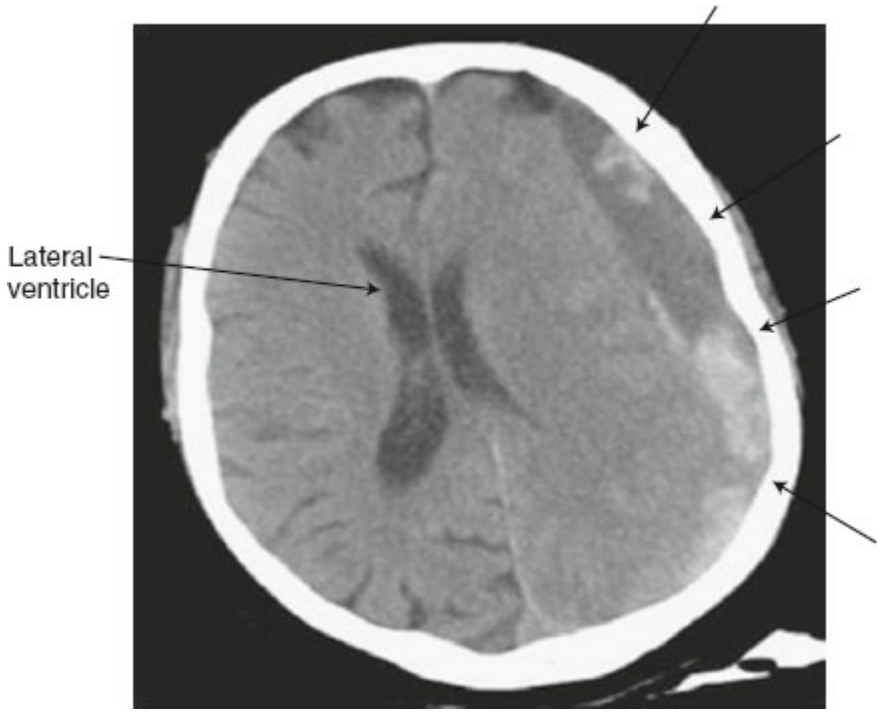


Subdural Hematoma (Fig. 48-11)

Small subdural hematomas are easily missed (up to 40% of the time)

CT: Extra-axial fluid collection, concave inner border, high (<1 wk) to low (>3–4 wks) density, “swirl” sign (mixture of hyperdense fresh bleeding & hypodense old clot; indicating active bleeding)

Figure 48-11. Subdural Hematoma with Midline Shift



Check for the extent of mass effect (loss or obscuration of adjacent sulci, ipsilateral ventricular compression, inward displacement of corticomedullary junction, midline shift)

Caution needed for bilateral hematoma (often w/o midline shift): too small ventricles for the age

Epidural Hematoma

Often associated with skull fx

CT: Extra-axial biconvex homogenous fluid collection, mass effect, marked stretching of vessels

Differentiation from subdural hematoma: usually not cross suture lines, convex inner border, homogenous ("swirl" sign is rare)

TOXICOLOGY

HEIKKI NIKKANEN, MD

Decontamination

Activated charcoal (AC)

Most widely used of any technique for GI decontamination

Significant proven benefit in clinical trials has been difficult to demonstrate

Use of AC does carry the risk of aspiration pneumonitis

Limitations of AC—poor adsorption of alcohols, acids, bases, metals

Adsorptive capacity of AC ~1 g of xenobiotic per 10 g of charcoal

Recommendation: single-dose AC if the ingestion occurred within an hour

Multiple dose–activated charcoal (MDAC)

Some toxins have significant enterohepatic or entero-enteric recirculation

MDAC disrupts this cycle by adsorbing the substance as it passes though the intestinal mucosa

Consider for OD of sustained release preps or medications known to form concretions

Risks are similar as those for a single dose of AC

Watch for ileus

Toxins Amenable to MDAC
Carbamazepine
Dapsone
Phenobarbital
Quinine
Theophylline
Yellow oleander

Whole bowel irrigation

Method of propelling the intestinal contents rapidly through the gut

Indications:

Toxic ingestion of sustained-release preps

Ingestion of a large amount of a highly toxic substance not well adsorbed by AC

Removal of drug packets from the intestine

Enhanced elimination

Hemodialysis & CVVH

Exchange transfusion

Plasmapheresis

Manipulation of urinary pH

Ion exchange resins

Indications

Low volume of distribution (Vd)

Molecular Wt <500 daltons

Some larger molecules with high flux dialyzers

Substances Amenable to Dialysis	
Conventional Hemodialysis	High flux Hemodialysis
Aspirin	Carbamazepine
Toxic alcohols	Phenobarbital
Lithium	Phenytoin
Theophylline	
Valproic acid	

Plasmapheresis or exchange transfusion

Indications

Toxin molecular wt too great for dialysis

Toxin highly protein bound

Patient (pt) cannot tolerate dialysis (infants)

Not in common use—discuss with toxicologist

Manipulation of urinary pH

Enhancing excretion of acidic substances in nephron

Limits diffusion back through the tubule by ionizing the molecule

Less able to pass through a lipid bilayer

Used in treatment of salicylate & uranium toxicity

Initial bolus sodium bicarbonate at 1–2 mEq/kg

Infusion of a solution of 132 mEq of sodium bicarbonate in 1L D5W at 1.5–2 × maintenance

Goal urine pH >7.5

Arterial pH should not be allowed to exceed 7.55

Keep serum K above 4 mmol/l

Metabolic Toxins

Salicylates

Compounds including:

Aspirin

Oil of wintergreen (methylsalicylate)

Pepto-Bismol (bismuth subsalicylate)

Others

Kinetics

Readily absorbed in the small intestine

Low volume of distribution

Toxic-therapeutic window is relatively narrow

Half-life increases significantly with small increases in dose

Toxicity can be significant in either acute or chronic dosing

Mechanisms include uncoupling of oxidative phosphorylation

Results in metabolic acidosis, hyperthermia, & hypoglycemia

Stimulation of the respiratory center results in hyperpnea & tachypnea

Primary respiratory alkalosis

Increased capillary permeability causes pulmonary edema

Clinical picture

Tachypnea & hyperpnea

Tinnitus (aspirin concentration above 30 mg/dl)

CNS effects from agitation to coma. Seizures possible

Hyperthermia

Nausea & vomiting

Pulmonary edema may be present

Lab analysis

ABG shows primary metabolic acidosis & primary respiratory alkalosis

Anion gap is present

Aspirin concentration, ABG, basic metabolic panel should be repeated at 2-hr intervals

Done nomogram is not accurate at predicting morbidity or mortality.

Absorption is erratic

Aspirin concentration of >60 mg/dl in chronic or 90 mg/dl in acute toxicity is considered indication for dialysis. Concentration of >30 mg/dl should prompt urine alkalinization

Treatment

Supportive care

If pt is intubated, it is essential to maintain the min volume as close to the pt's own efforts prior to intubation as possible. Failure to do so may result in acidemia & significant worsening of clinical picture. Sodium bicarbonate may be required to supplement ventilator efforts

Dehydration must be corrected, as many pt will be significantly volume depleted

Seizures can be treated with benzodiazepines or barbiturates

AC administration, even late after overdose, should be strongly considered. Pt with fluctuating aspirin concentrations may have an aspirin concretion present in the gut & may benefit from multiple-dose AC

Manipulation of urinary pH is useful to enhance elimination of aspirin

Correction of hypokalemia must be done concurrently

Consider hemodialysis for certain cases:

Concentrations as described above

Seizure or coma

Pulmonary edema

Renal failure

Refractory metabolic derangement

Toxic Alcohols

Most common agents: methanol (MeOH) & ethylene glycol (EG)

Methanol is a solvent & component of windshield washing fluid

EG is the base for a number of industrial chemical reactions & is present in automotive coolant

Others include:

Isopropanol

Benzyl alcohol

Diethylene glycol

EG ethers

Toxic alcohols are metabolized by:

Alcohol dehydrogenase (ADH)

Aldehyde dehydrogenase

Resulting in a metabolic acidosis & the formation of a toxin

Rapidly & completely absorbed in the stomach & the small intestine

Not adsorbed by AC

They both have volumes of distribution below 1 l/kg

Figure 49-1 shows the metabolism of these alcohols to their toxic metabolites

Majority of MeOH is converted to formate

In cases in which ADH has been inhibited, excretion of MeOH goes along 1st-order kinetics, with a half-life of 1–3 days

EG is more readily excreted by the kidney

Formate toxicity:

Damage to the retina from oxidant stress due to inhibition of cytochrome oxidase & depletion of glutathione

Ischemia or hemorrhage in the basal ganglia can also occur

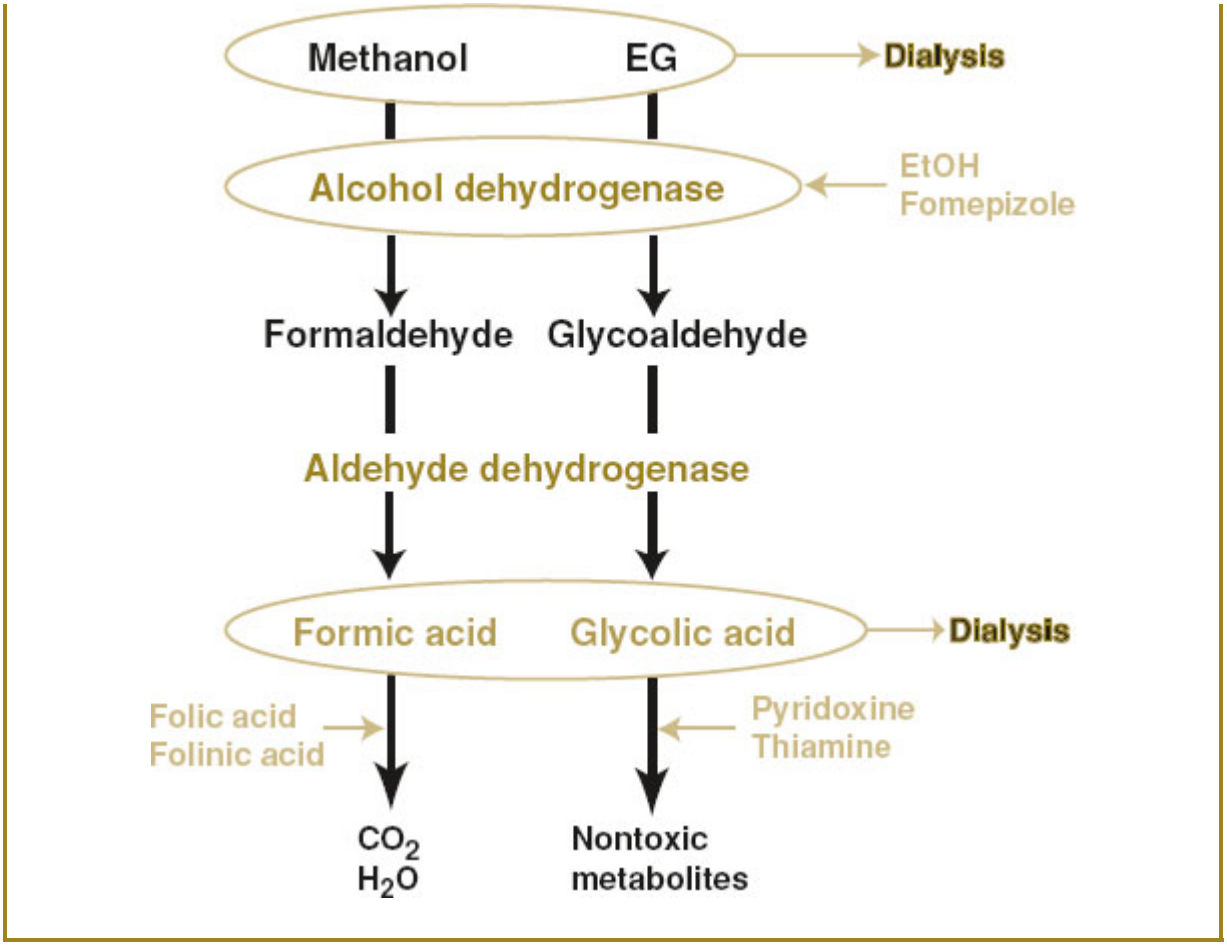
EG toxicity:

