VCMC ICU POCKET BOOK

“THE GREEN BOOK”

VERSION 2.0

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The contents of this pocket book are to be used as a guide. Healthcare professionals should use sound clinical judgment and individualize patient care. This pocket book is not meant to be a replacement for training, experience, continuing medical education or studying the latest literature and drug information.
# VCMC ICU Pocket Book Table of Contents

## General
- General Comments and Expectations ........................................ 4
- The Role of the Third Year .................................................. 10

## ICU Presentations
- ICU Note Format ............................................................... 12
- Cerner ICU Orientation ....................................................... 13

## Cardiovascular
- BLS Algorithms ..................................................................... 15
- ACLS Algorithms ................................................................. 17
- Bradycardia Algorithm ......................................................... 17
- Narrow Complex Tachycardia Algorithm .................. 18
- Wide Complex Tachycardia with Pulse-......................... 19
- Pulseless Arrest Algorithm .................................................... 20
- Post-Cardiac Arrest Care ....................................................... 21
- Hemodynamic Monitoring ..................................................... 22
- Acute Coronary Syndrome .....................................................
  - STEMI ........................................................................... 27
  - NSTEMI/Unstable Angina ............................................... 28
  - Thrombolysis for MI ...................................................... 29

## Heart Failure
-................................................................. 31

## Caridiogenic Shock
- Pressors .............................................................................. 35
- Hypertensive Crisis ............................................................... 36
- Acute Pulmonary Embolism ...................................................
- Cardiac Tamponade .............................................................. 40
- Aortic Dissection ................................................................. 42
- Inpatient Management of Hypertension .................... 43

## Pulmonary
- Airway Emergencies ............................................................. 45
- Rapid Sequence Intubation .................................................... 46
- The Difficult Airway ............................................................... 48
- Ventilator Management .......................................................... 52
- Ventilator Weaning ............................................................... 61
- Post Extubation Laryngeal Edema ......................................... 62
- Non-invasive ventilation ......................................................... 63
- ARDS .............................................................................. 64
- Ventilator Associated Pneumonia/................................. 65
- Hospital-acquired Pneumonia/ ........................................... 66
- Healthcare-Associated Pneumonia ..................................... 68
- Community-Acquired Pneumonia ........................................ 69
- Acute Asthma/Status Asthmaticus ....................................... 71
- COPD Exacerbations ............................................................. 72
- Tracheostomy ..................................................................... 73

## Gastroenterology
- Cirrhosis ............................................................................. 76
- Gastrointestinal Bleeding .................................................... 80
- Mesenteric Ischemia ............................................................. 82
- Ischemic Colitis .................................................................... 83
- Bowel-obstruction/Pseudo-obstruction ............................. 84
- Pancreatitis ......................................................................... 85
- Stress Ulcer Prophylaxis ...................................................... 86

## Renal
- Acute Renal Failure ............................................................. 87
- Assessment of Intravascular Volume ............................... 89
- Crystalloid/Colloid Fluid Chart .......................................... 92

## F/E/N
- Nutritional support in the ICU .............................................. 93
- Acid Base Interpretation ....................................................... 96
- Sodium Interpretation .......................................................... 103
- Hyperkalemia ..................................................................... 106
- Hyper-/Hypo-calcemia ......................................................... 106

## Hematology/Oncology
- Transfusion Medicine .......................................................... 107
- Bleeding ............................................................................. 111
- Hemorrhagic Shock ............................................................. 113
- Bleeding with Warfarin Therapy ......................................... 114
- Bleeding with Heparin Therapy ......................................... 117
- Bleeding with Novel Anticoagulants ............................... 118
- Bleeding in Liver and Kidney Disease ......................... 119
- Coagulopathy of Trauma ...................................................... 120
- Massive Transfusion Protocol ............................................ 122
- Thrombocytopenia ............................................................... 125
- DIC ................................................................................. 126
- TTP ................................................................................. 127
- HIT ............................................................................... 128
- DVT Prophylaxis ................................................................. 131
- Oncologic Emergencies ....................................................... 132

## Sepsis
- Definitions/Pathophysiology ............................................... 134
- Workup and Evidence .......................................................... 136
- Management Recommendations ...................................... 137
- Code Sepsis Policy ............................................................... 141
- Abdominal Compartment Syndrome ......................... 143
- Apache II Score ................................................................. 144

Topics in Normal Print are considered core curriculum. Topics in Italics are considered supplemental.
<table>
<thead>
<tr>
<th>Topic</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infectious Disease</td>
<td></td>
</tr>
<tr>
<td>Workup of Fever in the ICU</td>
<td>145</td>
</tr>
<tr>
<td>Antibiotic Use in the ICU</td>
<td>149</td>
</tr>
<tr>
<td>Procalcitonin</td>
<td>151</td>
</tr>
<tr>
<td>Vancocmycin Antiogram</td>
<td>154</td>
</tr>
<tr>
<td>Catheter-Related Blood</td>
<td>156</td>
</tr>
<tr>
<td>Workup of Fever in the ICU</td>
<td>158</td>
</tr>
<tr>
<td>Invasive Candidal Infections</td>
<td>160</td>
</tr>
<tr>
<td>HIV Infected Patients in the ICU</td>
<td>162</td>
</tr>
<tr>
<td>Anaphylaxis</td>
<td>163</td>
</tr>
<tr>
<td>Necrotizing Soft Tissue Infection</td>
<td>164</td>
</tr>
<tr>
<td>Clostridium difficile</td>
<td>165</td>
</tr>
<tr>
<td>Multi-Drug Resistant Pathogens</td>
<td>167</td>
</tr>
<tr>
<td>Endocrine</td>
<td></td>
</tr>
<tr>
<td>DKA</td>
<td>169</td>
</tr>
<tr>
<td>Intensive Insulin Therapy in the ICU</td>
<td>170</td>
</tr>
<tr>
<td>Insulin Infusions</td>
<td>171</td>
</tr>
<tr>
<td>Glucommander Down Time Protocol</td>
<td>173</td>
</tr>
<tr>
<td>Relative Adrenal Insufficiency</td>
<td>174</td>
</tr>
<tr>
<td>Endocrine Emergencies in the ICU</td>
<td>175</td>
</tr>
<tr>
<td>Neurology</td>
<td></td>
</tr>
<tr>
<td>Delirium in the ICU</td>
<td>176</td>
</tr>
<tr>
<td>Agitation in the ICU</td>
<td>178</td>
</tr>
<tr>
<td>Altered Mental Status</td>
<td>179</td>
</tr>
<tr>
<td>Coma</td>
<td>180</td>
</tr>
<tr>
<td>Weakness in the ICU</td>
<td>182</td>
</tr>
<tr>
<td>Myasthenia gravis</td>
<td>182</td>
</tr>
<tr>
<td>Guillain-Barré Syndrome</td>
<td>183</td>
</tr>
<tr>
<td>Critical Illness Polyneuropathy</td>
<td>184</td>
</tr>
<tr>
<td>Wound Botulism</td>
<td>184</td>
</tr>
<tr>
<td>Analgesia and Sedation in the ICU</td>
<td>185</td>
</tr>
<tr>
<td>Procedural Sedation</td>
<td>188</td>
</tr>
<tr>
<td>Neuromuscular Blockade</td>
<td>189</td>
</tr>
<tr>
<td>Alcohol Withdrawal Delirium</td>
<td>190</td>
</tr>
<tr>
<td>Status Epilepticus</td>
<td>192</td>
</tr>
<tr>
<td>Neuroleptic Malignant Syndrome</td>
<td>194</td>
</tr>
<tr>
<td>Serotonin Syndrome</td>
<td>194</td>
</tr>
<tr>
<td>Ischemic Stroke</td>
<td>195</td>
</tr>
<tr>
<td>Thrombolysis for Ischemic Stroke</td>
<td>199</td>
</tr>
<tr>
<td>Intracranial Hemorrhage (ICH)</td>
<td>201</td>
</tr>
<tr>
<td>Subarachnoid Hemorrhage (SAH)</td>
<td>202</td>
</tr>
<tr>
<td>Management of ICH/SAH</td>
<td>203</td>
</tr>
<tr>
<td>Induced Hypothermia Protocol</td>
<td>204</td>
</tr>
<tr>
<td>Determination of Brain Death</td>
<td>207</td>
</tr>
<tr>
<td>Trauma in the ICU</td>
<td></td>
</tr>
<tr>
<td>Trauma Severity Scoring</td>
<td>208</td>
</tr>
<tr>
<td>Traumatic Brain Injury and Management of Elevated Intracranial Pressure</td>
<td>209</td>
</tr>
<tr>
<td>Spinal Cord Injuries</td>
<td>212</td>
</tr>
<tr>
<td>Obstetrics in the ICU</td>
<td>217</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td></td>
</tr>
<tr>
<td>End of Life Discussions in the ICU</td>
<td>219</td>
</tr>
<tr>
<td>End of Life Care in the ICU</td>
<td>220</td>
</tr>
<tr>
<td>Organ Donation</td>
<td>221</td>
</tr>
<tr>
<td>Pronouncing Death</td>
<td>223</td>
</tr>
<tr>
<td>Poisonings and Toxicdromes</td>
<td>224</td>
</tr>
<tr>
<td>Hypothermia/Near drowning</td>
<td>226</td>
</tr>
<tr>
<td>Hyperthermia/Malignant Hyperthermia</td>
<td>227</td>
</tr>
<tr>
<td>Envenomations</td>
<td>228</td>
</tr>
<tr>
<td>Pressure Ulcers</td>
<td>229</td>
</tr>
<tr>
<td>Prophylaxis</td>
<td></td>
</tr>
<tr>
<td>Summary</td>
<td>230</td>
</tr>
<tr>
<td>DVT Prophylaxis</td>
<td>131</td>
</tr>
<tr>
<td>GI Prophylaxis</td>
<td>86</td>
</tr>
<tr>
<td>Ventilator-Associated Pneumonia</td>
<td></td>
</tr>
<tr>
<td>Prophylaxis</td>
<td>65</td>
</tr>
<tr>
<td>Pressure Ulcer Prophylaxis</td>
<td>229</td>
</tr>
<tr>
<td>Prevention of Catheter-related Blood Infections</td>
<td>158</td>
</tr>
<tr>
<td>Central Line Tips</td>
<td>231</td>
</tr>
<tr>
<td>Phone Numbers, Contacts, etc.</td>
<td>232</td>
</tr>
<tr>
<td>Procedures (on Video in the VCMC Library):</td>
<td></td>
</tr>
<tr>
<td>Central Venous Catheter insertion</td>
<td></td>
</tr>
<tr>
<td>Arterial Line Placement</td>
<td></td>
</tr>
<tr>
<td>Tube Thoracostomy</td>
<td></td>
</tr>
<tr>
<td>Endotracheal intubation</td>
<td></td>
</tr>
<tr>
<td>Lumbar Puncture</td>
<td></td>
</tr>
<tr>
<td>Thoracentesis</td>
<td></td>
</tr>
<tr>
<td>Paracentesis</td>
<td></td>
</tr>
<tr>
<td>Pulmonary Artery Catheter Insertion</td>
<td></td>
</tr>
</tbody>
</table>

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**GENERAL COMMENTS ABOUT THE ICU ROTATION**

The ICU Rotation can be a particularly challenging experience given the acuity of illness and intensity of the life-and-death issues that may happen. It is the time to learn to care for the most intensely sick patients and to learn the pathophysiology of disease at the sick end of the spectrum. It is a tiring month but one from which you can get an enormous amount of experience and learning. If you learn how to care for sick people during residency, it will help your care of your less-sick patients immensely. If you don’t learn how to take care of sick patients in residency, you likely never will. Be involved and read as much as you can.

Discuss all potential admissions with the ICU Attending. If you would like the Attending to be there, specifically ask for them to come in.

**What Patients Go to the ICU? (by no means an exhaustive list):**

- Acute Coronary Syndrome
- Unstable Arrhythmias
- Hypertensive Emergency
- Acute Aortic Dissection
- Persistent hypotension after 30 ml/kg fluid bolus
- Elevated lactic acid level (>4) or rising/stable lactate despite appropriate resuscitation
- Need for Pressors, Nitroprusside, or Nitroglycerine drips
- Pancreatitis with 4 or more risk factors
- Active GI Bleeding with the potential for decompensation
- Altered Mental Status / concern for airway protection / GCS 8 or less
- DKA with a pH<7.25 or anion gap > 20
- Sodium level <115
- Thyroid Storm
- Intoxications/Poisonings with sequelae
- Severe Alcohol Withdrawal / Agitation
- Status Epilepticus
- Severe hypoxia, hypercarbia, or respiratory distress
- Most head trauma; most multi-trauma; most intracranial hemorrhages
- Anyone who “looks sick”

**Transfers to the ICU/ to VCMC in general from other institutions:**
The ICU Attending should be aware of all potential transfers, and is responsible for accepting / not accepting patients. If the patient being transferred is in need of subspecialty care (e.g. orthopedics, surgery, ENT, GI, Neurosurgery, Oncology, etc.), it is imperative that the subspecialist in question is aware of the patient prior to transfer and that they also agree to accept the patient.

**Definitive Observation Unit (“DOU”) Capabilities:**
- Insulin drips, though blood sugars are checked every 2 hours (vs. q 1 hour in the ICU).
- Ativan for alcohol withdrawal (limit = 32mg in 24 hours) (16mg in 24 hours on the floor)
- Continuous O₂ Sat monitoring (only four continuous Sat monitors exist on 3 North, so ask your charge nurse if one would be available for your patient). Stable nitroglycerine drips when the nitro is not being titrated. Diltiazem drips. Nitroprusside, nicardipine, dexametomidine, and vasopressor drips are for the ICU only.
Code Blue:
A “Code Blue” is called for patients in cardiopulmonary arrest. The ICU Resident is responsible for both the airway and for running the code.

Code Yellow – Tier 1:
A “Code Yellow Tier 1” is called for patients with traumatic injuries in which there is a high probability for immediate surgical intervention. For Code Yellow Tier 1’s, the ICU Resident is responsible for the patient’s airway. Tier 1 criteria are met in the following instances:
- Hemodynamic instability (SBP < 90 mm Hg, pulse > 120 in adults; age-specific hypotension/tachycardia)
- Respiratory distress, intubated pre-hospital, unstable airway
- Glasgow Coma Scale (GCS) ≤ 8 or is unresponsive with a traumatic mechanism
- Penetrating wounds of the head, neck, or torso (chest, abdomen, back or buttocks)
- Major traumatic amputation
- Burns with associated trauma or respiratory distress
- Paralysis
- Transferred acute trauma patients who fulfill the above criteria or have “unstable” vital signs or require blood products to maintain “normal” vital signs

The hospital staff is to allow the paramedic to present their information prior to starting questioning of all awake, non-intubated patients. Often the Medicine resident or the surgery resident on-call will be running the code. The ICU Resident is not responsible for attendance at Tier 2 Traumas, though their help is often greatly appreciated during MCI (Mass Casualty Incident) activations.

Code Maternity
A “Code Maternity” will be called on patients with post-partum hemorrhage of at least 500 ml blood AND either evidence of hemodynamic instability OR ineffective response to pitocin, methergine and hemabate and/or misoprostol. The ICU resident is required to respond immediately to the bedside of a patient for whom a code maternity has been called (with the same urgency as a Tier 1 trauma), along with the anesthesiologist on call, obstetrician on call, nursing supervisor and lab tech.

Rapid Response:
A “Rapid Response” is called by health care staff when specific concerning criteria are met or staff is “worried” about a patient and is unable to reach the primary medical team. The ICU Resident is expected to respond immediately to all Rapid Response calls in the hospital and at the Hillmont psychiatric facility. The ICU resident is responsible for “running” the Rapid Response. Also responding to Rapid Response calls are a Respiratory Therapist, an ICU Nurse, the ICU Attending (daytime), a Laboratory Technician, and the charge nurse.

Criteria for activation of the Rapid Response include bradycardia (HR<50) or tachycardia (HR>130), BP<90/55, altered mental status, hypopnea (RR<10) or tachypnea (RR>28), FiO2>50% or O2 Sat<90%, acute significant bleed, seizure, or ‘failure to respond to treatment’. Goal of the Rapid Response team is to identify “pre-arrest states” and reduce non-ICU/ER arrests, and to facilitate transfer to higher acuity area if needed. The Rapid Response team
should not take over care – the primary team is still responsible for patient care if they are present.

**Code Sepsis:**
A “Code Sepsis” will be called on patients with a positive sepsis screen (3 vital sign abnormalities + evidence of new infection) who have a lactate>4 or SBP<90 BEFORE a fluid bolus (understanding that some patients will not be in shock). The hope is that shock can be avoided (and not just treated) by responding promptly to at-risk patients.

The ICU resident is required to respond urgently to the bedside of a patient for whom a code sepsis has been called outside of the Emergency Department (ED physician responsible for management in the Emergency Department), along with the ICU attending (daytime hours), trauma support nurse, respiratory therapist (rapid response therapist), phlebotomist (to be dispatched by lab clerk) and radiology technician. A sign-in sheet will be started to measure response times.