Oxalic acid precipitates with calcium to form crystals which primarily injure the kidney, although deposition of such crystals can be seen in a number of tissues

Tubular necrosis & cortical necrosis occur, although renal failure is usually reversible over weeks to months

HypoCa+, the other result of this reaction, can result in dysrhythmias & CV shock

Figure 49-1. The Metabolism of Toxic Alcohols to Their Toxic Metabolites



Early clinical picture of methanol poisoning may be subtle

Its metabolism is slower than that of EG

Less inebriation than EG

GI sx are common

The hallmark of MeOH poisoning is “snowy” or blurry vision

Headache, chest pain, & shortness of breath can occur

Late clinical picture of MeOH poisoning

Coma or respiratory arrest ominous findings

Physical exam findings may include tachypnea, hyperpnea, dilated pupils, & hyperemia of the optic discs. Imaging of the brain may reveal infarction or hemorrhage of the basal ganglia

Early clinical picture of EG poisoning

Inebriation

Late clinical picture of EG poisoning

Coma or seizures

Cardiovascular toxicity, with QT prolongation, dysrhythmias, & hypotension

AGMA develops

Oliguric renal failure occurs

Lab analysis

Early after ingestion of a toxic alcohol may be normal unless the serum osm is measured & an osmolar gap is noted

As the metabolism progresses, the osm gap gradually decreases & is replaced by an anion gap metabolic acidosis

An unexplained osmolar gap of 25 mOsm or more should prompt treatment for toxic alcohol poisoning & confirmatory testing

Serum samples should be sent for gas chromatography/mass spectrometry analysis for toxic alcohols, but treatment should not be withheld while waiting for the results, which may take many hrs

Treatment

Correction of the metabolic acidosis with IV fluid & sodium bicarbonate

All suspected or proven cases should receive antidotal therapy with fomepizole or EtOH to inhibit ADH

Hemodialysis removes the toxic alcohol, corrects acidosis, & removes the toxic metabolite. Hemodialysis also removes EtOH & fomepizole, which means that dosing must be adjusted accordingly

For MeOH, folinic acid at a dose of 1 mg/kg IV every 4 hrs helps metabolize formate

For EG, pyridoxine & thiamine should be given to help with metabolism of glyoxalic acid to nontoxic substances

Cyanide

Sources

Cyanide is used in a number of lab & industrial processes

Product of combustion of a number of synthetic textiles, silk, & wool

Acetonitrile & acrylonitrile can cause delayed toxicity as they are converted to cyanide after absorption

Administration of sodium nitroprusside at high rates can result in elevated cyanide levels, esp. in pt with hepatic or renal dysfunction

Mechanism

Cyanide is considered a "cellular toxin" as it inhibits mitochondrial cytochrome oxidase, disrupting aerobic metabolism

Tissues with high-energy requirements or with great sensitivity to hypoxia are most affected

Lactic anion gap metabolic acidosis results

The clinical picture is 1 of shock & coma, although early on, restlessness or agitation may be seen

Hx is usually more important than the physical examination in making the dx

Lab testing should include simultaneous ABG & VBG, as the inability of the tissues to extract oxygen results in similar pO_2 measurements in both samples. A lactate of above 8 mmol/l is a reasonable indicator of cyanide poisoning

Management of toxicity

Supportive care & observation in pt with normal hemodynamic parameters & mental status

More severely poisoned pt require antidotal therapy with hydroxocobalamin

Recently approved for use by the FDA

Vitamin B_{12} precursor combines with CN- to form vitamin B_{12}

As effective as the previous 3-part cyanide antidote kit, without the adverse effects of hypotension or the development of methemoglobinemia

Secretions may be turned a reddish color, & certain lab measurements relying on colorimetric analysis may be affected

Dose is 5-g IV infusion over 15 min, with a 2nd equal dose to be given if clinical improvement is incomplete

Neurotoxins

Carbon Monoxide

CO sources

Incomplete combustion of hydrocarbon fuel, whether that is charcoal, wood, gasoline or diesel, heating oil, natural gas, or propane

Methylene chloride, a solvent used as a dry cleaning agent & paint stripper. It is metabolized in the liver to form CO

Mechanism of action of CO is complex

Binds to Hb more avidly than oxygen

Impairs dissociation of oxygen from Hb

Tissue effects which are more important from a pathologic standpoint

Binding to iron-containing proteins & enzymes such as myoglobin & cytochrome oxidase, which causes cellular hypoxia

Binding to endothelium & platelets releases nitric oxide, which causes vasodilation & the generation of peroxynitrate. This molecule has a number of pathologic effects on endothelial & lipid tissue

Clinical picture of acute CO poisoning is confusing

Common nonspecific sx such as headache, weakness, or nausea

More severe cases may present with measurable end-organ dysfunction. Cardiac & neurologic findings, esp. syncope & cerebellar abnormalities, are worrisome

Some neurologic abnormalities develop in days to wks after poisoning & are termed delayed neurologic sequelae. Follow-up neuropsychiatric testing should be arranged for severely poisoned pt

Evaluation of the pt for CO toxicity

ABG or VBG with co-oximetry

ECG

Chest radiograph

Lactate in case of smoke exposure

Treatment with normobaric (NBO) or hyperbaric (HBO) oxygen

Equilibration of CO into the tissues from the blood takes hrs, & enhancing the elimination can be done with oxygen

Measurement of COHb yields the concentration in the blood compartment, however, & the tissue effects are more significant. Therefore, a near-normal COHb in the setting of an exposure & an end-organ deficit should not exclude treatment

Use of HBO over NBO is somewhat controversial but most toxicology texts recommend its use

For ICU pt, HBO should be strongly considered

Typically, a single treatment or "dive" is done but can be repeated for persistent signs or sx. The only absolute contraindication to HBO is untreated pneumothorax

Lithium

Kinetics: rapidly & completely absorbed in the small intestine

Bimodal distribution, with an initial serum peak in the 1st few hrs & subsequently a redistribution into the cells over the course of a week

The Vd varies between 0.4 l/kg & 0.9 l/kg, & lithium is not bound to protein

It is renally eliminated, with a half-life from 12 to 48 hrs depending on serum concentration. Lithium overdose can be a result of an acute ingestion, an increase in dose, or worsening renal function

Mechanism of action—may block the effect of some neurotransmitters, & as it is a small cation, it may substitute for potassium or sodium in some cellular functions, with abnormal result

Lithium toxicity in the acute setting is primarily neurologic, but attention should also be paid to cardiovascular examination

Intoxication	Mild	Moderate	Severe
Reflexes	Tremor	Hyperreflexia	Clonus
CNS	Confusion	Delirium, agitation	Seizures, coma
Nonneurologic	N/V/D	Tachycardia	Hyperthermia, hypotension

N/V/D: nausea, vomiting, diarrhea.

Chronic lithium toxicity can cause significant renal dysfunction, including nephrogenic diabetes insipidus

Lab testing

Serum electrolytes, ECG, & urine analysis

Lithium concentration should be drawn >6 hrs after any acute ingestion to avoid an erroneously high result. There is poor correlation between lithium concentration & severity of poisoning in chronic or acute on chronic situations

Treatment includes

Fluid resuscitation to maintain normal urine output

Benzodiazepines or barbiturates for agitation or seizure

Cooling for hyperthermia

Dialysis should be considered for pt with:

Severe sx

Renal failure

Lithium concentration >3.5 mEq/l in chronic toxicity

If dialysis is done, a repeat lithium level should be drawn 6 hrs after dialysis, & the pt should be closely monitored for recurrence of sx

INH (Isoniazid)

Kinetics

Rapidly absorbed from the small intestine

Volume of distribution of 0.6 l/kg

Metabolized by N-acetyltransferase

Toxicity

Inhibits pyridoxine phosphokinase, which converts pyridoxine to its active form

Binds to the active form, forming an inactive compound which is easily excreted

The resultant decrease in pyridoxine activity causes a decrease in gamma-aminobutyric acid concentration & catecholamine synthesis

Clinical picture

Ingestion of as little as 2 g of INH in an adult can cause toxicity

10 g is considered a lethal dose without treatment

GI sx predominate in the early stages

Progression to CV collapse, metabolic acidosis, seizures, & coma

Seizures are usually not controlled by anticonvulsant therapy

Coma may persist for some time after the pt has been stabilized

Lab analysis

Comprehensive metabolic panel

PT & PTT

Urine analysis

ABG or VBG

CK to evaluate for rhabdomyolysis

Treatment

Ventilatory support, fluids, pressors

Sodium bicarbonate to correct metabolic acidosis

Benzodiazepines or barbiturates can be used for seizure

Pyridoxine antidote therapy

Dose equivalent to the ingested amount of INH should be given intravenously

If the amount is not known, 75 mg/kg of body wt can be used

If the pt has refractory metabolic acidosis or renal failure, hemodialysis can be used to remove INH & treat the metabolic abnormalities

Organophosphate Poisoning (see Chapter 50)

Cardiovascular Toxins

Calcium Channel Blockers (CCBs)

Kinetics

Absorption in the small bowel is rapid, bioavailability is 90% or greater

There is 1st-pass metabolism, & blood concentrations reach a maximum within a few hours. Although there are 5 classes of CCB, 3 represent the majority of CCBs prescribed

Class	Agent			Activity
Phenylalkylamine	Verapamil			Cardiac & vascular
Benzothiazepine	Diltiazem			Cardiac
Dihydropyridine	Nifedipine	Nimodipine	Nicardipine	Vascular
Diarylpropylether	Bepridil			
Tertraline	Mibefradil			

Mechanism of action

Variable activity on cardiac or vascular L-type calcium channels is the basis for therapeutic activity of these medications, depending on which class of CCB is used

In overdose, receptor selectivity is lost, & even peripheral tissue calcium channels are affected in a clinically significant way

Supratherapeutic concentrations of CCBs also result in prolonged metabolism & excretion

Clinical picture

CO decreases, SVR decreases, & bradycardia with AV block can be seen

Pulmonary edema may be due to reduced CO or direct effect on the pulmonary capillary endothelium

Blockade of L-type calcium channels in the pancreas reduces the secretion of insulin, resulting in hyperglycemia. The degree of hyperglycemia can be used to predict the degree of toxicity

Assessment of the pt

Baseline lab studies, with particular attention to the glucose & lactate

ECG which may show high-degree AV blockade

Physical exam findings of peripheral vasodilation & warm skin consistent with distributed shock

Treatment

Supportive care, which may require multiple pressors

Alpha-adrenergic agent for increasing vasomotor tone

Beta-adrenergic agent for increasing CO

Amrinone may be useful, as it directly increases the opening of calcium channels via inhibition of phosphodiesterase III, resulting in an increase in cyclic AMP

Bradycardia may be responsive to atropine. Cardiac pacing may yield an increase in HR but has not been shown to increase BP

Calcium at high doses—common strategies

Bolus dosing of calcium chloride at 1 g every 2–3 min until a response is seen

One gram every 15 min until the clinical response is seen, or until 4 doses have been given

Continuous infusion at 0.2–0.4 mg/kg/hr, or titrated to a serum calcium of 8 mg/dl

Glucagon provides increased cyclic AMP, via a G-protein–mediated mechanism

A bolus dose up to 10 mg until clinical improvement, followed by an infusion of the effective total bolus dose, given every hour

Hyperinsulinemia–euglycemia therapy has been used as an effective antidote for CCB toxicity for a number of yrs

Its postulated mechanism includes increasing cellular uptake of glucose by making up for the decrease in insulin secretion as well as overcoming insulin resistance in the tissues

Bolus dosing of 0.5–1 U/kg is followed by continuous infusion of 0.5–1 U/kg/hr

Glucose should be checked frequently (q15min) for the 1st hour & at least hourly thereafter. Glucose may need to be given in bolus or continuous infusion

Potassium should be checked hourly & replenished as needed

Intralipid, or lipid emulsion, is a component of parenteral nutrition that has been used as an antidote in the treatment of lipophilic toxins

Most experience has been with systemic toxicity of local anesthetics

Has been tried as a last-ditch measure in severe poisonings of other types including CCB

One proposed dosing regimen is a bolus of 1.5 ml/kg of 20% lipid emulsion, followed by an infusion at 0.25 ml/kg/min for 30–60 min

This therapy is clearly an off label use that should be reserved for extreme circumstances

Lab analysis of the blood may be made difficult by the lipid load for the next 12–24 hrs. Ultracentrifugation of the sample prior to analysis may be helpful

Cardiac bypass or intra-aortic balloon pump can be used in very severe refractory cases

Digoxin

Kinetics

Not very well absorbed in the GI tract in pill form

Vd of 5.6 l/kg. It is, therefore, not amenable to dialysis

It is renally excreted, with a half-life of over 24 hrs. In overdose, this will be prolonged further

Mechanism of action

In overdose, the sodium–potassium ATPase pump in cell membranes becomes dysfunctional, leading to an intracellular elevation in calcium & serum elevation in potassium

Clinical picture

Conduction abnormalities including ectopy, tachydysrthymias, & bradydysrhythmias

Cardiogenic shock

Nausea & vomiting are common

Altered mental status or visual changes (yellowing of vision) can occur

Lab analysis

Measurement of serum K is of use in determining the severity of poisoning

Mortality 35% with a potassium above 5 mEq/l & 100% in pt with potassium above 6.4 mEq/l

A digoxin concentration can be difficult to interpret due to a number of factors

Treatment

A combination of h/o digoxin ingestion, a state of cardiac shock, cardiac dysrhythmia, & hyperkalemia (for acute ingestions) should prompt treatment for digoxin toxicity

Atropine or pacing for bradycardia

Magnesium is of some theoretical benefit because it is thought to increase activity of the sodium–potassium ATPase pump

Antidotal treatment with digoxin-specific Fab fragments is the most important intervention. Calculation of the amount to administer depends on what is known about the ingestion

Antidotal Treatment with Digoxin-Specific Fab Antibody Fragments	
Data Used for Dosing	**Vials to Be Given (Roundup)**
Amount ingested	(0.8 × ingested amount in mg)/0.6 mg
Serum digoxin concentration	([Digoxin] in ng/ml × 5.6 l/kg × pt wt kg/1,000)/0.6 mg
Acute OD—empiric rx	10–20 vials
Chronic OD—empiric rx	6 vials

Hepatic and GI Toxins

Acetaminophen

Kinetics of acetaminophen (APAP) are predictable

Absorbed in the small bowel

Vd of 1 l/kg

The majority of APAP is conjugated & excreted renally. Only about 5% is metabolized via CYP2E1 & CYP1A2 to the toxic metabolite, n-acetyl-para-benzoquinone-imine (NAPQI). With therapeutic dosing & normal glutathione stores, NAPQI is rapidly metabolized & excreted

Mechanism of action

In cases of overdose, glutathione is depleted & toxicity results

Exact mechanism is unclear but hepatic injury occurs in a centrilobular pattern

Mitochondrial dysfunction has been suggested as a mechanism

The clinical course of APAP poisoning has been artificially divided into 4 phases

Four Phases of the Clinical Course Following Acetaminophen Toxicity			
Phase I (Day 1)	**Phase II**	**Phase III**	**Phase IV**
Asymptomatic	LFTs rise further	Jaundice	Death or recovery
Nausea & vomiting	RUQ pain	Hepatic encephalopathy	
LFTs rise	Synthetic function off	Multi-system organ failure (MSOF)	

Dx & treatment

On the basis of the hx

Occasionally can be inferred from the physical examination & lab analysis

Use of Rumack–Matthews nomogram

If the ingestion occurred at a single point in time, & there were no coingestants that might interfere with gastric emptying, the nomogram can be used

If the APAP concentration as a function of time is above the possible hepatotoxicity line, treatment with n-acetylcysteine (NAC) should be initiated

If the ingestion is complicated by coingestants or unclear timing, the nomogram cannot be used

APAP overdose pt admitted to the ICU typically have massive ingestion, liver synthetic dysfunction, or hepatic encephalopathy. They should be treated with NAC regardless of timing of ingestion or APAP level

Dialysis can also be used to remove APAP in cases in which the concentration is severely elevated (over 1,000 mcg/dl)

Stopping NAC therapy in ICU pt should be done only when the LFTs are on a clear downward trend, with normal PT & PTT, & a zero APAP level

Dose & route of NAC should be chosen in conjunction with the hospital pharmacist or the local poison control center

Chronic lab monitoring includes comprehensive metabolic panel, PT, &PTT, lactate, & VBG or ABG daily, or more often in cases of hepatic failure

Criteria for liver transplantation are presented in the table later. Pt should be evaluated for transplant as soon as a concern develops

Criteria for Liver Transplantation Following Acetaminophen Toxicity	
Arterial pH <7.3	INR >2 at 24 hrs postingestion
Serum creatinine >3.3	INR >4 at 48 hrs postingestion
Initial lactate >3.5 mmol/l	INR >6 at 72 hrs postingestion
Lactate after resuscitation >3.0 mmol/l	Grade III or IV encephalopathy

Caustics

Alkaline and Acidic Substances

Drain cleaners, oven cleaners, automatic dishwasher detergents, brake dust removers, & other industrial chemicals

Cause significant injury to the skin & the mucosa

Alkalis cause a so-called "liquefaction" necrosis, as they cause softening of the tissues they come into contact with. This allows deeper penetration into the body

Acids, on the other hand, cause a coagulation that can limit the depth of injury. Ingestion of either substance can cause significant injury to the esophagus & the stomach

Burns to the GI tract are classified into 3 grades, & the progression of injury into 4 stages

Three Grades of Burns in the GI Tract and the 4 Stages of Progression Following Caustic Injury		
Grade	**Lesion**	
1	Erythema	
2a	Superficial ulcers	
2b	Deep or circumferential ulcers	
3	Full thickness ulcers, necrosis	
Stage	**Time**	**Pathophysiology**
I	Minutes	Necrosis
II	Hours	Thrombosis
III	Days	Sloughing
IV	Weeks to months	Stricture formation

Even brief skin contact with highly concentrated caustics can cause full-thickness burns. In the days to wks that follow an esophageal injury, tissue strength is diminished & perforation can occur

Treatment

No AC or gastric lavage, as they have not been shown to be of benefit. Lavage may damage tissues; AC can obscure the view during endoscopy

Steroid therapy is of no use in grade I injuries & can be harmful in grade III injuries. A prospective trial failed to demonstrate benefit in preventing strictures in pt including those with grade II injuries

Early consultation of the gastroenterology & surgical services is essential in order to determine the extent of the injury. Perforation, which can be seen on chest radiograph or CT scan, usually requires prompt surgical intervention

DISASTER PREPAREDNESS

GEOFFREY S.F. LING, MD, PhD, COL (RET.)

Basic Principles (Birch K. *JR Army Med Corps.* 2009;155:122–124)

Casualty management begins with planning. The expected chaos surrounding any mass casualty situation necessitates being prepared with a well-rehearsed well-trained team.

If there is any suspicion of a CBRNE (chemical, biological, radiologic, nuclear, or explosive) event, then casualty management begins with protecting medical providers (HazMat suits, etc.). A triage area needs to have clean & unclean areas clearly identified with definitive demarcation lines. After providing emergency care to save life and/or provide a rapid antidote, the patient (pt) must be decontaminated before proceeding to higher levels of medical care. A pt may then proceed into the medical treatment facility.

Planning

Disaster plan needs to be in place at all times

List of trained providers with 24/7 contact information

Assembly point identified, must be specific location (cafeteria or staff lounge)

Predetermined tasks for key personnel

Command structure with alternates for every key position, committees consisting of all involved disciplines, establish relationships with other medical treatment facilities

Key medical groups: emergency medicine, trauma surgery, primary care, pathology, critical care, infectious dz, psychiatry, preventive medicine, pharmacy

Other key groups: hospital administration, casualty/mortuary affairs, engineering, pt administration, security, public affairs, clergy

TRIAGE

This is a critical aspect of effective disaster management

Formulate triage plan prior to any disaster or mass casualty

Triage committee should include physicians, nurses, ethics, clergy, hospital administrator

Criteria for triage must be made well in advance of any disaster so as to ensure that all ethical issues are considered

Criteria must not be made by the triage officer at the time of disaster

Triage area needs to be before & outside of treatment areas

Triage officer

Ideally ED/trauma physician but may be a critical care physician

If a contaminated environment, should be instead a nonphysician (nurse, dentist, physician assistant, EMT)

Empowered to make disposition decisions based on nature of injury, prognosis

Must know pt load (anticipated & present), status of decontamination lanes, supply, evacuation chain, etc.