The abbreviated VCMC Code Sepsis Policy is on page 141.

**Pediatric Patients in the ICU:**
Occasionally, patients under the age of 21 with chronic conditions that make them eligible for California Childrens Services (CCS) end up in the ICU due to Pediatric ICU (PICU) staffing or other issues. Upon stepdown from the ICU, a CCS paneled provider (one of the pediatricians) will generally need to be involved with caring for these patients. Please let Pediatric Attendings know when any patient under the age of 21 with a chronic medical condition (i.e. diabetes, cerebral palsy, etc.) needs to be admitted to the ICU and is not going to the PICU.

**Emergency Department Admissions:**
ICU patients should be moved out of the ER and up to the ICU expeditiously. Examine the patient quickly and review the labs and ER management to determine whether the patient truly is an ICU candidate. If the patient is unstable, call your attending early for help.

It is often difficult for the ER nurses to perform ICU-level care while continuing to manage their other patients and keep the flow of patients moving in the ER. To help them, move the patients to the ICU expeditiously. If there are key orders (e.g. antibiotics in sepsis, insulin drips, etc.) that need to be done in the ER, speak to the ER nurse directly AND order and initiate them as one-time orders outside of your signed (but not initiated) admission orders (akin to writing orders in on the old paper ER charts on the bottom right corner).

**Circumstances Requiring ICU Attending Notification (day or night):**

| **Any time there is concern about a patient** | **Change in ventilator mode** |
| **Any unstable patient** | **Persistent cuff leak** |
| **Any potential procedures** | **Inability to suction through endotracheal tube** |
| **New Admissions (including trauma patients)** | **Inability to bag valve mask ventilate a patient** |
| **Persistent hypotension** | **Persistent high pressure alarms on ventilator** |
| **Increasing vasopressor requirement** | **Change in neurologic status** |
| **Need for intubation or re-intubation** | **Persistent oliguria** |
| **Worsening hypoxia** |
Procedures in the ICU:
The ICU rotation is the rotation in which you should obtain the majority of your procedural experience during your residency. You should be familiar with the indications, relative contraindications, and techniques for these procedures prior to doing them.

Pre-procedural checklists must be filled out prior to all procedures (JCAHO regulations). If you are unable to obtain consent from the patient due to technical issues (e.g. they are intubated and sedated), you should attempt to contact the family regarding what you would like to do. Informed consent is to be given. If no surrogate decision-maker is available, 2 physicians may sign for the procedure in the Progress Notes in the patient’s chart. This is to be done prior to performing the procedure. “Time out” (right procedure, right patient, right lateralization) is to be performed prior to the procedure and documented in your note. If you have a syringe with any liquid, it is government regulation that it be labeled, with sterile labels from the Line Cart.

All chest tubes, arterial lines, lumbar puncture, paracentesis, thoracentesis, and deep lines must be performed with aseptic technique, including hat, mask, gown, gloves, and eye protection. Widely draping patients with “half sheets” is also key to maintaining the sterility of your procedure. Use Chlorpreps (Chlorhexidine) for skin preparation for all procedures outside of lumbar punctures, for which Betadine is used. Allowing these antiseptics to dry prior to penetration of the skin is important. Washing hands prior to gowing is also of paramount importance. In hospital, all central line placements must have an additional CDC form filled out in an effort to reduce Catheter-Related Blood Stream Infections (CRBSI’s).

Please write procedure notes following the procedure you perform, and write the procedure, date, and your name on the discharge summary form. There is a procedure form template on the www.venturafamilymed.org website which you may use.

ICU Attendings will often like to be present for procedures done, particularly when we are in the building. Please page your attending prior to a procedure if they are in the building, or if you need help. As a general rule, you will be allowed 2 attempts on procedures. If your 2 attempts are unsuccessful, expect that the next more-senior resident or attending will be stepping in. It is up to the discretion of the attending if a procedure is too high risk, or under too difficult of a clinical circumstance, for a more junior resident to be attempting it.

Procedures in the ER are often performed under less-than-optimal conditions. They should be replaced under more sterile technique within 24 hours of ICU admission.

MRSA Screening:
As mandated by State Law in January 2009, all admissions to the ICU, all dialysis patients, all patients previously hospitalized within 30 days, as well as all transfers to the hospital from another institution such as a nursing home, require MRSA screening via nasal swab. The two orders sentences to select are “MRSA Swab Nurse Collect” and “MRSA Screen”, both found on the ICU General Admission and MED General Admit powerplans.
Family Discussions:
Family interactions are an extremely important part of the care of ICU patients. Try to speak in “layman’s terms” as much as possible, avoiding medical jargon that may be confusing. Be sure that the discussion is in the key family members’ primary language, and get a translator if you need one. It is exceedingly helpful to the ICU staff for the family to elect one “spokesperson” who can disseminate information to the rest of the family, make important decisions when they need to be made, and be the person to contact to give updates when there are significant changes in their family member’s clinical status. Try to ask the family to elect a spokesperson early on and put their name and contact number into Cerner (task your MOA with this).

As a general rule, you should avoid giving ‘false hope’ to families. Phrases such as “we are doing everything we can”, and “it is up to the patient’s body if (s)he responds to our therapy” can be very helpful. See “Code Discussions in the ICU” in Miscellaneous online for more in-depth discussion of this topic. Code status should be clarified early on.

Visitor Guidelines:
(From ICU Policies and Procedures via Medical Staff Office Website)
- Visiting hours are limited to 10 minutes every hour on the hour, and limited to immediate family members/ significant others. Special arrangements may be made by speaking with the patient’s nurse. In general, only two visitors are to be at the bedside at one time.
- No children under the age of 13 will be permitted to visit except under special circumstances.
- Attorneys and investigators of any type are not permitted to interview patients unless approval by the attending physician has been given and patient is agreeable to said visitation.
- Visiting will be curtailed at change of shift and during ICU rounds to assure confidentiality of patient information.

ICU Standards:
There are national standards to which all Intensive Care Units are measured and compared. VCMC uses a software program called ICU Tracker to collect data from all areas of patient care and create reports that allow us to measure our performance, both internally and compared to other ICUs (comparing to other ICUs is called ‘benchmarking’). The reports generated are only as good as the data collected and entered into the system, reliant on the time and effort put into your preparation for rounds and your communication with the attending staff, nurses, RTs and each other. The ultimate goals of this data collection are to recognize areas of relative weakness and to improve the quality of patient care, and we very much appreciate your role in this process.

Some outcomes measured and benchmarked with other hospitals include the following:
- Mortality Rates (ICU, Hospital, Long-term, adjusted for severity of illness)
- ICU Length of Stay
- Duration of Intubation
- Median Ventilator Hours
- ICU Readmission Rates
- Unplanned Extubations
- Reintubation Rates
- Rate of Ventilator Associated Pneumonia
- Rate of Catheter-Related Blood Stream Infections
- Rate of Urinary Catheter-Related Infections
- Incidence of Pressure Ulcers, particularly Grade III or higher
- Rates of Stress Ulcer and DVT Prophylaxis for appropriate indications
- Rates of Stress Ulcers and DVTs
GOALS AND EXPECTATIONS IN THE ICU

- Daily multidisciplinary rounds
  - Generally 9am, unless codes or other work impact that meeting time.
  - With residents, attending, nurse, respiratory therapist, nutritionist, pharmacist, infection control nurse, and infectious disease physician as possible attendees

- Call the attending for all admissions and all unstable patients. Please give the attending formal presentations over the phone. Tell the attending to come in if you need them to be there. It should go without saying that all patients admitted to the ICU require a dictated full History and Physical by the primary resident, with emphasis on the Assessment and Plan. A written summary should also briefly detail the assessment and plan in addition to the full dictation. All transfers into the ICU merit an accept note from the accepting ICU resident.

- Keep track of your admissions on the Microsoft Word document on the computer in the ICU to improve continuity with your night float (NICE). This list should be updated daily.

- When questions come up on rounds, the best attempt should be made by the resident taking care of the patient to answer the question (take guesses, and explain your logic). If the primary resident doesn’t know, they should ask their more senior resident (e.g. intern asks their second year, second year asks their third year) in order to preserve resident-to-resident teaching.

- Transfer summaries are EXCEEDINGLY HELPFUL to the accepting medicine/surgery team for patients being transferred out of the ICU. Except for the most straight-forward of patients or admissions less than 24-48 hours, transfer summaries should be dictated the day the patient leaves the ICU. Please complete your Trauma Summary Forms with any diagnoses and procedures performed while in the ICU. Update your diagnoses and problem lists. Use “PM Conversation” as well as “Physician Contact” to update the name of the resident and attending to whom the patient is going.

- Remember: 1 hour in the morning is worth 3 in the afternoon. Get patients seen, orders written, and plans made early. Let us know how things are going. Anticipate feedback from us.

- Issues that should be addressed in your assessment and plan on a daily basis are the following:
  - Number of days on antibiotics
  - Presence and duration of invasive lines/tubes
  - Presence or absence of GI/DVT/VAP prophylaxis (and, if absence, why?)
  - Family discussions and code status
  - Is patient ready to be extubated (if applicable)?
  - Does the patient need to remain in the ICU?
The Role of the Third Year in the ICU

It should go without saying that the daytime senior resident is responsible for being physically in the hospital and available on a moment’s notice to the ICU at all times between the hours of 7am and 6pm, with the exception of Mondays, Wednesdays and Fridays from 1pm through 5pm when the resident has obligations in AFMC. On clinic days, the senior resident is expected to have concluded their clinical work in AFMC by 5pm and to have physically returned to the hospital to be present from 5pm to 6pm. The Intern should not be alone as the sole provider of ICU care in the hospital. Attendings are available 9am through 5pm in-house each weekday.

What Differentiates a Good ICU Senior Resident from a Stellar ICU Senior Resident

Manages the patients in the ICU, manages their own time as well as their Intern’s time in an effective and efficient manner

- Examples:
  - Start rounds on time
  - Present patient data quickly without leaving out details
    - cadence, avoid or delay distractions during rounds, minimize or delegate looking up data during presentations
  - Move quickly from patient to patient

Multi-tasks appropriately

- Delegates tasks, including to attending if necessary
- Develops a plan for the day at the end of rounds restating the most urgent tasks

Presents both precise and concise assessments, and coherent plans based on those assessments, as opposed to looking to the attending to guide the therapy

Finds new and Interesting Problems and initiating thoughtful discussion on rounds about them

Brings up likely scenarios in the assessment and what they plan to do about the scenario should it arise

- e.g. “ICP trended up last night, now normal but likely to have more trouble today; will do check Chem 7 and Serum Osm and give Mannitol…”

Demonstrates efficiency in procedures (starts them and carries them through, while maintaining proper procedural technique and minimizing risk to the patient)

Sets a good example by

- Filling out forms that need to be filled out
- Obtaining proper consents for procedures from patients and/or family members
- Maintaining proper sterile barrier conditions, hand-washing, personal hygiene, etc.

Evaluates patients quickly in the ER, expedites their moving to the ICU quickly

Maintains effective communication with nursing and RT and PT/OT staff

Calls the attending for any concerns that the attending should know about

Reads the literature, focusing on their patient load

Takes control of your ICU

- Decides how and when to round
- Delegates tasks
- Leads discussions with staff, family
- Thinks of your attending as a clinical not logistical resource
**ICU Systems-Based Presentations**

**RN Report:** Will present all relevant subjective and objective data, including Significant overnight events, Significant physical assessment findings, Significant Vital Signs (Tmax, arrhythmias, etc), Is and Os (totals; +/- net), IV gtts and rate, Lines (IVs, CVC, Foley) & sites, Invasive hemodynamic measurements (i.e. SvO2, CVP, ICP), Feeds (type & rate; if held, why?), Blood sugars (range), BM, RASS Score, Pain (scale & score), CAM-ICU, Sleep, Skin integrity, Family/Social Issues, and Specialty Bed

**RT presentations:** Will present ventilator information, ABG, secretions, etc.

**Start with a One-Liner:** i.e. 55 year old male Hospital Day #8, ICU day #6, Ventilator Day #6 for sepsis secondary to community acquired pneumonia. For patients admitted overnight and not yet discussed at rounds, you may start with a couple of lines of what brought the patient into the hospital/ICU.

**Systems-based Presentations:**

- Arrange your presentation as Assessment and Plan together for each system. You may include subjective/objective data with each system as you see fit, but do NOT repeat what has already been said in RN/RT report.
- Start with the patient’s most significant problem.
- If the patient is on a ventilator, Pulmonary should be in your top 2 or 3 systems, to discuss while the Respiratory Therapist is still present at rounds.
- After you have discussed your main problem or couple of problems, then start at the top and sequentially go through the remainder of the systems not yet talked about.

<table>
<thead>
<tr>
<th>System</th>
<th>Assessment/Plan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuro/Psychiatric</td>
<td>• Include if delirium is present. If so, what’s your plan?</td>
</tr>
<tr>
<td></td>
<td>• Include current sedation goal and your plan for sedative changes</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td></td>
</tr>
<tr>
<td>Pulmonary</td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td></td>
</tr>
<tr>
<td>Renal</td>
<td></td>
</tr>
<tr>
<td>Hematologic</td>
<td></td>
</tr>
<tr>
<td>Infectious Disease</td>
<td>• Include day numbers for antibiotics, with the day the antibiotic was started as day #1</td>
</tr>
<tr>
<td></td>
<td>• Include day #s for lines, with the day the line was inserted as day #1</td>
</tr>
<tr>
<td>Endocrine</td>
<td></td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td></td>
</tr>
<tr>
<td>Derm</td>
<td></td>
</tr>
<tr>
<td>Fluids/Electrolytes/Nutrition</td>
<td></td>
</tr>
<tr>
<td>Prophylaxis</td>
<td></td>
</tr>
<tr>
<td>Lines</td>
<td>• Include day numbers and if the line needs to be continued</td>
</tr>
<tr>
<td>Code Status/ Family Updated?</td>
<td></td>
</tr>
<tr>
<td>Disposition</td>
<td></td>
</tr>
</tbody>
</table>
DATE/TIME

*R__ ICU PROGRESS NOTE* (during Cerner down time)

PT:
MRN:

Meds:

O/N events:

Subjective:

<table>
<thead>
<tr>
<th>BP:</th>
<th>MAP:</th>
<th>Pulse (art /cuff):</th>
<th>Ventilator Mode:</th>
</tr>
</thead>
<tbody>
<tr>
<td>RR:</td>
<td>Osat:</td>
<td>/</td>
<td>Vent rate:</td>
</tr>
<tr>
<td>BG:</td>
<td>i/Os:</td>
<td>/</td>
<td>PIP/Pplat:</td>
</tr>
<tr>
<td>UOP:</td>
<td>Drains:</td>
<td>/</td>
<td>PEEP:</td>
</tr>
</tbody>
</table>

Gen:
Neuro:
HEENT:
Resp:
CV:
Abd:
Ext:
Skin:
Lines:

Labs:

Micro:

Radiology/Studies:

Lines/d#:

ASSESSMENT/PLAN:
1. Neuro/Psychiatric:
2. Cardiovascular:
3. Pulmonary:
4. Gastrointestinal:
5. Renal:
6. Hematologic:
7. Infectious Disease:
8. Endocrine:
9. F/E/N:
10. Dermatology:

---------------------------------- # ___ 

Return to Table of Contents
Electronic Health Record (EHR) Cerner ICU Orientation

ED Admission Specifics

- In no other rotation is the issue of “sign” versus “initiate” more important than in the ICU.
  - “Signing” is akin to the paper chart way of writing full admission orders that, in the past, were placed into the patient folder and not seen until the patient reached the floor.
  - “Initiating” is akin to the paper chart way of writing one-time orders in the bottom right corner of the front page of the ER chart
  - For orders that need to be started immediately in the ED, initiate those outside of the admission orders that you’re signing. Also TELL YOUR NURSE in the ED about the orders you want to get going in the ED – more than ever, verbal communication outside of Cerner is so important.
    - For DKA patients, initiate the insulin bolus outside of any powerplan. You should probably also initiate the “PHA Adult IV Insulin Orders Using Glucommander” entire powerplan, but SEPARATE from the ICU General Admission powerplan which you will be signing
    - For patients who need pressors started in the ED, initiate the “PHA Adult IV Titratable Medication Vasoactive” orderset in the ED
    - For patients who need serial labs frequently right from the start, order and initiate those labs outside of a powerplan
  - “ICU General Admission” powerplan should be used for nearly all ICU admissions. The exceptions would be trauma patients, for which TRA Trauma Admit should be used.
    - The TRA Trauma ICU Specific powerplan adds a couple of ICU specific things: ICP monitoring, CVP monitoring, 3% saline, ocular lubricant, and tranexamic acid

Step ups from the floor to ICU

- Even if the patient already has “MED General Admit” powerplan orders, it is best to order “ICU General Admission” powerplan, then click the “Merge View” (the shuttlecock badminton looking thing on your orders) to see which orders you need to cancel from the medicine orders and which ones you would like to keep. The powerplan orders between Medicine and ICU are different enough as to want to do it this way.
  - Alternatively, you may perform your Transfer Medication Reconciliation first, which will also let you look at all home medications that may not have been continued on admission, then do the same process as above; it is not required to do it this way.
- Initiate your ICU General Admission orders even if you are still on the floor. It will get medications cooking/ labs cooking quicker, even if all orders may not be able to be performed on the floor

Step downs from ICU

- You may choose to order the “MED General Admit” powerplan, then click “Merge View” to see which orders you need to cancel from the ICU orders and which ones you would like to keep. The powerplan orders between ICU and Medicine are different enough as to want to do it this way.
- Alternatively, you may perform your Transfer Medication Reconciliation (which is now ‘all orders reconciliation’) first, which will also let you look at all home medications that may not have been continued on admission, then do the same process as above; it is not required to do it this way.
- Initiate your Med General Admit orders even if you are still physically in the ICU. Inform your nurse that you are doing so.
ICU Specific Orders

- **IV Drips** will be under one of two powerplans: “PHA Adult IV Titratable Medication Vasoactive” and “PHA Adult IV Titratable Medication Neurologic”. You will find pressors/antihypertensives in the former and sedatives and paralytics in the latter. Look at both the “Details” and “Continuous Details” tabs—there are required fields on both, but also suggestions under the “Details” as to the appropriate starting dose to be filled in under “Continuous Details”. Slightly cumbersome but incredibly effective and helpful/averts many phonecalls from pharmacy.
  - It is a CMS (Centers for Medicare and Medicaid) regulation that there be not more than one titratable medication listed for the same indication (i.e. you cannot have propofol and midazolam both titrated to a RASS score of -2 to -3). To order appropriately, one medication should be ordered at a non-titratable rate; we are pending approval of “PHA NON titratable IV Drip Medications” sub phase to order a non-titratable rate for all but one medication; the rate will need to be adjusted in the order manually by the ordering provider.