Casualty sorting by treatment requirement:

Delayed: care is needed but delaying care will not affect outcome

Immediate: emergency care is needed to save life (ABC or antidote)

Minimal: minor care by nonphysician, admission not needed, quick disposition

Expectant: survival unlikely even with optimal treatment, care exceeds avail. resources

Decontamination

Decontamination lanes should be established prior to medical treatment facility

Decontamination teams are nonmedical personnel

The “clean line” must be strictly adhered to & guarded by armed security

Evacuation sorting

Urgent (within 2 hrs), priority (within 4 hrs); routine (within 24 hrs)

Evacuation

Identify tertiary medical treatment facilities that pt, once stabilized, can be evacuated to

Transportation assets need to be dedicated to medical mission

Alternative modes & routes of transportation need to be identified

Combat

Medical treatment facilities at each echelon of care render only that care necessary to save life & sufficient to stabilize the pt for evacuation. The goal is to transport the pt to a safe area far away from the combat theater, where definitive medical treatment may be provided

A well-established, rehearsed evacuation system ensures flow of pt continually to higher levels of care. This prevents medical treatment facilities from filling their avail. bed space or exhausting their resources

Bacterial Biological Warfare (Ramasamy S, et al. *BJ Pharmacol.* 2010;161:721–748)

Anthrax (Inglesby TV, et al. *JAMA.* 2002;287:2236–2252)

Signs & sx

Early: fever, malaise, fatigue, cough, & mild chest discomfort

Late: hemorrhagic mediastinitis, severe respiratory distress with dyspnea, stridor, & shock

Clinical course: rapid progression to death 1–3 days after late sx onset

Dx: PCR or ELISA tests early, positive Gram & Wright stains late, CXR: widen mediastinum (late finding)

Treatment: ciprofloxacin 400 mg, IV every 12 hrs, may switch to oral when clinically stable. Treat for 60 days. Alternatives are penicillin or doxycycline

Ppx: ciprofloxacin, 500 mg, PO every 12 hrs for 4 wks

Alternative: doxycycline. Vaccine is avail.

This is not transmitted human-to-human

Plague (Inglesby TV, et al. *JAMA.* 2000;283:2281–2290)

Signs & sx

Early: swollen glands (bubo), fever, chills, malaise, fatigue, headache, myalgia

Late: high fever, cough with bloody sputum, pneumonia, sepsis

Clinical course: fatal within 24 hrs of pneumonia onset if not treated

Dx: gram-negative coccobacillus with bipolar safety pin appearance, florescentantibody or antibody test

Treatment: streptomycin, 15 mg/kg, IM, every 12 hrs for 10–14 days

Alternatives are gentamicin, ciprofloxacin, doxycycline

Ppx: doxycycline

Transmission: human-to-human is contagious; also rat-to-human via flea

Tularemia (Dennis DT, et al. *JAMA.* 2001;285:2763–2773)

Signs & sx

Early: fever, chills, headache, myalgia, coryza, sore throat

Inhalation tularemia presents as a nonspecific febrile illness with pneumonitis developing over days to wks (much slower than anthrax or plague)

Ulceroglandular type: painful ulcerative skin lesions, pneumonia (less common)

Typhoidal type: fever, cough, substernal chest pain, pneumonia (more common)

Clinical course: begins as nonspecific febrile illness & then over days to wks progresses to pneumonia leading to respiratory failure, shock, & then death

Dx: florescent-labeled antibody stain by a reference lab. Gram stain reveals tiny pleomorphic gram-negative bacilli

Treatment: Streptomycin, 1 g, IM, every 12 hrs for 10 days

Alternatives are gentamicin, chloramphenicol, ciprofloxacin, doxycycline

Ppx: not recommended. Postexposure treatment if evidence of fever with ciprofloxacin 500 mg, PO, every 12 hrs. Alternative: doxycycline

Transmission: human-to-human does not occur

Q Fever

Signs & sx

Early: high fever, chills, headaches, myalgia, headache, malaise, nonproductive cough, nausea, vomiting, diarrhea

Late: pleuritic chest pain, rales, 50–60% have abnormal CXR

Clinical course: lasts up to 2 wks & resolves. Fatality is uncommon

Dx: blood test for serum antibodies

Treatment: doxycycline, 100 mg PO × 21 days. Alternatives: macrolides, quinolones

Ppx: vaccine is avail.

Transmission: human-to-human is rare

Brucellosis

Sign & sx are fever, chills, malaise, headache, myalgia, arthralgia, lumbar back pain (from osteoarticular infxn), mental status changes, depression. Osteoarticular infxn leads to lumbar back pain, extremity joint pain, effusion, & immobility

Dx: Rose-Bengal plate test for rapid screening. Blood or bone marrow cx to confirm dx

Treatment: doxycycline 100 mg, PO, every 12 hrs for 6 wks.

Alternatives are streptomycin, gentamicin, rifampicin, quinolones, or Bactrim

Ppx: no vaccine

Transmission: human-to-human is unusual

Glanders & Melioidosis (*Glanders, Textbook of Military Medicine: Medical Aspects of Biological Warfare.* 121–146)

Signs & sx:

Early: fever, chills, sweats, myalgia, headache, pleuritic chest pain, cervical adenopathy, hepatosplenomegaly, papular/pustular rash

Late: pneumonia, sepsis

Clinical course: fatal if untreated

Dx: blood cx. Methylene or Wright stain of exudates reveals small bacilli with safety pin configuration

Treatment: doxycycline 100 mg, PO, every 12 hrs with Bactrim, PO, for 20 wks plus chloramphenicol, PO, for 1st 8 wks. For severe cases, ceftazidime at 40 mg/kg, IV, every 8 hrs for 14 days, then switch to mild case oral regimen for remaining 18 wks

Alternatives are ciprofloxacin, imipenem, & meropenem

Ppx: none

Transmission: human-to-human via secretions is possible

Viral Biological Warfare

Viruses that have been weaponized are smallpox & Venezuelan equine encephalitis (VEE)

Small Pox (Henderson DA, et al. *JAMA.* 1999;281:2127–2137)

Signs & sx

Early: fever, chills, malaise, vomiting, headache, backache

Late: vesicles, most often on face & extremities

Clinical course: up to 40% fatality rate

Dx: electron microscopy of vesicular fluid reveals brick-shaped virons, PCR, Guarnieri bodies are seen under light microscopy

Treatment: supportive care. There is no clinical evidence demonstrating cidofovir efficacy in humans

Ppx: vaccine

Transmission: human-to-human is contagious

Venezuelan Equine Encephalitis

Signs & sx are spiking high fevers, chills, malaise, rigors, headache, photophobia, myalgia in lower back & legs. Later, sore throat, nausea, vomiting, & diarrhea. Neurologic sx are unusual in natural VEE but much more common if exposed to an aerosol weapon. If the CNS is affected, then lethargy, somnolence, & confusion occur early, followed by seizures, ataxia, paralysis, & coma

Clinical course: low fatality rate

Dx: IgM serology, viral isolation. CSF analysis reveals monocytic leukocytosis & elevated opening pressure.

Treatment: supportive

Ppx: candidate vaccine is in clinical trial

Transmission: human-to-human is suspected but not proven

Chemical Warfare (Thiermann H, et al. *Chem Bio Interactions.* 2013;206:435–443)

6 types of chemical weapons (agents): pulmonary/choking, cyanide/blood, vesicants/blistering, nerve agents, incapacitating agents, & riot control. Riot control agents will not be discussed here.

Hallmark of treatment begins with terminating exposure. This should be done by removing the victim from exposure, placing a gas mask, & active cleansing of clothes & skin.

Pulmonary Agents

The prototypic pulmonary or choking agent is phosgene (CG).

Detection: odor of “new mown hay or grass,” M18A2 & ICAM

M8 & M9 paper & M256A1 tube assays will not detect them

Decontamination: fresh air & copious water irrigation

Triage

If seen within 12 hrs of exposure:

Immediate: pulmonary edema is present. Early development of pulmonary edema predicts a severe exposure

Such pt need admission to an ICU

Delayed: dyspnea is present. Close monitoring & retriage every hour

Minimal: known exposure & asymptomatic

Expectant: pulmonary edema, cyanosis, & hypotension within 6 hrs of exposure will not survive, even with maximal medical therapy. If >6 hrs, then may survive only if intensive care is immediately avail.

If seen beyond 12 hrs of exposure:

Immediate: pulmonary edema is present. Such pt need admission to an ICU within a few hours

Delayed: dyspnea is present. Close monitoring & retriage every 2 hrs. Recovering pt can be discharged in 24 hrs

Minimal: asymptomatic or resolving dyspnea

Expectant: hypotension in spite of intensive care treatment

Also, pt with pulmonary edema, cyanosis, & hypotension

Signs & sx are eye & airway irritation, dyspnea, chest tightness, & delayed pulmonary edema

Treatment: terminate exposure & decontaminate

Ventilation: an artificial airway should be placed if there is hoarseness or stridor as this portends laryngeal spasm

Frequent suctioning, supplemental oxygen, & positive pressure ventilation will likely all be needed For bronchospasm: theophylline, β-adrenergic agonists, or parenteral steroids may be used

CV: continuous close monitoring of hemodynamic status is paramount as pulmonary edema & positive pressure ventilation may lead to hypotension. Maintain euvolemia & consider applying antishock garments

Limit activity: rest is crucial. Even if pt appears well, enforce bed rest to include litter evacuation

Abx: not needed unless clear evidence of infxn

Blood Agents

Cyanide is the prototypic blood agent. Among other effects, it binds to iron in cytochrome a_3 & methemoglobin

Detection: M256A1, M18A2, ICAM; M8 & M9 paper assays will not

Decontaminate: skin decontamination is typically not needed. However, if the clothing is wet & contaminated, then clothing & skin will need decontamination

Triage:

Immediate: convulsions, apnea but circulation is intact. Immediate antidote treatment will be lifesaving

Minimal: exposed but showing minimal sx. Antidote may relieve sx but is not necessary to save life

Delayed: recovering from exposure or responding to antidote therapy

Expectant: apneic with circulatory arrest

Signs & sx: anxiety or apprehension, agitation, vertigo, subjective weakness, nausea, & muscular trembling. This can worsen to coma, seizures, respiratory, & cardiac arrest. Physical signs include severe respiratory distress without cyanosis or, occasionally, cherry red skin. Lab tests are blood cyanide levels, metabolic acidosis, elevated venous blood oxygen content.

Treatment: Cyanokit^R (hydroxocobalamin) or Cyanide Antidote Kit^R (contains amyl nitrite pearls, sodium nitrite, & sodium thiosulfate) & supportive care

Vesicants

Mustard (HN), Lewisite (L), & phosgene oxime (CX)

Mustard

Mustard's effects are delayed by several minutes as it must dissolve into sweat, tears, or extracellular fluid

Detection of HN: M8 & M9 paper assays, M256A1, M18A2, & ICAM

Triage

Immediate: moderately severe to severe pulmonary effects. Delayed: skin lesion affecting over 50% of body surface area (BSA)

Minimal: skin lesions affecting less than 50% BSA

Expectant: severe pulmonary effects <6 hrs after exposure

Decontamination: this is the most effective way to treat

Signs & sx: asymptomatic latent period (hrs), followed by erythema & then blistering of skin, conjunctivitis, eye opacity, airway irritation. Nausea & vomiting are usually due to stress reaction & not a direct effect of HN

Treatment: supportive care

Pt's body fluids & blister fluid do not contain HN

Lewisite

Similar to mustard, except Lewisite causes immediate tissue response

Phosgene oxide

Similar to mustard except phosgene oxide causes immediate tissue response but does not blister. Instead, it causes wheal-like lesions

Nerve Agents

There are 5 nerve agents: GA (Tabun), GB (Sarin), GD (Soman), GF, & VX plus pesticides (malathion, parathion, diazinon, trichlorfon, etc.), & herbicides (tribufos, merphos). They are in order of lowest to highest toxicity. These are all organophosphorus cholinesterase inhibitors

Detection: M8 & M9 paper assays, M256A1, M18A2, & ICAM will all detect nerve agents

Triage

Immediate: severe sx of seizures, loss of consciousness, difficulty breathing, apnea, flaccid paralysis. Immediate treatment can be life-saving

Expectant: no BP

Delayed: recovering from severe exposure following treatment but still requires ventilatory assistance

Minimal: walking & talking

Decontamination: necessary

Signs & sx: rhinorrhea is usually the 1st sign with miosis being the characteristic sign. Low dose: miosis, rhinorrhea, difficulty breathing from bronchoconstriction, nausea, vomiting, muscle fasciculation. Large dose: miosis, diarrhea, loss of consciousness, seizure, apnea, flaccid paralysis, copious secretions

Treatment: atropine, 2 mg, IM & pralidoxime chloride (2-PAM), 600 mg, IM Mark 1 kits are these 2 medications packaged together as self-administration autoinjectors. The course of therapy is for victims to self-administer a single Mark 1 kit & then seek buddy aid immediately. If, after 10 min, there is no improvement or if the victim is showing signs of severe exposure, then the buddy should administer 3 Mark 1 kits, followed by diazepam, 10 mg, IM

After this, additional atropine doses should be given on the basis of resolution of airway secretions & resistance

Incapacitating Agents

There are 2 incapacitating agents, BZ & Agent 15. Both are atropinic agents

Detection: none

Triage:

Immediate: cardiopulmonary compromise & severe hyperthermia

Physostigmine should be used cautiously in such pt

Instead, efforts should focus on ABCs & cooling

Delayed: suffering significant CNS sx. Physostigmine should be considered

Minimal: minor CNS or peripheral nervous system sx. Will likely not require physostigmine

Expectant: severe cardiopulmonary collapse in a situation in which treatment & evacuation are not possible

Decontamination: necessary

Sign & sx: mydriasis, dry mouth, dry skin, decreased level of consciousness, delirium, inattention, impaired memory

Treatment: physostigmine use is controversial due to its toxicity profile. If used, 45 mcg/kg IM, 30 mcg/kg slow IV infusion (over 4 min or more), or 60 mcg/kg PO (in orange juice as it is bitter). This may be repeated every hour with titration of dose to the pt's mental status. Also, diazepam 2 mg, IV, every 15 min as needed to control agitation. Supportive care (a well-established clinical team for airway, breathing, & circulatory management).

Nuclear Radiation (Pandey BN, et al. *Int J Rad*. 2010;86:613–635)

Detection: No specific test is avail. for determining severity of exposure. Tools such as Geiger counters & dosimeters can be helpful if findings are positive

Decontaminate: copious water irrigation

Triage:

Immediate: early onset of severe nausea & vomiting, headache, severe body burns

Minimal: delayed (hours) onset of nausea following exposure

Delayed: asymptomatic

Expectant: exposure to >10 Gy is typically fatal

Signs & sx: Radiation sickness develops quickly with rapidity related to exposure severity. The higher the exposure, the earlier sx manifest. The most common signs & sx are nausea, vomiting, & muscle weakness. Fever & diarrhea follow. Bloody emesis & stools, bleeding from mucous membranes, hair loss, & bone marrow suppression appear later. Following exposure to an explosive event, burn injuries may need to be managed.

Treatment: Potassium iodine is used to block radioactive iodine uptake into the thyroid gland. If used, 130 mg PO. DTPA (diethylenetriamine pentaacetate) is used to bind plutonium, americium, & curium. If used, ca-DTPA is administered 1 g IV or 1 g inhalation/nebulizer. This is followed by zn-DTPA 1 g IV every day. Prussian Blue is used to block intestinal uptake of cesium & thallium. It is administered at a dose of 500 mg PO. Filgrastim can be used to stimulated leukocyte production if a pt has been exposed to the severity of bone marrow suppression. If used, 10 mcg/kg SQ every day. Other options for leukocyte production stimulation are sargramostim & pegfilgrastim.

ICU CALCULATORS, CALCULATIONS, DRUGS

SUJATHA PENTAKOTA, MD

Hemodynamic Formulas

Variable	Calculation	Normal
Cardiac index(CI)	CO/BSA	2.5–4.0 l/min
Stroke volume	CO × 1,000/HR	60–90 ml/beat
MAP	DBP + PP/3	60–110 mm Hg
SVR	$\frac{\text{MAP} - \text{CVP}}{\text{CO}} \times 80$	800–1,500 dynes × sec/cm^5
PVR	$\frac{\text{PAP} - \text{PAWP}}{\text{CO}} \times 80$	150–250 dynes × sec/cm^5
LVSW	SV × (MAP – PAWP) × 0.0136	58–104 gm-m/beat
RVSW	SV × (MPAP – PAWP) × 0.0136	8–16 gm-m/beat
CO	HR × SV	5–8 l/min
Corrected QT (QTc) = Bazett formula = QT interval/$\sqrt{}$RR interval		

Fick Cardiac Output

Oxygen consumption (l/min) = CO (l/min) × arteriovenous (AV) oxygen difference

CO = oxygen consumption/AV oxygen difference

Oxygen consumption must be measured (can estimate with 125 ml/min/m^2, but inaccurate)

AV oxygen difference = Hb (g/dl) × 10 (dl/l) × 1.36 (ml O_2/g of Hb) × ($SaO_2 - SvO_2$)

SaO_2 is measured in any arterial sample (usually 93–98%)

SvO_2 (mixed venous O_2) is measured in RA, RV, or PA (assuming no shunt) (normal ~75%)

$$\therefore \textbf{CO (l/min)} = \frac{\text{Oxygen consumption}}{\text{Hb (g/dl)} \times 13.6 \times (SaO_2 - SvO_2)}$$

Respiratory Formulas

Variable	Formula	Normal Value
Alveolar oxygen tension	$PAO_2 = (FiO_2 \times [P_{atmos} - PH_2O]) - (PaCO_2/RQ)$	110 mm Hg on FiO_2 0.21
Alveolar–arterial oxygen gradient	A–a gradient = $PAO_2 - PaO_2$	10 mm Hg at FiO_2 0.21. ↑ 5–7 mm Hg per 10% ↑ in FiO_2. At FiO_2 1.0, should be <150 mm Hg
Oxygen extraction ratio	$OER = VO_2/DO_2 \times 100$ $(CaO_2 - CvO_2)/CaO_2 \times 100$	22–32%
Partial pressure of arterial carbon dioxide	$PaCO_2 = K \times \frac{VCO_2}{(1 - V_d/V_t) \times VA}$	35–45 mm Hg
Arterial oxygen content	$CaO_2 = (SaO_2 \times Hb \times 1.34) + 0.003\ (PaO_2)$	17–20 ml/dl
Mixed venous oxygen content	$SvO_2 = SaO_2 - (VO_2/Q \times Hb \times 13)$	12–15 ml/dl
Intrapulmonary shunt	$Qs/Qt = (CcO_2 - CaO_2)/(CcO_2 - CvO_2)$	5%
Physiologic dead space	$V_d/V_t = PaCO_2 - PeCO_2/PaCO_2$	Negligible
Oxygen consumption	$VO_2 = Q \times ([CaO_2 - CvO_2])$	200–250 ml/min
Delivered oxygen	$DO_2 = Q \times CaO_2$	520–570 ml/min/m^2
Static compliance	TV/plateau pressure – PEEP	0.05–0.07 l/cm H_2O
Dynamic compliance	TV/PIP – PEEP	80–100 ml/cm H_2O
Airway resistance	PIP – plateau pressure/ peak inspiratory flow	4–6 cm $H_2O \cdot l^{-1} \cdot sec^{-2}$

PAO_2, partial pressure of alveolar oxygen; FiO_2, fraction of inspired oxygen; P_{atmos}, barometric pressure (760 mm Hg at sea level); PH_2O, water vapor pressure; RQ, respiratory quotient; $PaCO_2$, partial pressure of carbon dioxide in blood; K, constant; VCO_2, carbon dioxide production; V_d/V_t, dead space ratio of each tidal volume breath; VA, minimum ventilation.

Acid–Base Equations (also see Chapter 7)

Base deficit (mEq/l) = 0.5 × body wt in kg × (24 – [HCO_3])

Anion gap = (Na^+ + K^+) - (Cl^- + HCO_3). Normal AG = 3-12 mEq/l.

Delta gap = Anion gap - 12 (normal anion gap)

Corrected anion gap: AG needs to be corrected for albumin level. For every 1 g/dl decrease in albumin from 4 g/dl, AG decreases by 2.5.

Delta Gap

Δ gap = (AG − 12) – (24 − HCO_3) = 0 ± 6

$$\text{Delta ratio} = \Delta \text{ anion gap}/\Delta\ [HCO_3^-] = \frac{AG - 12}{24 - HCO_3}$$

Positive delta gap signifies a concomitant metabolic alkalosis or respiratory acidosis.

Negative delta gap signifies a concomitant normal anion gap metabolic acidosis or chronic respiratory alkalosis.

$$\text{Calculated osmolarity} = 2(Na^+) + \frac{\text{BUN (mg/dl)}}{2.8} + \frac{\text{Glucose (mg/dl)}}{18} + \frac{\text{EtOH}}{4.6}$$

Normal serum osmolarity = 285–295 mOsm/l

Osmolar gap = measured osmolarity – calculated osmolarity (normal <10)

Fractional excretion of sodium:

FENA: Urine Na × serum Cr/(urine Cr × serum Na) × 100

FENA <1: Prerenal

It may also be seen in pt with post ischemic ATN, ATN superimposed upon a chronic prerenal dz, in 10% of pt with nonoliguric ATN, in AKI due to radio contrast media or heme pigments, acute glomerulonephritis or vasculitis, hepatorenal syndrome & in some cases of AIN, & (rarely) acute urinary tract obstruction.