- MINDS protocol for alcohol withdrawal is listed under “ICU Alcohol Withdrawal Protocol”
- For bleeding patients, “PHA Coagulopathy Reversal” should have everything you need.
- Ventilator orders are listed as either ad hoc order “Ventilator Settings” or under “ICU Ventilator Sedation and Analgesia”. These may be modified and should have the most up-to-date ventilator plan on a daily basis
- “PHA IV Fluids”, “PHA Chest Pain”, and “PHA Fever” are all helpful subphases for being on call
- Dietary supplements (i.e. Unjury, Banana flakes) (update 1/21/14): The problem that was occurring in the past was that nurses would not get tasked to give supplements, and were not reliably doing it because there was no task for it. The other problem is that you don't want the nurses to get tasked ALL the time because, on patients who get meal trays with the supplements already on them, the nurses don't need to be involved. The solutions:
  - On patients getting diet trays: Order supplements as ”Dietary Supplements". The nurses do not get tasked to give those supplements.
  - On patients NOT getting diet trays (usually patients on tube feeds): Order supplements as ”Tube Feeding Supplements". Nurses DO get tasked to give these supplements.

ICU Data – where to find it??

- Data like CPP, ICP, CVP, and other three initial acronyms may be found in the “Adult ICU Systems Assessment” under the “Interactive View and I&O” tab
  - Click on your “Interactive View and I&O” tab. If you do NOT see “Adult ICU Systems Assessment”, do the following:
    1. Click on “Interactive View and I&O” tab
    2. On the top line, click “View”, then hover over “Layout”, then click on “Navigator bands…”
    3. There are 5 different ICU bands, each with different data, which are worth exploring. These all start with the words “adult icu”

ICU Documentation in Cerner

- Create your own systems template; Lepore’s are available by emailing him; feel free to use them if you want (not necessary)
- Label your notes, “Critical Care Progress Notes”
CARDIOVASCULAR

Basic Life Support
Universal Algorithm for CPR (International Liaison Committee on Resuscitation)
(applies to infants through adults (but not neonates))

Unresponsive patient, not breathing
or only occasional gasps

Start ‘Good quality’ CPR
(2010 guidelines changed from ABC to
CAB—Compressions, Airway, Breathing)

Assess Rhythm

Shockable rhythm: (V-fib, V-tach)
Give 1 shock
Immediately resume CPR

Unshockable rhythm: (PEA/ Asystole)
Unshockable rhythm: (PEA/ Asystole)
Immediately Resume CPR

Advanced Cardiac Life Support: (while minimizing interruptions to compressions):
• Consider advanced airway
• Continuous chest compressions after advanced airway in place
• Consider capnography
• Obtain IV/ IO access
• Consider vasopressors and antiarrhythmics
• Correct reversible causes†

‘Good quality’ CPR:
• push hard to a depth of at least 2 inches (5 cm)
• rate of at least 100 compressions per minute (Bee Gees “Stayin’ Alive”=103 beats/minute)
• allow full chest recoil after each compression
• minimize interruptions in chest compressions.

Immediate post-cardiac arrest monitoring and support
Including consideration of:
• 12-lead ECG
• Perfusion/ reperfusion
• Oxygenation and ventilation
• Temperature control
• Reversible causes

† Reversible Causes:
• Hypovolemia
• Hypoxia
• Hydrogen ion (acidosis)
• Hypo/hyperkalemia
• Hypoglycemia
• Hypothermia
• Toxins
• Tamponade, cardiac
• Tension pneumothorax
• Thrombosis (coronary or pulmonary)
• Trauma
## Basic Life Support

<table>
<thead>
<tr>
<th>Maneuver</th>
<th>Adolescent and older</th>
<th>One year to adolescent</th>
<th>Infant under 1 year of age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Circulation</td>
<td>Check carotid pulse</td>
<td>Check brachial or femoral pulses for up to 10 seconds</td>
<td></td>
</tr>
<tr>
<td></td>
<td>for up to 10 seconds</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Compression site</td>
<td>Lower sternum between nipples</td>
<td>Sternum just below nipple line</td>
<td></td>
</tr>
<tr>
<td>Compression method: push hard and fast and allow complete recoil; if two providers, no pauses for ventilation</td>
<td>Heel of one hand with other hand on top</td>
<td>Heel of one hand</td>
<td>2 fingers (lone provider) or 2 thumbs and encircling hands (two providers)</td>
</tr>
<tr>
<td>Compression depth</td>
<td>At least 2 inches</td>
<td>1/3 – ½ the depth of the chest</td>
<td></td>
</tr>
<tr>
<td>Compression rate</td>
<td>Approximately 100 beats/min (Bee Gee’s “Stayin’ Alive” tempo is 103, close enough to 100)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Compression:ventilation ratio</td>
<td>30:2 (one or two providers)</td>
<td>30:2 (lone provider)</td>
<td>15:2 (two providers)</td>
</tr>
<tr>
<td>Airway</td>
<td>If no suspected neck trauma: Head tilt-chin lift</td>
<td>If suspected neck trauma: jaw thrust</td>
<td></td>
</tr>
<tr>
<td>Rescue breathing without chest compressions</td>
<td>1 breath every 5-6 seconds</td>
<td>1 breath every 3-5 seconds</td>
<td></td>
</tr>
<tr>
<td>Rescue breathing for CPR with advanced airway</td>
<td>1 breath every 6-8 seconds</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Airway obstructed by foreign body</td>
<td>Abdominal thrusts</td>
<td>Up to 5 repetitions of back slaps and chest thrusts</td>
<td></td>
</tr>
<tr>
<td>Defibrillation</td>
<td>Use adult pads</td>
<td>Witnessed collapse or hospital arrest: use AED immediately with pediatric pads (if available)</td>
<td>Manual defibrillator preferred; dose for VF is 2-4 Joules/kg</td>
</tr>
<tr>
<td>Defibrillation AED</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Newborn CPR

Compression-ventilation ratio of 3:1 for resuscitation of the newborn in the delivery room, with a pause for ventilation whether or not the infant has an advanced tracheal airway in place. Consider higher ratio if arrest is thought to be of cardiac etiology.

For term newborns, begin resuscitation with air rather than 100% oxygen.

ACLS Rhythms
Bradycardia Algorithm

- Heart rate <60/min
- Patient is symptomatic?

No  
Observe closely

Yes

- Maintain a patent airway
- Assure breathing is adequate; give O₂
- Cardiac monitor
- Vital signs and continuous oximetry
- Establish vascular access

- Signs/symptoms of poor tissue perfusion caused by bradycardia?
  - Altered mental status
  - Chest pain
  - Hypotension
  - Signs of shock
  - Acute heart failure

Adequate perfusion  
Inadequate perfusion

- Observe
- Monitor

- Consider administration of antidotes for beta blockers, calcium channel blockers or digoxin if patient has been taking them
- Prepare for transcutaneous pacing
  - Mobitz type II 2° AV Block
  - Complete heart block
- While awaiting pacer, consider using:
  - Atropine 0.5 mg IV doses (repeat dose q 3-5 min, max 3 mg)
  - Dopamine 2-10 mcg/kg/min
  - Epinephrine 2-10 mcg/min

- Prepare for transvenous pacing
- Identify and treat contributing causes
- Consider cardiology consultation

Narrow-complex Tachycardia with a Pulse

Determine whether the patient’s tachycardia is producing hemodynamic instability and serious signs and symptoms or whether the signs and symptoms (i.e. pain and distress of AMI, tachycardia from fever, sepsis, hypovolemia, etc.) are producing the tachycardia

Favor underlying problem causing symptoms:
- Pulse < 150
- Sinus tachycardia
Note: Chronic a-fib that has gotten more rapid, or acute a-fib conversion from sinus rhythm can be a ‘sinus tachycardia equivalent’ in some patients

Favor tachyarrhythmia causing symptoms:
- Pulse >150
- SVT (regular), A-fib or MAT seen on ECG

- Aggressive identification and treatment of the underlying cause
- Assess and support ABCs
- Oxygen
- Cardiac Monitor to identify rhythm; monitor blood pressure and oximetry; IV access

If regular narrow complex, may consider trial of adenosine prior to cardioversion

Synchronized cardioversion
- IV access
- Procedural sedation if patient is conscious
- Biphasic superior to monophasic defibrillator
- Anterior-posterior pads superior to right-left pads
- Narrow and regular: 50-100 J
- Narrow and irregular: 120-200 J biphasic, 200 J monophasic

Is patient unstable from tachycardia? (Unlikely rate-related symptoms if HR<150)
- Altered mental status; angina; hypotension; signs of shock; acute heart failure

Yes

Obtain ECG, confirm QRS<0.12 seconds

No

Regular
- SVT
- Atrial flutter with regular block
- Vagal maneuvers
- Adenosine rapidly
  - 6 mg IVP, then
  - 12 mg IVP
- Beta blocker or calcium channel blocker †

Irregular
- Afib
- Atrial flutter with variable block
- MAT
- Adenosine rapidly
  - 6 mg IVP, then
  - 12 mg IVP
- Beta blocker or calcium channel blocker †

Unexpectedly Fast
HR>200-220/min

Consider an accessory pathway
- Amiodarone 150 mg IV over 10 minutes, then start drip at 1 mg/min x 6 hrs, then 0.5 mg/min x 18 hrs
- Procainamide is alternative (see page 19)

† Note: Significant caution advised in using negative inotropes in patients with marginal blood pressure or in patients with severe pulmonary hypertension – their use may lead to severe hypotension

Wide-Complex Dysrhythmias with a Pulse

**Factors favoring V-Tach**
- Capture beats
- Fusion beats
- AV dissociation
- QRS concordance in precordial leads
- QRS>0.14 sec
- Marked RUQ axis
- QRS R/S ratio in V6<1

**Monomorphic V-tach**
- Amiodarone 150 mg IV over 10 min, then 1 mg/min x 6 hrs, then 0.5 mg/min x 18 hrs
- Procainamide 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
- Sotalol 100 mg (1.5 mg/kg) over 5 minutes; avoid if prolonged QT

**Torsades de pointes/Polymorphic V-tach**
- Treat as V-fib and deliver high-energy unsynchronized shocks
- Magnesium 2 gm IV over 2 min., then infuse 3-10 mg/min x 24-48 hours

**Contributing factors:**
- Hypovolemia
- Hypoxia
- Hydrogen ion (acidosis)
- Hypo/hyperkalemia
- Hypoglycemia
- Hypothermia
- Toxins
- Tamponade, cardiac
- Tension pneumothorax
- Thrombosis (coronary or pulmonary)
- Trauma

**Is patient unstable from tachycardia?**
- Altered mental status; angina; hypotension; other signs of shock; acute heart failure
- Unlikely rate-related symptoms if HR<150/min

**Synchronized cardioversion**
- IV access
- Procedural sedation if patient is conscious
- Biphasic superior to monophasic defibrillator
- Anterior-posterior pads superior to right-left pads
- 100-200 J for biphasic

**Unexpectedly fast HR>200-220/min**
- Consider an accessory pathway

- Amiodarone 150 mg IV over 10 minutes, then start drip at 1 mg/min x 6 hrs, then 0.5 mg/min x 18 hrs
- Procainamide is alternative

**Note:** For Idioventricular Rhythm (“Slow V-Tach”, or “Ventricular Escape Rhythm”) with Pulse <100, observation with correction of underlying cause (K<4, Mg<2, correcting Digoxin toxicity, ruling out ischemia and thyroid dysfunction) is indicated; no specific pharmacologic or cardioversion therapy is indicated with stable BP. With low BP, pressor support may be indicated.
Pulseless Arrest Algorithm

- BLS
- Administer oxygen
- Attach defibrillator

**VF or Pulseless VT**
- Shock x 1
  - Biphasic: 120-200 J
  - Monophasic: 360 J
- Resume CPR

**Asystole or PEA**
- CPR x 5 cycles
- Vasopressor (when IV/IO)
  - Epinephrine* 1 mg q3-5 min
  - Vasopressin* 40 U x 1 to replace 1st/2nd dose of epi
  - Atropine NOT recommended due to lack of efficacy

**If Pulseless VT or VF**
- Shock x 1 as above
- Resume CPR after shock
- Vasopressor (when IV/IO)
  - Epinephrine* 1 mg q3-5 min
  - Vasopressin* 40 U x 1 instead of 1st/2nd dose of epi

**Asystole/PEA**
- CPR x 5 cycles
- ? Pulse/? rhythm

**VF/VT**
- CPR x 5 cycles
- ? Pulse/? rhythm

**If Pulseless VT or VF**
- Shock x 1 as above
- Resume CPR after shock
- Antiarrhythmics
  - Amiodarone 300 mg IV +/- additional 150 mg IV x 1
  - Lidocaine no longer recommended
  - Consider magnesium sulfate 2 gm IV for torsades de pointes

CPR Notes
- Compressions continuous & hard
  - 30:2 compression/ventilation ratio
  - Rate: 100/min
  - Allow full recoil of the chest
  - Use ResQPod on ETT
  - Quantitative waveform capnography

Search for and treat reversible causes:
- Hypovolemia
- Hypoxia
- Hydrogen ion (acidosis)
- Hypo/hyperkalemia
- Hypothermia (Hypoglycemia)
- Toxins
- Tamponade, cardiac
- Tension pneumothorax
- Thrombosis (pulmonary)
- Thrombosis (coronary) (Trauma)

* - Meds may be given via endotracheal tube if vascular access unavailable at 2-2.5x standard IV doses
Adult Immediate Post-Cardiac Arrest Care

**Return of Spontaneous Circulation (ROSC)**
Signs include the following:
- Return of pulse and blood pressure
- Abrupt sustained increase in $P_{ETCO2}$ (end tidal CO2)
- Spontaneous arterial pressure waves with intra-arterial monitoring

**Optimize Ventilation and Oxygenation**
- Maintain $O2$ Sat ≥ 94%
- Consider advanced airway and waveform capnography (end tidal CO2)
- Do NOT hyperventilate; goal $P_{ETCO2}$ 35-40 mm Hg or $PaCO2$ 40-45 mm Hg

**Treat Hypotension**
- IV/IO Bolus
- Vasopressor Infusion
- Consider treatable causes
- 12-Lead ECG

Consider Induced Hypothermia (page 195)

Follow Commands?
- Yes

Coronary Reperfusion
- Yes

STEMI or High suspicion of AMI
- No

Advanced critical care

Hemodynamic Monitoring

See “The Estimation of Effective Intravascular Volume in the ICU” (page 89)

Hemodynamic Parameters, Definitions and “Normal Values”:

Preload=Amount of Stretch on the Left Ventricle at the end of diastole/prior to systole
‘Fluid Responsiveness’=a fluid challenge will improve hemodynamics
Afterload=equivalent to the Systemic Vascular Resistance
Stroke Volume (SV)=amount of blood volume ejected from the heart with each systolic contraction; Depends on Cardiac Contractility as well as the Preload
Cardiac Output (CO) = amount of blood volume ejected from the heart per minute
    = Stroke Volume x Heart Rate
Cardiac Index=Cardiac Output divided by Body Surface Area (BSA)
Systemic Vascular Resistance (SVR)=pressure in the systemic arterioles against which the heart pumps
Systemic Vascular Resistance Index (SVRI)=Systemic Vascular Resistance divided by BSA
Central Venous Pressure (CVP)=Pressure in the Superior Vena Cava. Notoriously POOR at assessing preload and ‘fluid responsiveness’.
Pulmonary Capillary Wedge Pressure (PCWP)=Pulmonary Artery Wedge Pressure (PAWP)= equivalent to the Left Ventricular End-Diastolic Pressure; better but still not perfect for assessing preload or ‘fluid responsiveness’
Pulse Pressure =Systolic Pressure minus Diastolic Pressure
Mean Arterial Pressure (MAP)= (Pulse Pressure)/3 + Diastolic Pressure (≥65 is ideal)

Relationship of Cardiac Output and Perfusion

\[
\text{Oxygen Delivery} = D_{O_2} = \frac{c(Hb)(CO)}{SaO_2}
\]
\[
\text{Oxygen Consumption} = V_{O_2} = \frac{C(Hb)(CO)(SaO_2 - SvO_2)}{c(Hb)(CO)}
\]

Diagram: Created by Diagram Author.
Tools That Monitor Hemodynamics

<table>
<thead>
<tr>
<th>Monitoring Devices</th>
<th>Measurements Assessed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pressure cuff, Mentating Patient</td>
<td>Perfusion of brain</td>
</tr>
<tr>
<td>Urinal / Foley Catheter</td>
<td>Perfusion of kidneys</td>
</tr>
<tr>
<td>Add Central Line with CVP</td>
<td>Adds preload assessment (not ideal; see above)</td>
</tr>
<tr>
<td>Add Arterial Line</td>
<td>Adds Second-by-second Blood Pressure / MAP Monitoring</td>
</tr>
<tr>
<td>Add Central Line with SvO₂</td>
<td>Adds Oxygen Delivery-Consumption Data</td>
</tr>
<tr>
<td>Add Arterial Line with continuous Cardiac Index</td>
<td>Adds Cardiac Output Data (utilizes special tubing with standard arterial line)</td>
</tr>
<tr>
<td>Cardiac Index Art Line + SvO₂ Central Line</td>
<td>Adds all of the above Data; short of a Swan-Ganz catheter in that SVRI/PCWP is not assessed, but may be inferred</td>
</tr>
<tr>
<td>Swan-Ganz Catheter</td>
<td>All hemodynamics including SVRI, PCWP, CI</td>
</tr>
</tbody>
</table>

Echocardiogram should be considered for all patients with hemodynamic concerns.

Types of Shock, Overview (see specific sections)
Definition: A medical condition in which tissue perfusion and oxygen delivery is insufficient for the metabolic demands of the body. In shock, there is an imbalance between oxygen delivery to tissues and oxygen consumption by tissues.

<table>
<thead>
<tr>
<th>Type of Shock</th>
<th>Cardiac Index</th>
<th>Afterload (SVR)</th>
<th>Wedge (PCWP)</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiogenic, or Septic-Vasoconstricted</td>
<td>Low (&lt;2)</td>
<td>High</td>
<td>High</td>
<td>Dopamine initially, Consider Dobutamine depending on SVR</td>
</tr>
<tr>
<td>Hypovolemic</td>
<td>Low</td>
<td>High</td>
<td>Low</td>
<td>Fluid resuscitation</td>
</tr>
<tr>
<td>Distributive (sepsis, anaphylaxis, neurogenic)</td>
<td>Usually High</td>
<td>Low</td>
<td>Normal or Low</td>
<td>Fluid resuscitation</td>
</tr>
<tr>
<td>Obstructive (tension pneumothorax, massive PE, tamponade)</td>
<td>Low</td>
<td>High (NI or High w/ PE)</td>
<td>High</td>
<td>Treat the underlying cause</td>
</tr>
</tbody>
</table>

Core Management Concepts of Hemodynamic Monitoring
Entails the following:
1. Deciding who needs the monitors
2. Interpreting the monitors’ data
3. Changing therapies based on the monitors’ data
4. Evaluating responses to therapies and adjusting therapies based on responses
5. Knowing complications of monitors
6. Knowing when to safely remove the monitors based on the patient’s clinical status

Goals of Hemodynamic Monitoring

Adequate Perfusion of Organs/Improving Organ Function
Surrogate Measures of Adequate Perfusion/Improving Organ Function include:
1. Urine output at $\geq 0.5$ml/kg/hour or $\geq 30$ml/hour and mentating patient
2. Mean Arterial Pressure $\geq 65$mmHg
If first two goals are not met:
1. Lactic Acid $<2.0$ or falling
2. Cardiac Index/ Blood pressure Optimized (with blood pressure, urine output, etc.)
3. May consider: Central Venous Pressure of 8-12 mmHg (or 12-15 mmHg in mechanically ventilated patients to account for increased intrathoracic pressure or 12-15 mmHg in patients with diastolic dysfunction)
4. May consider: Central Venous Oxygen Saturation $\geq 70\%$ (but $<82-85\%$)

Not putting the patient into a fluid overload state
An Approach to the Diagnosis and Management of Shock States

**Cardiovascular**

**Hemodynamic Monitoring**

An Approach to the Diagnosis and Management of Shock States

**Goals Achieved?**

1. Urine output at ≥ 0.5ml/kg/hr or ≥ 30ml/hr, mentating patient?
2. Mean Arterial Pressure ≥ 65 mmHg?
3. Lactic acid level < 2 (note: normal lactate does not exclude shock)

**Goals NOT Achieved**

Assess Intravascular Volume Status (see page 89)

**Suspect Intra- Vascular Depletion**

“Fluid Challenge”: Volume resuscitation w/ Normal Saline 30 ml/kg bolus at a rate of 500-1000ml per 30 minutes (or colloid at a rate of 300-500ml per 30 minutes) to achieve goals (begin slower if elderly, history of CHF or CAD, or no suspicion of septic shock)

**Goals Achieved**

Consider “RUSH” Exam (Rapid Ultrasound in Shock) (evaluate Pump, Tank, and Pipes)

**Goals NOT Achieved**

Dynamic Assessment of Volume Status (see page 89, 90)

Suspect Intravascular Overload

- Consider “Diuresis challenge”
- See “Cardiogenic Shock” if BP also low (page 34) and consider dopamine infusion to raise blood pressure

**The Pump:** (to rule out pericardial effusion, evaluate left ventricular contractility, and detect right ventricular strain (as a possible sign of pulmonary embolism)) (phased array probe)

**View** | **Findings**
---|---
Subxiphoid | Effusion, cardiac standstill during CPR
Parasternal Long Axis | Effusion, LV dysfunction (look at mitral valve proximity to septum)
Parasternal Short Axis | Evaluate LV function as ‘good’, ‘moderate’, or ‘poor’;
| Evaluate for focal wall motion abnormality
| (SALPI= septal, anterior, lateral, posterior, inferior)
Apical 4 chamber | Effusion, RV enlargement, Septal bowing (r/o PE), LV dysfunction

**The Tank:** (to evaluate fullness of the tank (IVC measurements as surrogate for CVP), leakiness of the tank (pleural and peritoneal fluid), obstructed tank (pneumothorax), +/- pulmonary edema)

**View** | **Findings**
---|---
IVC measurement | See page 91 for IVC measurement correlation with CVP (phased array probe)
FAST exam | Looking for both pleural and peritoneal fluid (phased array probe)
Lung exam | (with linear probe): Pneumothorax with ‘barcode sign’, no comet tails or pleural slide

**The Pipes:** (to evaluate for abdominal aortic aneurysm, aortic dissection, DVT) (linear probe)

<table>
<thead>
<tr>
<th>RUSH Interpretation</th>
<th>Hypovolemic</th>
<th>Cardiogenic</th>
<th>Obstructive</th>
<th>Distributive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pump</td>
<td>Hypercontractile Small chambers</td>
<td>Hypocontractile Dilated chambers</td>
<td>Hypercontractile Pericardial tamponade RV Strain</td>
<td>Hypercontractile (early sepsis) Hypocontractile (late sepsis)</td>
</tr>
<tr>
<td>Tank</td>
<td>Flat IV Pleural/peritoneal fluid</td>
<td>Distended IVC Pleural/ peritoneal fluid</td>
<td>Distended IVC Absent lung sliding (pneumothorax)</td>
<td>Normal or flat IVC Pleural/ peritoneal fluid (source of sepsis)</td>
</tr>
<tr>
<td>Pipes</td>
<td>AAA, dissection</td>
<td>Normal</td>
<td>DVT</td>
<td>Normal</td>
</tr>
</tbody>
</table>

**Reference:** Emerg Med Clin N Am; 2010: 29-56. Adapted with permission from Richard Rutherford, MD.

Return to Table of Contents
Pulmonary Artery Catheters (PAC) = “Swan Ganz Catheter”

Data
- Meta-analysis of 13 Randomized Control Trials, total of 5051 patients analyzed
- Conclusion: “In critically ill patients, the use of the PAC neither increased overall mortality or days in hospital nor conferred benefit. Despite almost 20 years of randomized control trials, a clear strategy leading to improved survival with the PAC has not been devised. The neutrality of the PAC for clinical outcomes may result from the absence of effective evidence-based treatments to use in combination with PAC information across the spectrum of critically ill patients.”

Indications (see The Estimation of Effective Intravascular Volume in the ICU”, page 89)
- Assessment of shock states, assessment of pulmonary edema (cardiogenic vs. ARDS), guidance of therapy with combined oliguria or hypotension and pulmonary edema, optimization of cardiac index in cardiogenic shock, evaluation and drug titration for severe pulmonary hypertension, diagnostic evaluation of left-to-right cardiac shunts; most often helpful in patients with renal failure going to surgery (massive fluid shifts expected), or in ARDS with renal failure (not supported by studies)

Relative contraindications
- Severe coagulopathy or thrombocytopenia (platelet count<50,000), prosthetic right heart valve, endocardial pacemaker/defibrillator, right sided endocarditis, uncontrolled ventricular or atrial dysrhythmias, right ventricular mural thrombus; caution with left bundle branch block (5% risk of complete heart block); do not use if hemodynamics are optimized with less invasive methods!!

Complications
- Atrial or ventricular dysrhythmias, right bundle branch block (0.1-5% of insertions), pulmonary infarction, pulmonary artery rupture (0.2% incidence; leave balloon inflated if this occurs), catheter-related bloodstream infection, marantic or infectious endocarditis, mural thrombus, knotting of catheter; from cordis catheter placement: pneumothorax, arterial puncture, air embolus.

Reference Values

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal Values</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central Venous Pressure (CVP)</td>
<td>5-7cmH2O (low values most helpful)</td>
<td>Elevated with RV infarct, severe tricuspid valve disease, cardiac tamponade, heart failure, PEEP&gt;10mmHg, PE</td>
</tr>
<tr>
<td>Cardiac Output (CO)</td>
<td>4-8 Liters/minute</td>
<td>Cardiogenic shock is defined as Cardiac Index &lt; 2 L/min*m^2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Elevated: cirrhosis, thyrotoxicosis, AV fistula, beri-beri, pregnancy, fever, activity, delirium tremens, distributive shock Low: cardiogenic shock, tension pneumothorax, cardiac tamponade, massive pulmonary embolism, high PEEP, hypovolemia; falsely low with severe TR/PI or VSD</td>
</tr>
<tr>
<td>Cardiac Index (CI)</td>
<td>2.5 - 4 Liters/minute*meter^2</td>
<td></td>
</tr>
<tr>
<td>Systemic Vascular Resistance Index</td>
<td>900-1300 dynes/cm^2</td>
<td>Elevated: with cardiogenic shock, hypovolemia, obstructive shock</td>
</tr>
<tr>
<td>Systemic Vascular Resistance Index</td>
<td>1970-2390 dynes/cm^2*cm^2</td>
<td>Low: distributive shock, sepsis, cirrhosis, pregnancy, thyrotoxicosis</td>
</tr>
<tr>
<td>Right Ventricular End Diastolic Volume Index</td>
<td>60-90 ml/m^2</td>
<td>Goal is up to 130 ml/m2 in hypotensive septic patients; unreliable with severe TR</td>
</tr>
<tr>
<td>“Wedge”= Pulmonary Artery Wedge Pressure (PAWP)= Pulmonary Capillary Wedge Pressure (PCWP)</td>
<td>8-12cm H2O (Wedge&gt;18 is consistent with Left Ventricular volume overload)</td>
<td>Elevated: volume overload, ARDS, COPD, PE, PEEP&gt;10mmHg, Mitral/aortic valve disease, diastolic dysfunction, tension pneumothorax, vasopressor therapy, severe abdominal distension, RV infarct with fluid overload Low: Hypovolemia, Aortic/pulmonic insufficiency, post-pneumonectomy</td>
</tr>
</tbody>
</table>
Placement of Pulmonary Artery Catheter

<table>
<thead>
<tr>
<th>Insertion Site</th>
<th>RA Distance (cm)</th>
<th>RV Distance (cm)</th>
<th>PA Distance (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right IJ</td>
<td>15</td>
<td>25</td>
<td>40</td>
</tr>
<tr>
<td>Left IJ</td>
<td>20</td>
<td>30</td>
<td>45</td>
</tr>
<tr>
<td>Right SCV</td>
<td>10-15</td>
<td>20-25</td>
<td>35-40</td>
</tr>
<tr>
<td>Left SCV</td>
<td>15</td>
<td>25</td>
<td>40</td>
</tr>
<tr>
<td>Femoral</td>
<td>45-50</td>
<td>55-60</td>
<td>70-75</td>
</tr>
</tbody>
</table>

- Direct Catheter medially from Right IJ and Left SCV Locations
- Direct Catheter inferiorly from right SCV location (may need to rotate catheter counterclockwise once RV is reached)
- Direct catheter posteriorly from femoral vein locations and rotate catheter counter-clockwise once RV is reached

Pulmonary Artery Catheter Waveforms

PCWP is measured at the z-point, at end-expiration:
- z-point is defined as 0.08 seconds (2 small boxes on the EKG) after the QRS complex ends
- Note: Spontaneous inspiration yields decreased intrathoracic pressure with inspiration, where mechanical ventilation yields increased intrathoracic pressure with inspiration

"Over-wedging" of Swan Ganz Catheter
Due to catheter floating further and becoming lodged in a branch of the pulmonary artery Managed by inching back the catheter with the balloon deflated, with trials of balloon inflation until back in position.

Acute Coronary Syndrome

AB MONTH PISA is a mnemonic that can help you remember the various therapies you should consider for Acute Coronary Syndrome. (Aspirin, Beta Blocker, Morphine, Oxygen, Nitrates, Thrombolytics, Heparin, Plavix, Integrilin, Statin, ACE inhibitor). You should be familiar with the indications and relative contraindications of these therapies. In your notes, you should discuss therapies given. If a therapy is contraindicated, mention why you are not giving it in your note.

**ST-Elevation MI (STEMI)**

**Initial Evaluation**
Focused history / exam
12 lead EKG
(If EKG is non-diagnostic repeat in 5 minutes.)

**ST Segment Elevation or New LBBB**

- **≤ 12 hours**
  - Primary PCI
    - If able to be done in <90 min
      - Call Invasive Cardiologist
    OR
    - Thrombolysis (TPA) + Medical Rx

- **> 12 hours**
  - Primary PCI
    - If persistent or recurrent pain
      - Call Invasive Cardiologist
    OR
    - Medical Rx

**Primary PCI preferred over Thrombolysis:**
Cardiogenic shock
Acute pulmonary edema
Unstable ventricular arrhythmias
Any contraindication to TPA

**Thrombolysis preferred over Primary PCI:**
(Patient must qualify for fibrinolytic therapy; see Thrombolysis Protocol)
Total ischemic time including transport to PCI-capable facility > 120 minutes
May also be preferred when EMS has fibrinolytic capability

**Rescue PCI after TPA Indicated:**
<50% ST segment resolution by 90 min after TPA
Cardiogenic shock
Acute pulmonary edema
Unstable ventricular arrhythmias
Persistent Ischemia after TPA

**Initial drug therapy**
ASA 325 mg chewed, then 81 mg daily
NTG 0.4 mg SL every 5 min x 3 for pain
Metoprolol 5 mg IV every 5 minutes x 3, followed by 50 mg orally every 6 hours
Atorvastatin 80 mg orally stat and nightly
IV nitroglycerin, if persistent or recurrent pain (usual dose 5-200 mcg/min)
Discuss with Invasive Cardiologist before starting the following medications: *
*Clopidogrel* 300 mg stat, then 75 mg daily
*Enoxaparin* 1mg/kg every 12 hrs x throughout hospital stay or unfractionated heparin
Enoxaparin 30mg initial IV bolus may be given (not given at VCMC)
*GP IIb/IIIa inhibitor* (Tirofiban, Integrilin)
Captopril 6.25mg daily, start post MI day 2 or 3

**Post MI therapy**
Treadmill test prior to discharge if PCI not performed
High risk treadmill – consider early PCI and medical therapy
Low risk treadmill – continue medical therapy

**Long Term Medical therapy:**
ASA, clopidogrel, metoprolol, ACE inhibitor, statin, eplerenone if LVEF<0.4 AND either DM or CHF

**Risk Factor Management**

NSTEMI/Unstable Angina

Initial Evaluation
Focused history / exam
12 lead EKG
(If EKG is non-diagnostic repeat in 5 minutes.)