FENA = 1–2: Prerenal or Renal

FENA >2: ATN

Results not reliable in pt on diuretics. Hence in pt on diuretics, consider using:

Fractional excretion of urea: <35 in prerenal dz, >50 in ATN.

Fractional excretion of lithium: <15% (and usually below 10%) in prerenal dz.

Fractional excretion of uric acid: <12 in prerenal dz, >20 in ATN.

Estimation of GFR

Serum creatinine concentration

Creatinine clearance

Estimation equations based upon the serum creatinine: such as the Cockcroft–Gault equation & modification of diet in renal dz (MDRD) study equations

Creatinine Clearance

$$\text{Creatinine clearance (CrCl)} = \frac{\text{urine creat (mg/dl)} \times \text{total urine output in 24 hrs (ml/d)}}{\text{serum creat (mg/dl)} \times 1{,}440}$$

This gives CrCl in ml/min. This may be adjusted for the BSA using the formula:

CCr × 1.73/BSA to give CrCl in terms of ml/min/1.73 m^2.

The normal value for the creatinine clearance is 95 ± 20 ml/min in women & 120 ± 25 ml/min in men.

2 major errors can limit the accuracy of creatinine clearance

Incomplete urine collection

Increasing creatinine secretion as the GFR falls

Cockcroft–Gault equation

$$\text{CCr (ml/min)} = \frac{(140 - \text{age}) \times \text{lean body wt (kg)}}{\text{Cr (mg/dl)} \times 72}$$

In women, multiply by 0.85. This equation has to be adjusted for body surface area.

MDRD GFR calculator

GFR, in ml/min/1.73 m^2 = 175 × SCr (exp [-1.154]) × age (exp [-0.203]) × (0.742 if female) × (1.21 if black)

The MDRD study equation is reasonably accurate in non hospitalized pt known to have CKD, regardless of dx.

The MDRD study equation & Cockcroft–Gault equation appear to be somewhat less accurate in obese individuals.

The MDRD study equation & Cockcroft–Gault equation may not be similarly accurate in different age groups.

The MDRD study equation & the Cockcroft–Gault equation are less accurate in populations with normal or near-normal GFR.

Estimation equations may also be less accurate in populations of different ethnicities & from outside of the United States.

ICU Medications and Doses

Cardiac Meds

Norepinephrine	0.02–3 mcg/kg/min	Tachycardia, arrhythmias
Epinephrine	0.01–0.1 mcg/kg/min	Tachyarrhythmias
Vasopressin	0.01–0.04 units/min	Arrhythmias, asystole, ↓ CO, mesenteric ischemia
Phenylephrine	0.3 mcg/kg/min. Maximum 3 mcg/kg/min	↓ CO, hypersensitivity reactions
Dopamine	1–2 mcg/kg/min. Maximum 15 mcg/kg/min	Ectopic beats, tachycardia, angina pain, headache, nausea, vomiting
Dobutamine	1–2 mcg/kg/min. Maximum 10 mcg/kg/min	PVC, tachycardia, hypo/HTN
Milrinone	Bolus 50 mcg/kg 0.1–0.75 mcg/kg/min	PVC, NSVT, hypotension, headache

Pulmonary Vasodilators

Calcium channel blockers		
Diltiazem	Up to 720 mg/d	Edemas, headache, AVN block, dizziness
Nifedipine	Up to 240 mg/d	Flushing, peripheral edema, dizziness, headache, nausea, dyspepsia
Prostacyclins		
Epoprostenol	25–40 ng/kg/min IV	Flushing, jaw pain, & diarrhea
Treprostinil	50–100 ng/kg/min	Flushing, cough
Iloprost	2.5–5 mcg inhaled	
Endothelin antagonists		
Bosentan	Oral: 62.5 mg q12h × 4 wks Maximum 125 mg q12h	Edema, headache, inhibition of spermatogenesis, anemia, ↑ in transaminases
PDE-5 inhibitors		
Sildenafil	IV: 10 mg q8h PO: 20 mg t.i.d	Headache, flushing, diarrhea, myalgia, dyspepsia, erythema
Nitric oxide	20–40 ppm inhaled	Hypotension, withdrawal syndrome, hypoxemia, pulmonary edema
Endothelin antagonist		
Ambrisentan	PO: 5–10 mg/d	Peripheral edema, headache, nasal congestion, cough, dyspepsia
Macitentan	PO: 10 mg/d	Headache, pharyngitis, anemia, bronchitis, UTI
Guanylate cyclase (sGC) stimulator riociguat	PO: 2.5 mg t.i.d	Hypotension, palpitations, peripheral edema, headache, dizziness, dyspepsia
Prostacyclin IP receptor agonist	PO: 160 mcg BID	Headache, flushing, diarrhea, nausea, vomiting, jaw pain, limb pain, myalgia, arthralgia

Drugs Used in Hypertensive Emergencies

Nitroprusside	0.25–3 mcg/kg/min Maximum 10 mcg/kg/min	Onset: few seconds Duration: 2–3 min after infusion stopped	Nausea, vomiting, hypotension, tachycardia, thiocyanate, cyanide toxicity
Nitroglycerin	5–20 mcg/min. Maximum 40–400 mcg/min	Onset: 5–10 min Duration: 5–15 min after infusion stopped	Hypotension, tachycardia, headache
Nicardipine	3–15 mg/h	Onset: 15–30 min Duration: 1–4 hrs	Hypotension, tachycardia, headache, peripheral edema
Labetalol	IV bolus: 20–40 mg (maximum 80 mg) at 10–20 min intervals. Infusion 0.5–2 mg/min	Onset: 5–10 min Duration: 3–6 hrs	Hypotension, bradycardia, heart block, bronchoconstriction
Hydralazine	10–40 mg q4–6h	Onset: 2–4 hrs Duration: 10–30 min	Hypotension, tachycardia, headache. Drug-induced lupus-like syndrome, rash, peripheral neuropathy
Enalaprilat	1.25–5 mg IV q6h	Onset: 15–30 min Duration: 6–12 hrs	Hypotension, hyperkalemia, renal insufficiency, anaphylaxis, angioedema
Clonidine	0.1–0.3 mg PO q8–12h	Onset: 30–60 min Duration: 8–12 hrs	Drowsiness, dizziness, hypotension, bradycardia, dry mouth
Esmolol	Bolus: 500 mcg/kg Infusion: 50–100 mcg/kg/min	Onset: 1–5 min Duration: 15–30 min	Bradycardia, hypotension, bronchospasm
Phentolamine	Bolus: 5–10 mg Infusion: 0.2–5 mg/min	Onset: 1–2 min Duration: 10–20 min	Tachycardia, nausea, headache

Antiarrhythmic Agents

Class	Electrocardiographic Effect	Membrane Effect	Example
IA	↑ QRS & ↑ Q–T interval	Sodium channel block	Quinidine Procainamide Disopyramide
IB	↓ Q–T interval	Sodium channel block	Lidocaine Tocainide Mexiletine
IC	↑↑ QRS interval	Sodium channel block	Flecainide Propafenone Moricizine
II	↓ HR; ↑ P–R interval	β-Adrenergic receptor inhibition	Propranolol & others
III	↑ Q–T interval	Potassium channel block; slow sodium channel facilitator	Procainamide Sotalol Amiodarone Ibutilide
IV	↓ HR; ↑ P–R interval	Calcium channel block	Verapamil Diltiazem
Digitalis	↑ P–R interval; ↓ Q–T interval	Na^+, K^+ ATPase inhibition	Digoxin
Adenosine	↓ HR; ↑ P–R interval	Purinergic receptor agonist	Adenosine

Drug	Dose	Common Toxicities	Rare Toxicities
Quinidine	324–648 mg q8h	Diarrhea, thrombocytopenia, TDP (2–8%)	Hepatitis, bone marrow depression, cinchonism
Procainamide	15–18 mg/kg bolus, then 1–6 mg/min	Hypotension, slowing of conduction, diarrhea, nausea, vomiting	Torsades de pointes, drug-induced lupus syndrome
Disopyramide	100–200 mg 6 hrs 200–400 mg q12h	Precipitation of glaucoma, constipation, dry mouth, urinary retention, TDP	
Lidocaine	1–1.5 mg/kg bolus, then 1–4 mg/min		Confusion, slurred speech, drowsiness, paresthesias, seizures, bradycardia
Flecainide	50–200 mg q12h	Blurred vision, provocation or exacerbation of potentially lethal arrhythmias	Heart block
Propafenone	150–300 mg q8h	Reentrant ventricular tachycardia, exacerbation of heart failure, sinus bradycardia, bronchospasm	
Propranolol	Load: 1–3 mg IV, the 10–80 mg PO q6–8h	Bradycardia, hypotension, CHF, bronchospasm	

Sotalol	80–320 mg q12h	TDP	
Amiodarone	300 mg bolus, then 1 mg/min for 6 hrs, then 0.5 mg/min for ≥18 hrs	Bradycardia, hypotension, nausea	Heart block, pulmonary fibrosis, hypo/hyper thyroidism, corneal microdeposits, blue-gray discoloration of skin, optic neuropathy, Torsades de pointes
Ibutilide	1 mg IV over 10 min, may repeat once 10 min later	TDP in 6%	
Verapamil	5 mg/kg bolus, then 5–15 mg/h	Headache, flushing, edema	
Diltiazem	0.25 mg/kg bolus, then 5–15 mg/h	Bradycardia, hypotension, constipation	Heart block, heart failure
Digoxin	Loading: 5–15 mcg/kg; give 50% of load in initial dose, then 25% at 6–12 hrs intervals × 2	Nausea, vomiting, PVCs, bigeminy, trigeminy, ventricular tachycardia, ventricular fibrillation, PAT, nodal rhythms, accelerated junctional tachycardia & sinus bradycardia, AV conduction block	
Adenosine	6 mg IV, if not effective in 1–2 min can give 12 mg, may repeat 12 mg	Transient asystole, chest fullness & dyspnea	Bronchospasm, atrial fibrillation

Relative Potencies and Equivalent Doses of Representative Corticosteroids

Steroid	Glucocorticoid (Anti-inflammatory)	Mineralocorticoid (Sodium Retention)	Half-life (hrs)	Equivalent Dose
Cortisol	1	1	8–12	20
Cortisone	0.8	0.8	8–12	25
Fludrocortisone	10	125	12–36	NA
Prednisone	4	0.8	12–36	5
Prednisolone	4	0.8	12–36	5
Methylprednisolone	5	0.5	12–36	4
Triamcinolone	5	0	12–36	4
Betamethasone	25	0	36–72	0.75
Dexamethasone	25	0	36–72	0.75