Low Clinical Risk
Low clinical pretest likelihood of CAD
New onset angina > 2 weeks < 2 months
Crescendo angina @ high workload
Atypical chest pain
Normal EKG
Normal Troponin I > 6 hours

Higher Clinical Risk
Refractory ischemic chest pain
Recurrent or persistent ST deviation
Ventricular tachycardia
Hemodynamic Instability
Heart Failure or EF<40%
Cardiogenic Shock
Elevated Troponin I level
h/o CABG or PCI
Age>65

ER or Outpatient Treatment
Treadmill

Intermediate Risk
Ischemic pain resolved
No arrhythmias
Stable hemodynamics
No acute ST-T changes
DOU Admission

High Risk
Refractory ischemic pain
Persistent ST Deviation
Ventricular Tachycardia
Hemodynamic Instability
Heart Failure/Cardiogenic Shock
Call invasive cardiology for PCI or ICU admit

Post MI therapy
Treadmill test prior to discharge if PCI not performed
High risk treadmill – consider early PCI + medical therapy
Low risk treadmill – continue medical therapy

Long Term Medical therapy:
ASA, clopidogrel, metoprolol, ACE inhibitor, statin,
eplerenone if LVEF<0.4 AND either DM or CHF

Risk Factor Management

Preference for Invasive Strategy (PCI) Over Conservative Strategy in ACS:
Refractory angina
High Risk ACS (accelerated tempo of ACS symptoms ≤ 48 hours; ongoing rest angina for at least 20 minutes or with ST ↓ > 0.5mm; CHF, S3 or ↑ rales, New or ↑ MR murmur, hypotension, age > 75, New LBBB, Sustained Ventricular Tachycardia; Troponin ≥0.1ng/mL, ↑CK-MB)
Intermediate Risk ACS (prior MI, PVD, CVD, CABG or ASA use; Rest angina≥20 min resolved with rest /NTG; nocturnal angina; severe/progressive angina ≤ 2 weeks; age>70; old pathologic Q waves; diffuse ST↓ <1mm; T wave inversions; TnI <0.1ng/mL; slight ↑ CK-MB)
TIMI Risk Score ≥ 3 (1 point for each variable: age≥65; ≥3 CAD Risk Factors; known coronary stenosis ≥50%; ST ↓ ≥0.5mm; ≥ 2 anginal events w/i 24 hours; ASA use within 7 days; elevated Troponin I or CK-MB)
PCI in last 6 months
LVEF < 0.4
New ST depression ≥ 0.5mm
High-risk findings on stress test

Initial drug therapy
ASA 325 mg chewed, then 81 mg daily
NTG 0.4 mg SL every 5 min x 3 for pain
Metoprolol 5 mg IV every 5 minutes x 3, followed by 50 mg orally every 6 hours
Atorvastatin 80 mg orally stat and nightly
IV nitroglycerin, if persistent or recurrent pain (usual dose 5-200 mcg/min)

Thrombolysis for Myocardial Infarction

Candidate for thrombolysis in acute myocardial infarction:

DEFINITE Candidate:
- Patient who presents with chest pain consistent with a diagnosis of acute ST segment elevation MI and at least 0.1 mV of ST segment elevation in at least 2 contiguous EKG leads with time to treatment 12 hours or less, age less than 75 years.
- Patient who presents with chest pain consistent with a diagnosis of acute MI and a Bundle Branch Block (obscuring ST-segment analysis) with time to treatment 12 hours or less, age less than 75 yrs

PROBABLE Candidate:
- Patient 75 years or older who presents with chest pain consistent with a diagnosis of acute ST segment elevation MI and at least 0.1 mV of ST elevation in at least two contiguous EKG leads with time to treatment 12 hours or less.

Contraindications to Thrombolysis in Acute Myocardial Infarction:

<table>
<thead>
<tr>
<th>Absolute contraindications</th>
<th>Relative Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous hemorrhagic stroke at any time</td>
<td>Chronic severe hypertension</td>
</tr>
<tr>
<td>Ischemic or embolic stroke within 3 months</td>
<td>Uncontrolled HTN&gt;180/110 mmHg on presentation</td>
</tr>
<tr>
<td><strong>EXCEPT ischemic stroke within 3 hours</strong></td>
<td>History of prior CVA or known intracerebral pathology not</td>
</tr>
<tr>
<td>Known intracranial neoplasm</td>
<td>covered in absolute contraindications</td>
</tr>
<tr>
<td>Active bleeding or bleeding diathesis (does not include menses)</td>
<td>Use of anticoagulants in therapeutic doses (INR &gt; 2)</td>
</tr>
<tr>
<td>Suspected aortic dissection</td>
<td>Major surgery (&lt;3 weeks)</td>
</tr>
<tr>
<td>Significant closed head or facial trauma within 3 months</td>
<td>Traumatic CPR or prolonged CPR &gt; 10 minutes.</td>
</tr>
<tr>
<td></td>
<td>Non compressible vascular puncture</td>
</tr>
<tr>
<td></td>
<td>Recent (within 2-4 weeks) internal bleeding</td>
</tr>
<tr>
<td></td>
<td>Pregnancy</td>
</tr>
<tr>
<td></td>
<td>Active peptic ulcer</td>
</tr>
<tr>
<td></td>
<td>For streptokinase/anistreplase: prior exposure (&gt; 5 days ago) or</td>
</tr>
<tr>
<td></td>
<td>prior allergic reaction to these agents</td>
</tr>
</tbody>
</table>

Procedure:
- Cardiologist consultation is required for initiation of this protocol.
- The Attending Staff Physician is to be present during the procedure until the patient's condition is deemed stable.
- O₂ via nasal cannula at 2 liters/min-to keep O₂ sat > 90%
- Continuous EKG monitoring looking for arrhythmias or ST changes
- Monitor blood pressure q 5 minutes - notify MD immediately if BP > 160/90 or < 100 systolic
- NPO except for meds and sips of water

Labs:
- Admission laboratory tests:
  - EKG, Chest X-Ray on admission
  - CBC, electrolytes, creatinine, glucose, cardiac enzymes, INR, aPTT, and stool guaiac
- Repeat laboratory tests:
  - EKG repeated after first dose of RETAPLASE and after second dose.
  - Repeat EKG at 4 hours, 12 hours post admission and daily for 3 days.
  - Cardiac Enzymes: Repeat at 4, 8, 12 hours after admission, then twice daily for 48 hrs.
  - aPTT per Heparin Protocol; check first aPTT 6 hours after Heparin bolus
Thrombolytic Agents:
- Retepalase (Retavase ®): Used at VCMC: Door-to-needle time < 30 minutes
- Start Heparin 60 units/kg (max 5000 units) bolus followed by a constant infusion of heparin at 12 micrograms per hour (max 1000 units/hr) for 24 hours.
- After heparin bolus, start Retepalase 10 units over 2 minutes via a dedicated IV line in which no other medication is being infused.
- Repeat 10 units of reteplase 30 minutes after initiation of the first bolus.
- If reteplase is given through the heparin line, flush with normal saline before starting the reteplase bolus.
- Check aPTT at 6 hours (target 1.5 to 2 times control or 50-75 seconds)
- Other thrombolytics that may be used include streptokinase, alteplase, or tenecteplase

Adjunctive therapies:
- Aspirin 325 mg po chewed x 1, then 81 mg po daily (may give per rectum if NPO)
- Beta Blocker 5 mg IV q 5 minutes x 3 doses, then 50 mg po q 6 hours 15 minutes after last IV dose
  - Caution advised with acute CHF, PR interval > 0.24, 2nd or 3rd degree AV block, significant bronchospasm, concurrent use of diltiazem or verapamil, severe peripheral vascular disease
  - Hold for SBP < 110, pulse < 60, PR interval > 0.24 seconds
- Atorvastatin 80 mg po x 1, then 80 mg po daily
- Clopidogrel 300 mg po x 1, then 75 mg po daily; Contact Interventional Cardiology prior to starting this medication, as open surgery is contraindicated for 5 to 7 days after even 1 dose of clopidogrel
- ACE inhibitor (ACEI) (e.g. captopril 6.25 mg po bid)
  - Start within 24 hours if SBP>160 mmHg; otherwise start at 48 hours
  - Caution advised with creatinine > 2.5, potassium > 5, bilateral renal artery stenosis, allergy to ACEI
- Nitroglycerine 10 mcg/min; increase by 5 mcg/min until clinical response or SBP < 110 mm Hg
  - Indicated for Acute MI + recurrent ischemia, persistence of CHF, or HTN
  - Nitroglycerine 0.4 mg sublingual prn anginal pain may also be given
- Atropine 1mg/kg IV bolus (max 100mg); repeat 0.5mg/kg q 10 minutes (max total dose 3mg/kg); then begin continuous lidocaine drip at 1-4 mg/minute
  - Indicated for hemodynamically significant ventricular tachycardia
- Morphine 2mg IV q 5 minutes prn pain; hold for SBP < 100
- Dopamine/norepinephrine (“Levophed”) per ICU protocol for SBP < 90 mmHg or MAP < 65 mm Hg
  - Must be given through a central venous catheter

Clinical Evidence of Reperfusion:
- Prompt relief of pain after thrombolysis
- Decrease in ST elevation
- “Reperfusion arrhythmias”: late PVC's or slow Ventricular Tachycardia

Complications:
- Intracerebral hemorrhage (high index of suspicion with acute hypertension, new/severe headache, nausea, vomiting, drowsiness/coma, focal neurologic deficits)

- Stop thrombolytic, anticoagulants (heparin), and antiplatelet agents
- Check stat aPTT, fibrinogen, CBC with platelets

Abbreviations:  Hb, hemoglobin; PRBCs, packed red blood cells; Plts, platelets; Fbg, fibrinogen; FFP, fresh frozen plasma
References:  ACC/AHA Guidelines 2004; e44-54.  Adapted with permission from Daniel Clark, MD and Evan Slater, MD.
Heart Failure

Clinical Manifestations

- Symptomatic
  - Left Heart
    - Congestive Symptoms: dyspnea on exertion, orthopnea, paroxysmal nocturnal dyspnea
    - Low Output: exertional fatigue, cold extremities, decreased renal perfusion
  - Right Heart: Jugular Venous Distension, Hepatomegaly, Ascites, Edema
- Systolic Dysfunction: Poor contraction
- Diastolic Dysfunction (“Heart Failure with Normal Systolic Dysfunction”): Inadequate Relaxation

Etiologies

- Coronary Artery Disease, HTN, valvular cardiomyopathy, myocarditis, infiltrative cardiomyopathy (amyloidosis, hemochromatosis, sarcoidosis), constrictive pericarditis, toxin-induced cardiomyopathy (anthracyclines, alcohol), beriberi, thyrotoxicosis or peripartum cardiomyopathy

Precipitants of Acute Decompensated Heart Failure (ADHF)

- MI, cardiac ischemia, ARF, hypertensive crisis, medication or dietary noncompliance, pulmonary disease, anemia, pulmonary embolus, thyroid disease, substance abuse or arrhythmia

Classifications

<table>
<thead>
<tr>
<th>New York Heart Association (NYHA) Classification (Class represents current clinical status)</th>
<th>AHA/ACC Stages of Heart Failure (Stage represents worst clinical status)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class 1 No symptoms</td>
<td>Stage A Asymptomatic/risk factors for heart failure present</td>
</tr>
<tr>
<td>Class 2 Symptoms with moderate exertion</td>
<td>Stage B Asymptomatic/systolic dysfunction is present</td>
</tr>
<tr>
<td>Class 3 Symptoms with activities of daily living</td>
<td>Stage C Symptomatic/heart failure present</td>
</tr>
<tr>
<td>Class 4 Symptoms at rest</td>
<td>Stage D Symptomatic/end-stage heart failure</td>
</tr>
</tbody>
</table>

Adapted from ACC/AHA clinical practice guidelines on chronic heart failure in JACC, 2005; 46: 1116-43.

Clinical Findings in Patients with Suspected Heart Failure

<table>
<thead>
<tr>
<th>Clinical Finding</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive LR</th>
<th>Negative LR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspnea on exertion</td>
<td>100%</td>
<td>17%</td>
<td>1.2</td>
<td>0</td>
</tr>
<tr>
<td>Paroxysmal nocturnal dyspnea</td>
<td>39%</td>
<td>80%</td>
<td>2</td>
<td>0.8</td>
</tr>
<tr>
<td>Prior MI</td>
<td>59%</td>
<td>86%</td>
<td>4.1</td>
<td>0.5</td>
</tr>
<tr>
<td>Laterally displaced cardiac apex (PMI)</td>
<td>66%</td>
<td>95%</td>
<td>16</td>
<td>0.4</td>
</tr>
<tr>
<td>Dependent edema</td>
<td>20%</td>
<td>86%</td>
<td>1.4</td>
<td>0.9</td>
</tr>
<tr>
<td>S3 gallop</td>
<td>24%</td>
<td>99%</td>
<td>27</td>
<td>0.8</td>
</tr>
<tr>
<td>Hepatoglandular reflux</td>
<td>33%</td>
<td>94%</td>
<td>6</td>
<td>0.7</td>
</tr>
<tr>
<td>Jugular venous distension</td>
<td>17%</td>
<td>98%</td>
<td>9.3</td>
<td>0.8</td>
</tr>
<tr>
<td>Pulmonary rales</td>
<td>29%</td>
<td>77%</td>
<td>1.3</td>
<td>0.9</td>
</tr>
<tr>
<td>CXR showing cardiomegaly and/or pulmonary edema</td>
<td>71%</td>
<td>92%</td>
<td>8.9</td>
<td>0.3</td>
</tr>
<tr>
<td>ECG with anterior Q waves or LBBB</td>
<td>94%</td>
<td>61%</td>
<td>2.4</td>
<td>0.1</td>
</tr>
<tr>
<td>BNP&gt;500 pg/mL</td>
<td>90% PPV for HF (NOT reliable in critical illness)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BNP&lt;50 pg/mL</td>
<td>98% NPV excluding HF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BNP&lt;100 pg/mL</td>
<td>90% NPV excluding HF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NT-proBNP&gt;450 pg/mL (&lt;50 yrs)</td>
<td>95% PPV for HF (NOT reliable in critical illness)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NT-proBNP&gt;900 pg/mL (50-75 yrs)</td>
<td>95% PPV for HF (NOT reliable in critical illness)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NT-proBNP&gt;1,800 pg/mL (&gt;75 yrs)</td>
<td>95% PPV for HF (NOT reliable in critical illness)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NT-proBNP&lt;300 pg/mL</td>
<td>98% NPV excluding HF</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Initial Evaluation
- ECG, Chest X-Ray, 2D-Echocardiogram
- Labs: CBC, Chem 7, liver & fasting lipid panels, Troponin I, BNP/NT-proBNP & SaO₂
  - Other causes of ↑ BNP: septic shock, acute PE, ARDS, Cor pulmonale, renal failure (CrCl<60 mL/min), cirrhosis, thyrotoxicosis, pulmonary hypertension, subarachnoid hemorrhage
- Monitor: Strict I’s/O’s, daily weights, potassium, BUN/creatinine

Systolic Heart Failure Therapy (see Cardiogenic Shock section if Blood Pressure is low)
Step 1: Preload Reduction
- IV loop diuretics: furosemide 20-40 mg, bumetanide 2-4 mg or torsemide 10-20 mg
  - Double diuretic dose every 15-20 minutes until effective diuresis obtained
  - “Effective diuresis”= enough diuresis to relieve symptoms
- Refractory diuresis
  - Add thiazide diuretic: chlorothiazide 500 mg IV or metolazone 10 mg PO 30 minutes prior to loop diuretic
  - Furosemide drip: give bolus dose then start 10-20 mg/hour
  - Ultrafiltration: use if venous access, SBP>85 mmHg & no ESRD or shock
- Vasodilators (if BP>100/60 mmHg)
  - Nitroglycerin: 0.2-10 mcg/kg/min

Step 2: Afterload Reduction
- Start after euvolemic state achieved with diuretics
- ACE Inhibitor (ACEI)(usually begin with low-dose Captopril if not much blood pressure to work with)
- Angiotensin Receptor Blocker (ARB)
- Hydralazine + Nitrates if contraindication to the above
- Consider nitroprusside if severe heart failure

Step 3: Positive Inotropy
- Digoxin improves symptoms and decreases hospitalizations but does not improve survival (may improve survival if Digoxin level < 1.1 ng/ml)

Step 4: Negative Inotropy
- Start Beta-blockers (metoprolol, carvedilol, or bisoprolol) once the patient is euvolemic
- May continue home Beta-blockers in acute CHF if warm and adequate blood pressure; if cold extremities or low blood pressure, hold Beta blockers

Step 5: HMG-CoA Reductase Inhibitor
Improves survival in ischemic and non-ischemic systolic heart failure

Step 6: Aldosterone Antagonist
- Improves survival for NYHA Class III-IV
- Spironolactone 25mg daily or Eplerenone 25-50mg daily
- Avoid if creatinine>2.5mg/dL (men) or >2mg/dL (women)
- Avoid if Potassium > 5mEq/L. Potassium level must be monitored, particularly with ARB/ACEI

Diastolic Heart Failure Therapy
Step 1: Decrease Preload (diuretics as with Systolic Heart Failure)
Step 2: Control Systolic and Diastolic hypertension (ACEI,ARB,Beta-blocker,diltiazem,verapamil)
Step 3: Slow heart rate in Atrial Fibrillation/ Atrial Flutter
Step 4: Control Ischemia
Indication for Heart Transplantation
- Refractory CHF, ischemia or arrhythmias despite optimal medical therapy
- Poor candidates: pulmonary hypertension, sepsis, CA, advanced lung disease, cirrhosis, ESRD, substance abuse, age >60 or noncompliance

Prognosis in Acute Decompensated Heart Failure
- CART risk analysis-risk factors: BUN ≥43 mg/dL; creatinine ≥2.75 mg/dL; SBP < 115
  - In-hospital mortality: 22% if all 3 risk factors present; 2% if no risk factors present
- Pre-discharge BNP: >700 has 15x ↑ 6 mo. death or readmissions vs. <350 pg/mL
- Initial Troponin I ≥1 mcg/L has 8% in-house mortality vs. 2.7% if Troponin I normal

Non-pharmacologic interventions for Heart Failure management
- 2 gram/day sodium restriction
- Maintain BP < 120/80 mmHg
- Smoking Cessation
- Drink Alcohol in Moderation (or stop alcohol altogether if contributes to CHF etiology)
- Weight loss for obese patients
- Consider fluid restriction if Na < 130 (2 Liters/day) or Na < 125 (1.5 Liters/day)
- Education: Diet, medications, exercise, lifestyle modification

Devices to Consider in Chronic Heart Failure
- ICD if LVEF ≤0.3 with NYHA ≥ class 2 CHF on optimized medical therapy OR any history of cardiac arrest, VF or unstable VT and expected survival more than 1 year.
- Biventricular pacemaker if LVEF ≤0.35 and NYHA ≥ class 3 CHF on optimal med therapy, QRS duration ≥120 milliseconds and expected survival more than 1 year.

Forrester Acute Decompensated Heart Failure (ADHF) Diagram

Cardiogenic Shock

Definition:
- End-organ hypoperfusion due to cardiac failure
  - may be thought of as Congestive Heart Failure with hypotension/hypoperfusion
- Persistent Hypotension
  - Systolic Blood Pressure <80 to 90mmHg or mean arterial pressure 30mmHg lower than baseline
- Severe Reduction in Cardiac Index
  - <1.8 Liters/min/m² without support or <2.0 to 2.2 Liters/min/m² with support
- Elevated Filling Pressure (LVEDP>18mmHg or RVEDP>10 to 15mmHg)

Etiologies:
- Ischemia/ischemic cardiomyopathy
  - Cardiogenic shock complicates 5-8% of STEMI and 2.5% of NSTEMI
- Hypertrophic cardiomyopathy
- Myocarditis, Pericarditis
- Acute valvular regurgitation (e.g. endocarditis, chordal rupture)
- Severe AI, Stress in the face of significant aortic or mitral stenosis
- Cardiac Tamponade
- Massive Pulmonary Embolism
- Myocardial Depressant Factor Release in Sepsis

Pathophysiology:
- LV Pump Failure is the primary insult in most forms of Cardiogenic Shock
- RV Pump Failure is the cause of ~5% of Cardiogenic Shock complicating MI
- Neurohormonal compensatory systems often perpetuate/augment cardiogenic shock
  - (e.g. sympathetic, renin-angiotensin-aldosterone, endothelin, arginine, cytokine systems)

Diagnosis:
- See The Estimation of Effective Intravascular Volume in the ICU
- Swan-Ganz catheterization may be helpful in the diagnosis, but is not essential.

Treatment:
- Inotropic and vasopressor agents, used in the lowest possible doses
  - Higher doses are associated with poorer survival: inotropes increase myocardial ATP consumption such that short-term hemodynamic improvement occurs at the cost of increased oxygen demand when the heart is already failing and supply is already limited.
  - Dopamine is often the initial therapy of choice as it increases the amount of squeeze (inotropy) for any given preload (See Starling Curve, page 22)
  - Dobutamine is the medication of choice as it reduces afterload and increases inotropy/chronotropy, allowing the heart to unload in a forward direction and improve systemic perfusion
    - The down side of Dobutamine is worsening hypotension, either from the heart being unable to increase its cardiac output (CO) enough to compensate for the reduction in systemic vascular resistance (SVR), or when the patient was not in cardiogenic shock to begin with (17% of cases of ‘cardiogenic shock’ in 1 study were in fact in septic shock)
    - Lowering systemic vascular resistance can also worsen coronary perfusion in some cases.
  - Coronary reperfusion is indicated in the face of Acute Coronary Syndrome (SHOCK Trial: 13% absolute decrease in mortality at 1 year with early revascularization)
  - Intra-aortic Balloon Pump may be indicated for refractory cases (not done at VCMC)

### Net effects of Agonizing Receptors:

| Beta 1 Receptor: | Cardio-specific, Positive Inotrope, Positive Chronotrope (leading to increase in stroke volume and heart rate, and subsequently increases Cardiac Index) |
| Beta 2 Receptor: | Smooth muscle relaxation in lung and blood vessels, Decreases Systemic Vascular Resistance |
| Alpha Receptor: | Peripheral vasoconstriction, Increases Systemic Vascular Resistance (SVR) |

| Dopamine Receptor: | Increases Renal Blood Flow |
| Vasopressin Receptor: | Vasocostriction |


### Definitions:

- **Inotropy:** Strength of contraction (positive inotropy = increased contraction)
- **Chronotropy:** Heart rate (positive chronotropy = increased heart rate)
- **Lusitropy:** Amount of relaxation of the heart (positive lusitropy = better relaxation)

---

### Medication

<table>
<thead>
<tr>
<th>Medication</th>
<th>Usual Dose</th>
<th>Indications</th>
<th>Receptors Agonized</th>
<th>Hemodynamic Effects</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Norepinephrine (Levophed)</td>
<td>5 to 20 mcg/kg/min</td>
<td>Treatment of choice for “warm shock” (vasodilatory component of septic shock); CHF</td>
<td>Alpha &gt; Betal</td>
<td>Positive vasoconstrictor, positive inotrope, net neutral chronotrope.</td>
<td>“Levophed leaves ‘em dead” is an old adage: be sure the patient has received adequate volume resuscitation when using Norepinephrine.</td>
</tr>
<tr>
<td>Dopamine-Low Dose</td>
<td>&lt;5 mcg/kg/min</td>
<td>No indications (disproved for ARF)</td>
<td>Dopamine</td>
<td>Dilates afferent renal arterioles</td>
<td>Dopamine dose is often limited by tachycardia (120 is around the maximal desired heart rate). Dopamine may be administered by peripheral IV for a short time while obtaining central access. Avoid with tricyclic overdoses and with serotonin syndrome</td>
</tr>
<tr>
<td>Dopamine-Moderate Dose</td>
<td>5-20 mcg/kg/min</td>
<td>Treatment of choice for shock of unknown etiology, 1st or 2nd line for septic shock; may also be used in septic shock when the patient is “relatively bradycardic”; Effective for symptomatic bradycardia ~90% of the time</td>
<td>Dopamine, Beta 1</td>
<td>Positive Inotrope, Positive Chronotrope</td>
<td></td>
</tr>
<tr>
<td>Dopamine-High Dose</td>
<td>≥20 mcg/kg/min</td>
<td></td>
<td>Dopamine, Beta 1, Alpha</td>
<td>Positive Inotrope, Positive Chronotrope, and Vasocostrictor</td>
<td></td>
</tr>
<tr>
<td>Vasopressin “Low Dose”</td>
<td>0.01-0.04 U/min</td>
<td>Refractory Shock (“catecholamine resistant” shock)</td>
<td>Vasopressin</td>
<td>Vasoconstriction</td>
<td></td>
</tr>
<tr>
<td>Epinephrine</td>
<td>5-20 mcg/kg/min</td>
<td>First line for Anaphylactic Shock, May be used for Refractory Shock cases</td>
<td>Beta = Alpha</td>
<td>Positive Inotrope, Vasoconstrictor</td>
<td></td>
</tr>
<tr>
<td>Phenylephrine</td>
<td>100-180 mcg/kg/min</td>
<td>Vasodilatory hypotension (not 1st line)</td>
<td>Pure Alpha</td>
<td>Vasoconstrictor</td>
<td>Useful for spinal shock May cause reflex bradycardia</td>
</tr>
<tr>
<td>Isoproterenol</td>
<td>0.5-5 mcg/min</td>
<td>Positive Inotropy/ Chronotropy</td>
<td>Pure Beta</td>
<td>Positive Inotrope/ Positive chronotrope</td>
<td></td>
</tr>
</tbody>
</table>

**“Perfusors”**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Usual Dose</th>
<th>Indications</th>
<th>Receptors Agonized</th>
<th>Hemodynamic Effects</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dobutamine</td>
<td>20 mcg/kg/min</td>
<td>Cardiogenic Shock with high systemic vascular resistance; Vasoconstrictive phase of septic shock (“Cold shock”)</td>
<td>Beta-1, Beta-2</td>
<td>Positive inotrope, positive chronotrope, vasodilator</td>
<td>1 option during “Goal Directed Therapy” for septic shock when CVP is 8-12 but Svo2 is &lt;70%</td>
</tr>
<tr>
<td>Milrinone</td>
<td>See →</td>
<td>Congestive Heart Failure (not 1st line) Also decreases SVR</td>
<td></td>
<td>Positive Inotrope</td>
<td>Start with 50 mcg/kg over 10 min then 0.375-0.75 mcg/kg/min</td>
</tr>
</tbody>
</table>

### Other Vasoactive Agents

<table>
<thead>
<tr>
<th>Medication</th>
<th>Usual Dose</th>
<th>Indications</th>
<th>Receptors Agonized</th>
<th>Hemodynamic Effects</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitroglycerine</td>
<td>5-100 mcg/min</td>
<td>CHF, Acute Coronary Syndrome</td>
<td></td>
<td>Reduces Preload</td>
<td>The use of an arterial line is STRONGLY encouraged Usual dose 0.3 mcg/kg/min</td>
</tr>
<tr>
<td>Nitroprusside “Nipride”</td>
<td>0.1-1.0 mcg/kg/min</td>
<td>Hypertensive crisis, potentially subarachnoid hemorrhage</td>
<td></td>
<td>Decreases Systemic Vascular Resistance</td>
<td></td>
</tr>
</tbody>
</table>
Hypertensive Crisis (Hypertensive Emergency)

Definition
- Markedly elevated blood pressure associated with acute end-organ damage
  - Examples: hypertensive encephalopathy (headache, confusion and papilledema); CHF; acute coronary syndrome; Acute Renal Failure; aortic dissection; ischemic or hemorrhagic stroke; pre-eclampsia or eclampsia, microangiopathic hemolytic anemia
  - Treatment of hypertensive emergency is to cautiously reduce the Mean Arterial Pressure (MAP) by 25% with IV meds in the ICU
- Distinguish from hypertensive urgency: “severely elevated blood pressure” (“severe elevation” not clearly defined; varies from 180/110 to 220/120 depending on the patient’s baseline blood pressure), but no end-organ damage
  - May treat with oral agents and manage with close follow-up as an outpatient, reducing blood pressure with oral medications gradually over 24 to 48 hours
- May be difficult to determine ‘chicken and egg’ – hypertension as a cause or hypertension as a symptom of an underlying illness/ stress response

Management of Hypertensive Emergencies

<table>
<thead>
<tr>
<th>Medication</th>
<th>IV Dosages</th>
<th>Indications</th>
<th>Cautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitroprusside†</td>
<td>0.25-10 mcg/kg/min</td>
<td>Encephalopathy, CHF, or refractory HTN in stroke</td>
<td>Cyanide or thiocyanate toxicity‡</td>
</tr>
<tr>
<td>Labetalol</td>
<td>20-80 mg IV q10 min then 0.5-2 mg/min IV</td>
<td>Encephalopathy, ACS, aortic dissection, acute stroke, pre-eclampsia or pheochromocytoma</td>
<td>Bradycardia or heart block</td>
</tr>
<tr>
<td>Nitroglycerin</td>
<td>17-1,000 mcg/min</td>
<td>ACS, CHF</td>
<td>Headache (HA)</td>
</tr>
<tr>
<td>Nicardipine</td>
<td>5-15 mg/hour</td>
<td>Acute stroke, pre-eclampsia, or sympathomimetic crisis</td>
<td>Tachycardia</td>
</tr>
<tr>
<td>Hydralazine</td>
<td>10-20 mg IV q20 min</td>
<td>Pre-eclampsia, CHF</td>
<td>Tachycardia, HA</td>
</tr>
<tr>
<td>Enalaprilat</td>
<td>0.625-1.25 mg IV q6h</td>
<td>CHF</td>
<td>↓ renal function, ↑ K</td>
</tr>
<tr>
<td>Esmolol</td>
<td>500 mcg/kg load then 50-300 mcg/kg/min</td>
<td>ACS, aortic dissection or adjunct for pheochromocytoma</td>
<td>Bradycardia, or heart block</td>
</tr>
<tr>
<td>Phentolamine</td>
<td>5-15 mg IV q5 min (max 30 mg)</td>
<td>Pheochromocytoma, or sympathomimetic crisis</td>
<td>Add β-blocker after initiation for pheo</td>
</tr>
</tbody>
</table>

† - consideration should be given to the use of continuous blood pressure monitoring with an arterial line
‡ - risk higher with prolonged use >24 hours and with severe renal or hepatic impairment
Adapted from Chest, 2007; 131: 1949

Management of Hypertensive Urgencies and Emergencies in the Face of Sympathomimetic Agents:

In the face of sympathomimetic activation (e.g. Cocaine, methamphetamines, phencyclidine, MAO inhibitors in the face of tyramine-containing foods, pheochromocytoma), Beta blockers should be avoided for the concern for unopposed alpha adrenergic stimulation, coronary vasospasm, and paradoxical increase in blood pressure. Similarly, the alpha-beta blocker labetalol should also be avoided for the same concern. In the face of Myocardial Infarction and sympathomimetics, the treatments of choice are nitroglycerine and benzodiazepines. Beta blockers are to be avoided as above. Calcium channel blockers have been associated with an increase in mortality as well and should not be used.