ANTICOAGULANTS

Drug	Dosage	Half-life	Monitoring	Elimination	Use in HIT?	Antidote
Unfractionated heparin	Ppx: 5,000 units SubQ q8h DVT/PE Rx: 60 U/kg, then 12 U/kg/h	1–2 hrs	aPTT 1.5–2.5 × control	Renal	NO	Protamine
Low–molecular-weight heparin Enoxaparin (Lovenox) Tinzaparin (Innohep) Dalteparin (Fragmin)	1 mg/kg SubQ q12h 1.5 mg/kg SubQ q24h 175 U/kg SubQ q24h 120 U/kg SubQ q12h	 4.5–7 hrs 3–5 hrs 2–5 hrs	Xa levels in renal insufficiency, obesity, & old age	Renal	NO	Partial reversal with protamine
Direct thrombin inhibitors 1. Argatroban	0.5–2 mcg/kg/mintitrated to aPTT of 1.5–3 times control. Maximum 10 mcg/kg/min PCI: 350 mcg/kg bolus, 25 mcg/kg/min HIT: 2 mcg/kg/min (adjustments made as clinically indicated, not to exceed 10 mcg/kg/min) *ICU, HF, MOSF, severe anasarca, after cardiac surgery: 0.5–1.2 mcg/kg/min	40–50 min	aPTT q4h until steady state reached (1.5–2 times baseline), ACT	Hepatic	YES	NO
2. Bivalirudin (semisynthetic hirulog)	PCI: 0.75 mg/kg bolus, followed by 1.75 mg/kg/h during & up to 4 hrs postprocedure. HIT (unlabeled use): IV: normal renal function: initial dose: 0.15–0.2 mg/kg/h; adjust to aPTT 1.5–2.5 times baseline value	25 min	aPTT every 4 hrs until steady state reached (1.5–2 times baseline), ACT	80% enzymatic, 20% renal	YES	NO

3. Lepirudin DTI	HIT: omit bolus or ↓ 0.2 mg/kg in life- or limb-threatening thrombosis, followed by 0.10 mg/kg/h *ICU: no bolus, 0.005–0.10 mg/kg/h Hemofiltration: 0.005–0.01 mg/kg/h, no bolus Dialysis: 0.1 mg/kg bolus predialysis PCI: not indicated	80 min	aPTT every 4 hrs until steady state reached (1.5–2 times baseline)	Renal	YES	NO
Desirudin	15 mg SC q12h (for thromboprophylaxis before hip replacement)	60 (IV) 120–180 (SC)	aPTT	Renal	YES	NO
Fondaparinux (Arixtra) Indirect factor Xa inhibitor	DVT ppx: >50 kg: 2.5 mg per day SubQ Acute DVT/PE treatment: SubQ <50 kg: 5 mg per day 50–100 kg: 7.5 mg per day >100 kg: 10 mg per day	17–21 hrs	Anti-Xa activity of fondaparinux can be measured by the assay if fondaparinux is used as the calibrator	77% excreted unchanged in urine. T1/2: 17–21 hrs	YES Unlabeled use	NO
Danaparoid Factor Xa inhibitor (Organon)	HIT: bolus-IV 2,000 antifactor Xa units Then, 2,000 units subQ q12h	25 ± 100 hrs	Antifactor Xa assay	Renal	YES	NO
Coumadin	2–5 mg PO per day	40 hrs (20–60 hrs)	INR	Hepatic metabolism, renal excretion	NO	Vitamin-K, FFP, Four factor concentrate (Vitamin K dependant factors- 2,7,9 & 10) and Three factor concentrate (2,9 & 10) ± rFVIIa
Edoxaban	30–60 mg once daily	9–11 hrs	None	Renal 35%		NO

New Anticoagulants

Drug	Target	Route	Dose (VTE Prevention)	Half-life	Monitoring Required	Excretion	Antidote
Rivaroxaban	Direct factor Xa inhibitor	PO	10–40 mg per day	7–11 hrs	none	Renal 66% Hepatic 33%	None
Apixaban	Direct factor Xa inhibitor	PO	2.5 mg PO q12h	8–14 hrs	FXa inhibition assay or modified PT	Renal 25%	None
Otamixaban	Direct factor Xa inhibitor	IV		30 min	none	Biliary 75%	None
Dabigatran (DTI)	Factor IIa	PO	220 mg per day	14–17 hrs		Renal >80%	None

Pharmacologic Coumadin Reversal

Drug	Dose	Side Effects
Vitamin K (phytonadione)	1–10 mg q24h: subQ/PO/IV	IV form-anaphylaxis, HTN
Activated factor 7	15–90 mcg/kg	Thrombosis, HTN
Factor IX complex	INR 2–3.9: 25 U/kg INR 4–5.9: 35 U/kg INR >6: 6 U/kg	Thrombosis, DIC
Unactivated PCC products 4 factor-Kcentra Contains factors 2, 7, 9, & 10 in inactive forms 3 factor Bebulin VH Profilnine SD Contain factors 2, 9, & 10.		
Activated PCC FEIBA NF	Contains factors 2, 7, 9, & 10. Factor 7 is mostly activated.	

Insulin Preparations

Type	Action (hrs) Onset	Peak	Duration
Rapid			
Regular crystalline	0.5–0.7	1.5–4	5–8
Lispro	0.25	0.5–1.5	2–5
Aspart	0.25	0.6–0.8	3–5
Glulisine	–	0.5–1.5	1–2.5
Intermediate			
NPH	1–2	6–12	18–24
Lente	1–2	6–12	18–24
Slow			
Ultralente	4–6	16–18	20–36
Protamine zinc	4–6	14–20	24–36
Glargine	2–5	5–24	18–24

Diuretics

Drug	Mechanism and Site of Action	Dose	Duration of Action	Common Adverse Effects
Acetazolamide	Inhibitor of carbonic anhydrase—↑ excretion of bicarbonate Site: PCT	125–500 mg IV/maximum of 2 g PO	IV 4–5 hrs PO 8–12 hrs	Hypokalemia Aplastic anemia Hyperglycemia Thrombocytopenia Hypersensitivity in sulfa allergy pt
Mannitol	Osmotic diuretic Site: PCT	0.25–1 g/kg	1.5–6 hrs	CHF, hyper/hypotension, fluid & electrolyte imbalance
Furosemide	Inhibitors of Na-K-2Cl symport Site: thick AL of LOH	10–40 mg IV	6 hrs	Electrolyte imbalance Dehydration Deafness Hyperglycemia Hyperuricemia Hypersensitive reaction in sulfa allergy pt
Bumetanide	Inhibitors of Na-K-2Cl symport Site: thick AL of LOH	0.5–1 mg IV. Maximum 10 mg/d	2–4 hrs	Electrolyte imbalance Dehydration Deafness Hypersensitivity in sulfa allergy
Ethacrynic acid	Inhibitors of Na-K-2Cl symport Site: thick AL of LOH	IV: 25–100 mg over 5–10 min. Maximum 400 mg/d Oral: 50–200 mg/24 hrs	IV: 2 hrs Oral: 12 hrs	Can be used in pt with sulfa allergy
Torsemide	Inhibitors of Na-K-2Cl symport Site: thick AL of LOH	PO/IV: 20 mg per day, maximum 200 mg/d Infusion: 5–20 mg/h	PO 6–8 hrs	ECG abnormality, chest pain, nervousness
Chlorothiazide (DIURIL)	Inhibitor of Na-Cl symport Site: DCT	250–500 mg IV, maximum 2 g over 24 hrs	Oral: 6–12 hrs IV: 2 hrs	Enhances activity of loop diuretics in renal failure
Chlorothiazide	Inhibitor of Na-Cl symport Site: DCT	50–100 mg PO per day. Maximum 200 mg/d	Oral: 2–6 hrs	Cardiac dysrhythmia Cholestatic jaundice syndrome, pancreatitis pulmonary edema Toxic epidermal necrolysis

SEDATIVES (also see Chapter 8)

Drug	Route	Bolus	Infusion	Adverse Effects
Benzodiazepines				CNS depression, respiratory depression, paradoxical excitation
Midazolam	IV	1 mg repeated to effect	0.04–0.2 mg/kg/h	
Diazepam	IV	2–5 mg IV push q1–4h	NA	
Lorazepam	IV, IM	1–4 mg q4–6h	0.01–0.05 mg/kg/h	
Propofol	IV	0.3–0.7 mg IV push	10–100 g/kg/min	Hypotension, bradycardia, hypertriglyceridemia
Dexmedetomidine	IV	10 mcg/kg	0.2–0.7 g/kg/h	Hypotension/HTN, bradycardia
Ketamine	IV	1–2 mg/kg IV push	0.5–4.5 g/kg/h	Hallucinations, tachycardia
Barbiturates				Hypotension, tachycardia, respiratory depression
Pentobarbital	IV	3–5 mg/kg	1–3 mg/kg/h	
Thiopental	IV	3–5 mg/kg	2–5 mg/kg/h	
Butyrophenones				
Haldol	IV, IM	0.5–5 mg, repeat doses every 30–45 min. Maximum 80 mg PO/IV q6h		CNS depression, orthostatic hypotension, QTc prolongation, extrapyramidal side effects, neuroleptic malignant syndrome

IM, intramuscular; IV, intravascular; NA, not applicable.

Dosage and Mode of Administration of Common Nonopioid Analgesics

Drug	Route	Dose (mg)	Frequency
Ibuprofen	PO	200–400	q4–6h
Ketorolac	IV or IM	30–60 initially	Repeat 15–30 q4–6h
Indomethacin (Indocin)	PO, PR	25 (PO), 50 (PR)	q6–8h
Naproxen (Naprosyn)	PO	250–500	q12h
Acetaminophen	PO, PR	500–1,000	q4–6h
Aspirin	PO, PR	300–1,000	q4–6h

Standard Equivalents of Selected Opioid Analgesics

Drug	Oral Dose (mg)	Parenteral Dose (mg)
Alphaprodine HCl (Nisentil)	–	45
Codeine	200	130
Fentanyl (Sublimaze)	–	0.1
Hydromorphone HCl (Dilaudid)	7.5	1.5
Meperidine HCl (Demerol)	200	50
Methadone HCl (Dolophine HCl)	10	8.8
Morphine sulfate	60	10
Oxycodone HCl (Roxicodone)	30	15
Oxymorphone HCl (Numorphan)	–	1.5
Pentazocine (Talwin)	–	60

Acceptable drugs, IV drugs, & lockout intervals for use with postoperative pt-controlled analgesia pump.