Acute Pulmonary Embolism

Risk Factors for Venous Thromboembolic Events (VTE)
- Advanced Age >50
- Prolonged Immobility, Recent Prolonged Travel
- Major Surgery in last 4 weeks
- Recent Trauma
- Central Venous Catheter
- Previous Venous Thromboembolism
- Medical Conditions: Severe burns, active cancer, stroke with paresis, inherited thrombophilia, polycythemia, myeloproliferative disorder, obesity, CHF, nephrotic syndrome, inflammatory bowel disease, acute MI, acute respiratory failure, sickle cell disease, paroxysmal nocturnal hemoglobinuria and pregnancy
- Medications: tamoxifen, raloxifene, thalidomide, lenalidomide, darbepoetin, epoetin alfa, bevacizumab, hormone replacement therapy or systemic chemotherapy

Evaluation for Possible Pulmonary Emboli
- See Diagram Page 39

Treatment Options for Pulmonary Emboli
- Unfractionated heparin (UFH) 80 units/kg bolus→18 units/kg/hr titrated to PTT 1.5-2.5x upper limit of normal (preferred therapy over LMWH if concern for massive PE and considering thrombolytic therapy)
- Low Molecular Weight Heparin (LMWH), i.e. Enoxaparin 1 mg/kg SQ q12h or 1.5 mg/kg subcutaneous daily
  - AVOID if CrCl<15 mL/min; dose adjustment required for CrCl 15-30 mL/min
  - Follow anti-Factor Xa levels to adjust dosing for patient weight >155 kg
- Fondaparinux 5 mg, 7.5 mg or 10 mg subcutaneous daily (based on patient’s weight) (avoid with Creatinine Clearance <30)
- Warfarin, with goal INR 2-3
  - Overlap warfarin and LMWH/heparin/fondaparinux ≥5 d and until INR 2–3 for 24 hours
  - For patients with active cancer, do NOT use Warfarin; use LMWH or fondoparinux instead
- Direct thrombin inhibitor argatroban or fondaparinux indicated for patients with Heparin-Induced Thrombocytopenia (see page 128)
- Early ambulation is recommended for patients with DVT on anticoagulation.
- Inferior vena cava filter if warfarin contraindicated or if recurrent pulmonary embolus on therapeutic doses of anticoagulation.
- Graded compression stockings 30-40 mmHg at the ankle for ≥2 years after leg DVT

Advanced Therapies for Massive Pulmonary Emboli
- Consider IV thrombolytics in a hemodynamically unstable patient with a massive PE (see page 38)
- Consider catheter-directed thrombolysis for a massive, limb-threatening iliopelvic DVT with symptoms <14 days, good functional status, and life expectancy ≥1 year
- Pulmonary embolectomy is an option for patients at high risk of bleeding

Thrombolysis for Massive Pulmonary Embolism

Approximately 5% of patients with pulmonary embolism will experience hemodynamic compromise due to massive Pulmonary Embolism

Generally Accepted Indications:
- Cardiogenic shock (systolic blood pressure <90 mm Hg with end organ hypoperfusion) associated with massive acute Pulmonary Embolism (grade IB evidence per American College of Chest Physicians 2008 Guidelines = strong recommendation, moderate quality evidence)
  - For patients presenting as above, mortality rate 6.2% with thrombolytics vs. 12.7% with heparin alone (not quite statistically significant due to small sample size)
- During CPR for cardiac arrest if high suspicion for Pulmonary Embolism as the cause of the arrest (though studies have not borne out mortality benefit, survival in this situation is often very low and study sample would need to be much larger to detect any differences)

Controversial Indications:
- Hypotensive patients (SBP < 90 mm Hg) without evidence of shock
- Evidence of right heart strain or failure (up to 40-50% of patients with Pulmonary Emboli)
- In selected highly compromised patients who are unable to receive thrombolytic therapy because of bleeding risk, or whose critical status does not allow sufficient time for systemic thrombolytic therapy to be effective, we suggest use of interventional catheterization techniques if appropriate expertise is available (grade 2C = weak recommendation, weak or very weak evidence).
- Severe hypoxemia (has not been adequately studied)

### Thrombolysis: Absolute Contraindications

<table>
<thead>
<tr>
<th>History of intracranial hemorrhage, known intracranial neoplasm, arteriovenous malformation, or aneurysm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Significant head trauma or active internal bleeding</td>
</tr>
<tr>
<td>Known bleeding diathesis</td>
</tr>
<tr>
<td>Intracranial or intraspinal surgery within 3 months</td>
</tr>
<tr>
<td>Cerebrovascular accident within 2 months</td>
</tr>
</tbody>
</table>

### Thrombolysis: Relative Contraindications

<table>
<thead>
<tr>
<th>Recent internal bleeding, surgery or organ biopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recent trauma, including cardiopulmonary resuscitation</td>
</tr>
<tr>
<td>Venipuncture at noncompressible site</td>
</tr>
<tr>
<td>Uncontrolled hypertension</td>
</tr>
<tr>
<td>High risk of left heart thrombosis</td>
</tr>
<tr>
<td>Diabetic retinopathy</td>
</tr>
<tr>
<td>Pregnancy</td>
</tr>
<tr>
<td>Age &gt; 75 years</td>
</tr>
</tbody>
</table>

### Thrombolysis: Suggested Regimens:

- Streptokinase 250,000 units over 30 min, then 100,000 units/h over 24 h
- Urokinase 4,400 units/kg over 10 min, then 4,400 units/kg/h over 12 h
- Recombinant Tissue Plasminogen Activator (rt-PA) 10 mg bolus, then 90 mg over 2 hours
  - Despite the lack of data proving superiority, the American College of Chest Physicians (ACCP) guidelines suggest using the thrombolytic regimen with the shortest infusion time, which is currently rt-PA.

### Bleeding Risks:

- Meta-analysis of 847 patients
  - Risk of major bleeding 9% with thrombolytics vs. 5.7% with anticoagulation alone
  - Bleeding score developed: h/o bleeding = 2 points; creatinine > 1.2 mg/dL or anemia = 1.5 points; PE, cancer, or age >75 = 1 point
    - High risk for bleeding in patients with a score of > 4; low risk for bleeding = 0 points
- Most life-threatening complication = Intracranial hemorrhage in an estimated 3% of patients treated with systemic thrombolitics for pulmonary embolism

Clinical features of a pulmonary embolus: dyspnea, pleuritic chest pain, hemoptysis, tachycardia, tachypnea, fever or pleural rub

Low PTP and D-dimer* normal excludes a PE
Intermediate-high PTP or D-dimer* high

M-CTPA

Positive
PE present
Low-intermediate PTP
DUS of legs and serial M-CTPA or pulmonary angiogram
PE excluded

Intermediate probability
High PTP
Low PTP
DUS
Inter-high PTP
DUS
Intermediate PTP
DUS
Low PTP
DUS
Low probability
Inter-high PTP
DUS
Low PTP
DUS
Intermediate probability

High PTP
Low PTP
DUS


M-CTPA=multidetector CT pulmonary angiogram, DVT=deep venous thrombosis, VTE=venous thromboembolism, DUS=duplex ultrasound, neg= negative and pos = positive

* - D-dimer ≤ 500 ng/mL is normal
‡ - M-CTPA positive, PE present; negative, PE excluded.

Return to Table of Contents
Cardiac Tamponade

Definition
- “A hemodynamic condition characterized by equal elevation of atrial and pericardial pressures, an exaggerated inspiratory decrease in arterial systolic pressure (pulsus paradoxus), and arterial hypotension (often a late finding).”
- Beck’s Triad: Elevated Jugular Venous Pressures, Muffled Heart Sounds, and Hypotension
- Kussmaul’s Sign: Jugular Venous Distension during inspiration (reversal of normal pattern of decreasing jugular venous pressure during inspiration) usually seen in constrictive pericarditis

Etiologies: Transudative vs. Exudative vs. Blood
- Transudative: Pericarditis, CHF, Myocardial Infarction, Valvular Disease
- Exudative: Pericarditis, Uremia, TB, neoplasia, connective tissue disease, infection
- Blood: CHF, post-operative after cardiac surgery, cardiac rupture complicating acute MI, rupture of a dissecting hematoma of the proximal aorta, complication of percutaneous coronary intervention (very rare)

Pathophysiology
- Elevated intrapericardial pressure exerted on the heart throughout the cardiac cycle, decreasing venous return
- Pericardial pressure and right atrial pressure are elevated above normal and are equal to each other
- Extreme tamponade becomes fatal when venous pressure cannot increase to equal the pericardial pressure and maintain circulation.
- In severe cases, diminution of myocardial perfusion is aggravated by direct compression of the epicardial coronary arteries further impairing ventricular systolic function.

Spectrum of Clinical Manifestations
- Cardiac tamponade may be acute or chronic and should be viewed hemodynamically as a continuum ranging from mild (pericardial pressure of 10 mm Hg) to severe (pericardial pressure of 15 to 20 mm Hg).
- Mild cardiac tamponade is frequently asymptomatic, whereas moderate tamponade and especially severe tamponade produce precordial discomfort and dyspnea, and can progress to cardiovascular collapse and death
- As little as 50ml of acute fluid in the pericardial space can cause clinically significant tamponade, whereas a much larger quantity of fluid built up over time can be relatively asymptomatic
- Cardiac tamponade should be suspected in a patient with recent chest trauma who seems to be in shock, especially when the venous pressure is elevated.

Workup
- Physical Exam
  - Beck’s Triad as described as above
  - Pulsus paradoxus
    - Signifies an inspiratory fall in blood pressure exceeding 10mmHg (quantified by using a manual blood pressure cuff to measure the difference between when heart tones are appreciated but disappear during inspiration and when the heart tones no longer disappear)
    - Pulsus paradoxus is neither sensitive nor specific for tamponade
    - COPD, asthma, and pulmonary embolism are all non-tamponade causes of elevated pulsus paradoxus
  - Chest X-Ray

Return to Table of Contents
Bulbous or boot-shaped cardiac shadow

Echocardiogram
- The diagnostic modality of choice for diagnosis of pericardial effusions and tamponade
- Identification of Effusion: Size of “echo-free space” between the parietal and visceral pleurae:
  - Small effusions have an echo-free space of 5 mm
  - Moderate-sized effusions range between 5 and 10 mm and are circumferential
  - Large effusions are larger than 10 mm
  - Fluid adjacent to the right atrium is an early sign of pericardial effusion

Echocardiographic evidence of Tamponade
- Right ventricular diastolic collapse signifies that pericardial pressure exceeds early diastolic Right Ventricular Pressure; may not be present with Right Ventricular Hypertrophy
- Right atrial diastolic collapse is nearly 100% sensitive for tamponade but less specific
- Duration of right atrial collapse exceeding one third of the cardiac cycle increases specificity without sacrificing sensitivity
- Left atrial diastolic collapse is seen in about 25% of patients and is very specific for tamponade
- LV collapse is less common because the wall of the LV is more muscular
- The absence of any cardiac chamber collapse has a high negative predictive value (92%) for tamponade (meaning that in 8% of cases, there is tamponade without any chamber collapse!)

Clinically significant tamponade is a clinical diagnosis and “echocardiographic signs of tamponade” are not by themselves an indication for pericardiocentesis.

CT and MRI may also visualize pericardial effusions but are not the diagnostic modalities of choice

Management
- Pericardiocentesis
  - Indications for pericardiocentesis:
    - Clinical Evidence of Cardiac Tamponade
    - Suspicion for purulent pericarditis (bacterial, tuberculous, fungal)
    - Persistent (>3 months) large or progressive pericardial effusion (to make diagnosis)
  - Removal of small amounts of pericardial fluid (about 50 mL) produces considerable symptomatic and hemodynamic improvement because of the steep pericardial pressure–volume relation.
  - Unless there is concomitant cardiac disease or coexisting constrictive pericarditis, removal of all the pericardial fluid normalizes pericardial, atrial, ventricular diastolic, and arterial pressures and cardiac output.
  - With Echocardiographic guidance, pericardiocentesis carries a ~1.2% major complication rate

- Surgical Pericardial Window via subxiphoid incision, video-assisted thoracoscopy, or thoracotomy may be indicated

- When circumstances are deemed life-threatening, an immediate therapeutic trial of rapid infusion of fluid and diagnostic pericardiocentesis should be attempted. Otherwise, pericardiocentesis should be delayed until the presence of significant pericardial fluid can be demonstrated by prompt echocardiography.

Aortic Dissection

Clinical Presentation
- Acute onset of sharp or tearing, anterior chest pain radiating to interscapular area
- Clinicians suspected aortic dissection only 15-43% of the time.
- Associated signs: diastolic murmur (aortic insufficiency, 31.6%); pulse deficit (15.1-38%); focal neurological deficits (stroke, 4.7-17%); paraplegia (3-5%); acute limb ischemia (6-28%); acute MI (3.2%); and cardiac tamponade (4-25%)
- Associated symptoms: syncope (8-13%); dyspnea (heart failure from acute aortic insufficiency, 3-9%); and abdominal pain (mesenteric ischemia, 3.7%)

Risk Factors
- Age>50, HTN, bicuspid aortic valve, Marfan syndrome, Ehlers-Danlos syndrome, Turner syndrome, Giant cell arteritis, syphilitic aortitis, pregnancy, coarctation of aorta, adult polycystic kidney disease, Bechet’s disease, Takayasu’s arteritis, blunt chest trauma, cardiac or aortic surgery or cardiac catheterization

Work-up
- Systolic blood pressure difference between arms ≥ 20mmHg
- Chest x-ray: widened mediastinum in 44-80% and abnormal aortic contour (56-84%)
- CT scan of aorta with IV contrast (95% sensitivity, 90% specificity)
- MRI with contrast (98% sensitivity, 98% specificity)
- Catheter aortogram (90% sensitivity, 95% specificity)
- Transesophageal echocardiogram (TEE) (98% sensitivity, 91% specificity)
- Labs: chemistry panel, CBC, PT, PTT, Troponin I and EKG

Treatment of Acute Aortic Dissection
- Labetalol or esmolol drip titrated to keep SBP≤110 mmHg and HR<60
- Nitropresside drip can be added for blood pressure control if necessary
- Surgical repair or endovascular treatment indicated for all Stanford Type A AD patients
- Endovascular and med treatment preferred for appropriate Stanford Type B AD patients

Borrowed with permission from Joseph Esherick, MD.
An Approach to the Inpatient Management of Hypertension

1. **Determine the patient’s baseline blood pressure**
2. **Confirm the blood pressure reading** (manual check is preferable)
3. **Review Medications**, including home medications that may have been withheld
4. **Look for common underlying causes of hypertension in inpatients** by examining the patient:
   - Blood pressure in both arms to rule out coarctation or dissection
   - Heart and Lung Exam
   - Abdominal bruits?
   - Carotid bruits?
   - Edema?
5. **Rule out hypertensive emergency (acute target organ damage)** by history & physical:
   - no chest pain
   - no headache or altered mental status
   - no sign of increased intracranial pressure (check fundoscopic exam)
   - Check EKG, Chem 7, CBC, UA to rule out target organ damage
6. **Oral Regimens for Treatment of Hypertension**:
   - **Clonidine** 0.1mg or 0.2mg po initially, followed by 0.1mg every 45-60 minutes to a max of 0.8mg (**Note: Clonidine may slow resting heart rate**)
   - **Captopril** 25mg po q 1 hour to a maximum of 100mg (**Note: Caution with elevated creatinine (>1.4) or elevated potassium**)
   - **Labetalol** 200mg to 300mg po initially

**Properly obtained blood pressure:**
- Patient sitting at rest for at least 5 minutes
- Arm supported at level of heart
- No cigarettes/caffeine within 30 minutes
- Cuff bladder encircling at least 80% of arm
- No clothing under cuff

**Common Underlying Causes of Hypertension in the Inpatient** (not an exhaustive list):
- pain or anxiety
- alcohol withdrawal or other drug withdrawal
- physical stress of sepsis, infection, or other medical condition
- blood loss (before the patient's blood pressure goes down)
- elevated intracranial pressure
- renal failure
- too much Sodium in their IV Fluids and/or diet
- Drug interactions (e.g. Rifampin increases clearance of beta blockers and verapamil; antacids may decrease absorption of ACE inhibitors and diuretics; etc.)
- Autonomic responses: bladder distention, constipation, hypoglycemia, spinal cord injury

If acute findings are present, treat for hypertensive emergency (transfer to ICU, IV Blood pressure medications, etc.)

**Return to Table of Contents**
## An Approach to the Inpatient Management of Hypertension (continued)

### Sublingual Medications
- **Captopril** sublingual at same dose as po
- **Clonidine** sublingual at same dose as po

### Parenteral Regimens for Treatment of Hypertension in Patients who are NPO:
- **Metoprolol** 5mg IV at variable dosing intervals, to desired effect (usually given in the ED with acute MI, 5mg IV q 15 minutes x 3) (**Note: hold for Pulse < 60**)
- **Labetalol** 20mg IV over 2 minutes x 1; usual dose 40-80mg IV q10 minutes prn; Max 300mg IV; may be given as a drip, 0.4-1.0mg/kg/hr, max of 3mg/kg/hr) (**Note: hold for Pulse < 60**)
- **Diltiazem** 10-20mg IV bolus, followed by 5-15mg/hr. may repeat IV bolus 25mg x 1 (**Note: would **AVOID** IV Verapamil for increased risk of hypotension and AV Nodal Blockade; hold for pulse<60**)
- **Hydralazine** 5mg IV q 6 hours; Max dose 15mg IV q 6 hours

### Alternative Regimens:
- **Vasotec** (enalaprilat) 0.625-1.25mg IV q 6 hours; onset 15-60 minutes; has variable effect on blood pressure
- **Diuretics**: furosemide, Diuril (chlorothiazide)
- **transdermal Clonidine Patch** (**Note: this may take 1-2 days to achieve effect**)

### Anti-hypertensives and their mechanisms of action

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preload Reduction</td>
<td>Nitrates, diuretics</td>
</tr>
<tr>
<td>Afterload Reduction</td>
<td>ACE inhibitors, hydralazine, dihydropyridine Calcium Channel Blockers (i.e. all calcium channel blockers that end in ‘-ine’), nitroprusside, minoxidil</td>
</tr>
<tr>
<td>Negative Inotropy/Chronotropy</td>
<td>Beta blockers, non-dihydropyridine Calcium Channel Blockers (i.e. diltiazem, verapamil), clonidine (via central alpha-2 agonism)</td>
</tr>
<tr>
<td>Other</td>
<td>Aliskiren (renin inhibitor)</td>
</tr>
</tbody>
</table>

Harrison’s Principles of Internal Medicine. 16th Edition. 2005
PULMONARY

Airway Emergencies, General Concepts

Anticipate difficulties early, and have the appropriate support around you (e.g. your ICU attending, and for higher risk patients, anesthesiologist and/or surgeon, but call your ICU attending first). In a pinch, there is always an ER attending you could ask to join you in the ICU. Use your co-residents on-call as support as well.