Drug	Dose (mg)	Lockout Interval (min)
Morphine sulfate	0.2–3	5–20
Meperidine HCl (Demerol)	2–30	5–15
Fentanyl (Sublimaze)	0.02–0.1	3–10
Hydromorphone HCl (Dilaudid)	0.02–0.5	5–15

MISCELLANEOUS

	Indications	Dosage	Excretion	Side Effects
Acetylcysteine	Acetaminophen overdose Ppx for contrast-induced nephropathy	In acetaminophen overdose Oral: 140 mg/kg × 1 dose, 70 mg/kg every 4 hrs × 17 doses IV: 150 mg/kg × 1 dose, 50 mg/kg × 2 dose over 4 hrs, 100 mg/kg × 1 dose over 16 hrs	Excreted by kidneys	IV: anaphylactoid reactions, flushing, tachycardia, urticaria, nausea, vomiting
Adenosine	PSVT, WPW syndrome	6–12 mg IV bolus	Cleared by RBCs & endothelial cells	Transient new arrhythmia, facial flushing, headache, dizziness, chest pressure, dyspnea

Alprostadil (PGE1)	PHTN, maintain patent ductus arteriosus	0.05–0.1 mcg/kg/min	Pulmonary metabolism/renal excretion	IV: flushing, fever, apnea
Alteplase (recombinant tPA)	Fibrinolytic agent—lyse fibrin in thrombus in coronary artery, PA, cerebral artery; used for CVC clearance	Wt >67 kg 15 mg bolus & then 15 mg over 30 min. Institute heparin therapy & then infuse 35 mg of TPA over 1 hr. Total dose of tPA—100 mg Wt <67 kg—5 mg bolus, then 0.75 mg/kg over 30 min, heparin bolus & then 0.5 mg/kg tPA over 1 hr	Hepatic clearance	Hemorrhage, fever
Aminocaproic acid	Antifibrinolytic agent	Load: 5 g over 1 hr. Maintenance 6–24 g/24 hrs. Maximum 24 hrs dose: 30 g	Renal	Arrhythmias, bradycardia, edema, thrombosis, confusion, rash, agranulocytosis
Tranexamic acid	Antifibrinolytic agent	In trauma—associated hemorrhage: IV: load 1,000 mg over 10 min, followed by 1,000 mg over next 8 hrs	Renal	Hypotension, diarrhea, nausea, vomiting, blurred vision
Naloxone	IV 0.4–2 mg, may repeat every 2–3 min. Consider repeating the dose q20–60 min depending on type/duration of opioid/starting an infusion. For infusion, use 2/3 of the initial effective naloxone bolus	30–120 min	Hepatic	Tachycardia, HTN, pain, agitation (secondary to reversal of opioid & sedative effect), pulmonary edema
Flumazenil	Reversal of benzodiazepine effect	0.01 mg/kg up to 0.2 mg, repeat up to 1 mg	Hepatic	Agitation, seizures

STATISTICS AND EVIDENCE-BASED MEDICINE (EBM)

SUJATHA PENTAKOTA, MD

Evaluation of Published Research

Apply the following questions to the manuscript:

Are the results valid?

Was the assignment of pt to treatments randomized?

Were all pt who entered the trial properly accounted for & attributed at its conclusion?

Was f/u complete?

Were the pt analyzed in the groups to which they were randomized?

Were the pt, health workers, & study personnel blind to treatment?

Were the groups similar at the start of the trial?

Aside from the experimental intervention, were the groups treated equally?

What are the results?

How large was the treatment effect?

How precise was the estimate of the treatment effect?

Will the results help me in caring for my pt?

Can the results be applied to my pt care?

EBM Internet Sources

Cochrane database of systematic reviews: www.cochrane.org
Additional resources: www.cebm.net; www.openclinical.org; ktclearinghouse.ca/CEBM
Medline: www.pubmed.org

Definitions

Odds & odds ratios: odds are the probability of an event occurring divided by the probability of the event not occurring.

An odds ratio is the odds of the event in one group, for example, those exposed to a drug, divided by the odds in another group not exposed.

Relative risk: the relative risk is the ratio of the probabilities of 2 events; if *p* is the probability of the 1st event, & *q* is the probability of the 2nd, then the relative risk is *p/q*.

A Basic Guide for Systematically Evaluating and Applying Evidence-Based Medicine

<table>
<tr><th>Study</th><th>Is the Evidence Valid</th><th>What are the Results</th><th>Will the Results Help Me in My Patient Care</th></tr>
<tr><td>Diagnostic</td><td>Was there an independent, blind comparison with a reference (gold) standard of dx?
Was the diagnostic test evaluated in an appropriate spectrum of pt, similar to the practice population?
Was the reference standard applied regardless of the diagnostic test result?</td><td>A diagnostic test is validated by its degree of sensitivity, specificity, positive and negative predictive values.
For example, consider a 2 × 2 table of the diagnostic test and the result:
<table><tr><th>Diagnostic Test Result</th><th>Target Disorder Present</th><th>Absent</th><th>Totals</th></tr><tr><td>Positive</td><td>a</td><td>b</td><td>a + b</td></tr><tr><td>Negative</td><td>c
d</td><td></td><td>c + d</td></tr><tr><td>Totals</td><td>a + c
b + d</td><td></td><td>a + b + c + d</td></tr></table>
Sensitivity = a/a + c
Specificity = d/b + d
Likelihood ratio (LR) of a positive test = sens/1 – spec
Likelihood ratio of a negative test = 1 – sens/spec
Positive predictive value = a/a + b
Negative predictive value = d/c + d
Prevalence of a dz = a + c/a + b + c + d
Pre-test odds ratio = prevalence/1-prevalence
Post-test odds = pretest odds × LR</td><td>a. Is the test available, affordable, accurate, and precise in your setting?
b. Estimate your patient's pretest probability?
c. Will the posttest probability affect your management plan & benefit the pt?</td></tr>
<tr><td>Prognosis</td><td>Was a defined, representative sample of pt assembled at a common point in their dz course?
Was pt f/u sufficiently long & complete?
Were objective outcome criteria applied in a "blind" fashion?
In subgroups with different prognoses, was there an adjustment made for important prognostic factors & was there validation in an independent group of "test set" pt?</td><td>Represented as survival curve that depicts, at each point in time, the proportion of the original study population who has not yet had an outcome event.
How likely are the outcomes over time?
How large & precise are the estimates of the likelihood of outcome in the period of time (95% CI)?</td><td>Are the study pt similar to your pt group?
Will the results significantly impact your conclusions as to what to offer or tell your pt?</td></tr>
<tr><td>Treatment & RCT</td><td>Was the assignment of pt to treatment randomized?
Was the randomization concealed?
Were all the pt who entered the trail accounted for at conclusion?
Were the pt analyzed the groups to which they were randomized?
Were the pt & clinicians blinded to treatment?
Were the groups treated equally except for the experimental treatment?
Were the groups similar at the start of the trial?</td><td>Relative risk reduction (RRR)
RRR = control event rate – experimental event rate/control event rate
Absolute risk reduction (ARR): control event rate – experimental event rate.
Number of pt needed to treat to prevent one bad outcome (NNT): 1/ARR.</td><td>Were all the clinically important strategies & outcomes included?
Are the probabilities credible?
Was the robustness of the conclusion tested?</td></tr>
<tr><td>Systematic review</td><td>Is it an overview of randomized trials of treatment you are interested in?
Does it include a methods section that describes: finding & including all relevant trials?
Assessing their individual validity?
Were the results consistent from study to study?</td><td>How large & precise are the results?
This may be concurred from the 95% confidence interval.</td><td>Are the study pt similar to my pt population?
Were all clinically important outcomes considered?
Cost-benefit analysis—does benefit outweigh harm & costs?</td></tr>
<tr><td>Economic analysis</td><td>Is this report asking an economic question comparing well-defined alternative courses of action with a specified point of view from which the costs & effects are being viewed?
Does it cite good evidence of the efficacy of the alternatives?
Does it identify all the costs & effects you think should & did it select credible measures for them?</td><td>Two-step process:
1. Are the resulting costs or costs/unit of health gained impressive?
2. Could the uncertainty in the evidence change the results?
Check if the study includes a cost-effectiveness analysis/cost-benefit analysis/cost-utility analysis.</td><td>Could my pt expect similar health outcomes & costs?
Are the benefits worth the harm & costs?</td></tr>
<tr><td>Clinical decision analysis</td><td>Were all the clinically important strategies & outcomes included?
Are the probabilities credible?
Was the robustness of the conclusion tested?</td><td>Does one strategy result in a clinically important difference?
How strong is the evidence used in analysis?
How much does allowance for uncertainty change the results?</td><td>Do the probability estimates approximate my patients' clinical features? If not can you adjust them properly?
Do the utilities reflect my patients' values? Can they state their utilities in a stable & usable form?</td></tr>
<tr><td>Harm</td><td>Were there clearly defined groups of pt similar in all important ways other than exposure to the treatment?
Were treatment exposures & clinical outcomes measured in the same way in both the groups?
Was the f/u of study pt complete and long enough?
Do the results satisfy some "diagnostic tests for causation"?</td><td>Finding out if a treatment causes harm: calculate the strength of an association between a treatment & subsequent adverse outcomes.
In RCT/cohort study: Relative risk = (a/[a+b])/(c/[c+d])
Case-control study: Relative odds = RO = ad/bc
<table><tr><th>Exposure</th><th>Adverse Outcome Present</th><th>Absent</th><th>Totals</th></tr><tr><td>Yes</td><td>a</td><td>b</td><td>a + b</td></tr><tr><td>No</td><td>c</td><td>d</td><td>c + d</td></tr><tr><td>Totals</td><td>a + c</td><td>b + d</td><td>a + b + c + d</td></tr></table></td><td>Can the study results be extrapolated to this patient?
What are the patient's risks of the adverse outcome?
What are the patient's preferences, concerns, and expectations from this treatment?
What alternative treatments are avail.?</td></tr>
<tr><td>Clinical practice guideline</td><td>Were all important decision options & outcomes specified?
Was the evidence relevant to each decision option identified, validated, & combined in a sensible & explicit way?
Are the relative preferences the key stakeholders attach to the outcomes of decisions identified & explicitly considered?
Is the guideline resistant to clinically sensible variations in practice?</td><td>Does the guideline offer an opportunity for significantly improving the quality of current health care practice?
Is there a large variation in current clinical practice?
Does the guideline contain new evidence that could positively impact clinical practice?
Would the guideline significantly improve pt outcome?</td><td>Is the primary objective of the guidelines consistent with my goals?
Are the recommendations applicable to my pt?
What barriers exist to its implementation? Can they be overcome?</td></tr>
</table>

Adapted from Sackett DL, Richardson WS, Rosenberg W, et al. *Evidence-based Medicine: How to Practice and Teach EBM*. Edinburgh: Churchill Livingstone; 1998.

INDEX

Note: Page number followed by A, f, and t indicates appendix, figure, and table respectively.

A

B

C

D

E

F

G

H

J

K

L

M

N

O

P

Q

R

S

T

U

v

W

X

Z