If any doubt exists concerning the ability to ventilate the patient by bag and mask (i.e. morbid obesity), caution should be used in giving a sedative hypnotic agent that may cause the patient to become apneic or lose the airway reflexes. Paralytic agents should never be given if there is doubt as to the ability to ventilate the patient. Airway management in this case should be performed with the patient awake by an experienced anesthesiologist or critical care physician. Cricoid pressure should be used in all situations when the patient is known to have a “full stomach” or if there is doubt about the patient’s NPO status. Although difficult airways are not always predictable, if there is any concern, you should be prepared with a plan B, C, etc., with all of the necessary equipment readily available to achieve those plans.

Be sure that suction is available and that your laryngoscope is working prior to attempting to intubate. After 30 seconds of trying to intubate the patient without success, consider “bagging the patient back up” and trying again. As above, 2 attempts with the same technique is a general rule unless the clinical situation makes the procedure too high-risk. This is up to the discretion of the attending.

BiPap should only be used on awake patients who could pull the mask off should they vomit, to avoid aspiration. If your patient needs to be intubated, intubate them. Mortality goes up if you use BiPap on someone who needs intubation.

If your ET Tube is coming out and needs advancing, or for large cuff leaks, consider using a “Cook exchanger” to advance the tube (Seldinger-type technique). Alternatively, the placement of a laryngoscope through the endotracheal tube may be plan B, with advancing of the endotracheal tube over the laryngoscope once tracheal rings are visualized. Be sure the patient is sedated and paralyzed.

Think ahead. When your Etomidate and Succinylcholine have worn off and the patient is waking up, what medications will you be using to sedate the patient? Order ahead. If the patient is septic and hypotensive, ketamine as an IV infusion (+/- along with midazolam pushes) are generally used for ventilator sedation – this order has to be faxed to the pharmacy and mixed, and it takes time. In the interim, 100mg of Ketamine (slowly over 1-2 minutes to avoid hypotension) with 1 to 2 mg Versed is reasonable to administer in bolus form. Avoid Ketamine if you are concerned about elevated intracranial pressure or elevated intraocular pressure. (see page 186 regarding more details of sedatives)

Avoid non-depolarizing neuromuscular blockers in myasthenia gravis (or use the shortest-acting non-depolarizing neuromuscular blocker). You may use Succinylcholine in myasthenia gravis, but patients are often less-responsive to it. Use double the usual dose of Succinylcholine in myasthenia gravis.

Reversible Causes of Hypoxia

CDSPIES: Cardiac (e.g. CHF), Drugs (sedatives, narcotics), Spasm (asthma, COPD, bronchospasm), Pneumothorax, Infection, Embolism (Pulmonary Embolism), Secretions, Splinting

Other causes of respiratory acidosis or decreased pO2 include: Muscle weakness/deconditioning, severe neuromuscular disorders, myopathies, chest wall disorders, brainstem stroke, traumatic brain injury, intracranial hemorrhage, spinal cord injury, bronchiectasis, obesity-hypoventilation syndrome, aspiration pneumonitis, interstitial lung disease, severe pulmonary hypertension, pulmonary fibrosis, etc.
Rapid Sequence Intubation

Equipment necessary for intubation
- Supplemental oxygen, Bag valve mask
- Suctioning with Yankauer
- Functional laryngoscope (or other intubating device)
- Endotracheal tube (with 10ml syringe to inflate balloon, lubricant (‘Surgilube’))
- Oral Airway for use during bag valve mask ventilation (measure from corner of mouth to jaw angle)
- Laryngeal Mask Airway (LMA) and/or “Intubating LMA”
- Appropriate monitors (O₂ Sat monitor, EKG monitor, Blood pressure cuff)

Pre-Procedure
1. Evaluate the patient for a difficult airway (see page 48)
2. Call a CODE BLUE should there be an inability to ventilate or oxygenate the patient
3. Consider ‘awake intubation’ for patients with highest risk airway or in whom bagging the patient may prove to be difficult or impossible (preserving spontaneous respirations and not paralyzing or deeply sedating the patient, with experienced anesthesiologist or critical care physician)
   a. Mnemonic for difficulty with bag mask ventilation: MOANS: Mask seal (poor), Obesity (includes pregnancy), Aged, No teeth, Stiffness or Snores
4. Have your Attending (or the ED Attending) at the bedside for all intubations
5. For high risk airways, think through an alternate plan for airway management, including ‘awake intubation’ as above, intermediate airways (Laryngeal Mask Airway (LMA) or laryngeal (King))
   airway, or surgical airway

Procedure
1. Place patient in “sniffing position” (towel behind the occiput to elevate the head ~4 cm) if the patient is not in C-spine precautions
2. Preoxygenate the patient with FiO₂ 100% to an oxygen saturation of 100% (if possible), for at least 2 minutes (or 5 deep breaths of 100% oxygen via non-rebreather). Use caution if the patient is not NPO or otherwise at high risk for aspiration (see risk factors for aspiration, page 48). Also apply a nasal cannula with 15 liters per minute of oxygen flow to give an additional 30-90 seconds of time without desaturation
3. Apply cricoid pressure (not in cardiac arrest)
4. Consider prophylactic administration of lidocaine if there is a concern for elevated intracranial pressure (see below)
5. Give Induction agent (see below)
6. Give Paralytic agent (see below)
7. Attempt visualization of vocal cords and intubation
8. If attempt unsuccessful after 30 seconds, consider abandoning the attempt and return to “bagging” the patient, returning to step 2
9. After 2 unsuccessful attempts, a more senior physician should then take over the intubation. In very high-risk situations, it is the discretion of the attending physician as to who should be performing the intubation.
Options for Induction (see page 186 for medication details)

- Etomidate 0.2-0.3 mg/kg IV; dose may be titrated to effect; may cause adrenal suppression and may lead to adverse outcomes in septic patients; hypotension may be seen at higher doses
- Versed 0.3-0.35 mg/kg IV (0.15 mg/kg in debilitated patients)+/- fentanyl 50-100 mcg IV
- Ketamine (does not relax muscles) 1-2 mg/kg IV
- Dexmedetomidine (Precedex) 1mcg/kg IV load over 10 minutes, then 0.2-0.7 mcg/kg/hour IV (only for awake intubations) (be very cautious with load as may cause hypotension and bradycardia)
- Propofol 2-2.5 mg/kg IV given as 40mg q 10 sec until induction onset (hypotension side effect is prohibitive for anesthesia induction; may be considered in status asthmaticus for intubation as it does have beneficial effects on the airway reflexes and may relax bronchoconstriction)

Options for Paralytic

- Succinylcholine 1-2 mg/kg IV; there is no maximum dose
  - Higher doses (2 mg/kg), particularly a second dose, may cause bradycardia
  - Use double the usual dose in patients with myasthenia gravis
  - Contraindications to Succinylcholine: malignant hyperthermia, burns after 48 hours, spinal cord injury after 48 hours, crush injury after 48 hours, denervating injury after 48 hours
  - Relative Contraindications to Succinylcholine: Hyperkalemia (as Succinylcholine will often increase the potassium level transiently by ~0.5 mEq/L); renal failure is not a contraindication
- Rocuronium 0.5-1 mg/kg IV

Lidocaine for Elevated Intracranial Pressure

- There is doubtful utility to this practice, though it is still widely performed
- Dose: 1-1.5mg/kg IV x 1

The Difficult Airway

### Assessment of the Difficult Airway

1. **Mallampati Classification of the Upper Airway**

<table>
<thead>
<tr>
<th>Mallampati Classification</th>
<th>Class I</th>
<th>Class II</th>
<th>Class III</th>
<th>Class IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>View of Vocal Cords</td>
<td>90% grade I</td>
<td>100% unpredictable</td>
<td>100% unpredictable</td>
<td>90% grade IV</td>
</tr>
</tbody>
</table>

2. Neck extension at the Atlanto-Occipital Joint in Sniff Position
3. Thyromental Distance (inside of mandible to top of thyroid cartilage): if <3-4 finger breadths (~ 6.5 cm), anticipate ‘anterior larynx’
4. Assessment of Aspiration Risk (higher with full stomach (< 8 hours fasting) or unknown fasting status, trauma, intestinal obstruction/inflammation, gastric paresis (i.e. narcotics, diabetic gastroparesis, peritonitis), GERD, pregnancy, obesity)

### Conditions Associated with Difficult Airway

- Mnemonic for predictors of difficult laryngoscopy: LEMON
  - Look Externally (obese neck, beard, etc.; 3-3-2 (cm; mouth opening, mentum, mike=thyromental distances; smaller distances than these can portend anterior larynx)
  - Mallampati classification
  - Obstruction of airway
  - Neck Mobility (poor)
- Mnemonic for predictors or difficult intermediate air
- Abnormal facial anatomy/development (e.g. small mouth and/or large tongue, dental abnormality-overbite, prognathia, obesity, advanced pregnancy(+/-), acromegaly, congenital syndromes
- Inability to open mouth (e.g. masseter muscle spasm (dental abscess), tetanus, temporo-mandibular joint dysfunction, facial burns, post-radiotherapy fibrosis, scleroderma, rheumatoid Arthritis (TM arthritis))
- Cervical immobility/abnormality (e.g. short neck/obesity, poor cervical mobility (e.g. ankylosing spondylitis), previous cervical spine surgery/fusion, presence of cervical collar or halo, burns to neck/post-radiotherapy
- Pharyngeal and laryngeal abnormality (e.g. high or anterior larynx, deep vallecula (inability to reach base of epiglottis with blade of scope), anatomical abnormality of epiglottis or hypopharynx (e.g. tumor), subglottic stenosis, Mallampati Class IV

### The Difficult Airway: Options for Management

- Consider the relative merits and feasibility of basic management choices
  - Non-surgical technique for initial approach to airway management vs. surgical technique for initial approach to airway management
  - Awake intubation vs. Intubation attempts after induction of general anesthesia
- Preservation of spontaneous ventilation vs. ablation of spontaneous ventilation
  - If conventional laryngoscopy fails: do NOT persist with the same technique if two attempts fail
    - Imperative to have a thought process as to second (and even third) option
    - Multiple attempts at direct laryngoscopy cause trauma with each attempt, with increased edema, bleeding and secretions, leading to decreased success of another technique
    - Multiple attempts can lead to the “cannot intubate, cannot ventilate” scenario
    - Consider waking the patient up if control of the airway is not emergent
- With first attempt failure of direct laryngoscopy, consider the following:
  - Better sniff position
  - Better neck extension
  - Laryngeal Pressure
  - Change Head Elevation
- With second attempted failure of direct laryngoscopy, strongly consider allowing a more experienced intubator to step in; may also consider the following:
  - Different Laryngoscopy Blade
    - Different Size (size 3 or size 4 for both)
    - Macintosh (”Mac”): Placed in valecula and indirectly lifts epiglottis
      - Advantages: easier for beginners, easier to manipulate the tongue
      - Disadvantages: May pull cords out of view, may require cricoid pressure, more difficult visualization, more tempting to ”crank back” as opposed to pulling up
    - Miller blade (”straight blade”): Placed under epiglottis and directly lifts epiglottis
      - Advantages: better view, less likely to need cricoid pressure to see, better with short neck
      - Disadvantages: harder to control tongue, mouth puckers around blade, need an assistant to pull lip out of the way, more difficult for beginners
  - Different Glidescope blade
    - Different size (size 3 or size 4)
    - VCMC: the OR has a different Glide-scope blade and handle than the ICU Glidescope
  - Different technique
    - Direct Laryngoscopy
    - Glidescope
    - Eschman Stylette (”Bougie”)
      - To be used with conventional laryngoscopy or Glidescope
      - Has an anterior curvature to allow tube placement into the trachea, followed by Seldinger technique insertion of the ET Tube
      - Should feel tracheal rings (”washboard sign”); will not advance past the carina (”hang up sign”); absence of both likely to signify placement in the esophagus
    - Intermediate airway: Laryngeal Mask Airway or “Fast-track LMA” (or “Intubating LMA”)
      - Seal allows gentle positive pressure but does not protect the airway from aspiration
      - Leaks above 20 cm H2O pressure so stomach is not inflated
      - May not be able to ventilate patients with stiff lungs (ARDS) or who are obese
      - May be able to pass an ET tube through the LMA (see chart next page for ET tube size)
    - Intermediate airway: King Airway
      - Laryngeal airway: has an esophageal balloon and a laryngeal balloon
      - Enters esophagus 100% of the time inflate balloons withdraw until able to ventilate
      - This is a stable airway for up to 8 hours/ may transport patients with King airway in-place
      - May be exchanged for an ET tube in the following manner:
        - Withdrawing tube to the point where chest rise is almost lost and breath sounds are minimal with the balloon inflated, inserting an Eschmann stylette, deflating the balloon, removing the King Airway, and inserting an ET tube with guidance of laryngoscope; patient must be sedated and paralyzed for any tube exchange
      - Decreased incidence of aspiration due to presence of esophageal balloon
Intermediate Airway Sizing:

<table>
<thead>
<tr>
<th>Size Tube</th>
<th>Height</th>
<th>Cuff volume</th>
<th>ET tube size†</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Up to 5 kg</td>
<td>up to 4 mL</td>
<td>3.5</td>
</tr>
<tr>
<td>1.5</td>
<td>5-10 kg</td>
<td>up to 7 mL</td>
<td>4</td>
</tr>
<tr>
<td>2</td>
<td>10-20 kg</td>
<td>up to 10 mL</td>
<td>4.5</td>
</tr>
<tr>
<td>2.5</td>
<td>20-30 kg</td>
<td>up to 14 mL</td>
<td>5</td>
</tr>
<tr>
<td>3</td>
<td>30-50 kg</td>
<td>up to 20 mL</td>
<td>6</td>
</tr>
<tr>
<td>4</td>
<td>50-70 kg</td>
<td>up to 30 mL</td>
<td>6</td>
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<td>5</td>
<td>70-100 kg</td>
<td>up to 40 mL</td>
<td>7</td>
</tr>
<tr>
<td>6</td>
<td>&gt; 100 kg</td>
<td>up to 50 mL</td>
<td>7</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Size Tube</th>
<th>Height</th>
<th>Cuff volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>35-45”</td>
<td>25-35 mL</td>
</tr>
<tr>
<td>2.5</td>
<td>41-51”</td>
<td>30-40 mL</td>
</tr>
<tr>
<td>3</td>
<td>4-5 feet</td>
<td>45-60 mL</td>
</tr>
<tr>
<td>4</td>
<td>5-6 feet</td>
<td>60-80 mL</td>
</tr>
<tr>
<td>5</td>
<td>&gt;6 feet</td>
<td>70-90 mL</td>
</tr>
</tbody>
</table>

† = size of ET tube that can fit through internal diameter of LMA

- Intermediate Airway: Combitube
  - Mostly used by paramedics in the face of failed intubation and airway bail out
  - Contraindicated if intact laryngeal reflexes or known esophageal pathology
  - Unable to suction the trachea when the tube is placed in the esophagus
- Mnemonic for difficult intermediate airway placement: RODS
  - Restricted mouth opening, Obstructed airway, Disrupted or distorted oropharynx, Stiff lungs or C-spine
- Awake Intubation/ Fiberoptic Intubation
  - Performed only by experienced anesthesiologist or critical care physician
  - Must have awake and cooperative patient
  - Judicious use of sedatives – mandatory to not oversedate patient into loss of airway reflexes or airway obstruction
  - Procedure:
    - Nasal oxygen used; oxygen also insufflated down fiberoptic scope to reduce fogging
    - Glycopyrolate 0.2 to 0.3 mg 5 minutes before to dry mucosa
    - Topical anesthetic of upper airway, and then vocal cords, with atomized lidocaine 4%
    - Place bite block
    - Laryngoscope to directly visualize vocal cords → pass through vocal cords → pass endotracheal tube over the laryngoscope into the trachea
    - Sedate patient
- Transtracheal jet insufflation
  - Procedure:
    - Insert catheter through crycothyroid membrane
    - Jet ventilator attaches directly to wall O2 (O2 from wall = 50 PSI); may also use standard O2 tank; jet ventilator must have regulator
    - Start ventilation at 10 PSI; increase by 5 PSI increments until chest rise is seen
    - Need to open airway to allow for passive exhalation
    - Can oxygenate patient and buy time for a more permanent airway; does not ventilate
    - If catheter gets dislodged, can cause massive subQ emphysema
- Emergent Cricothyrotomy
  - Mnemonic for difficult cricothyrotomy placement: SHORT
    - Surgery/ disrupted airway
    - Hematoma or infection of the neck
    - Obese/ access problem
    - Radiation to the neck/Tumor of the neck
- Emergent Cricothyrotomy with Retrograde Intubation using a guidewire/bronchoscope
- Emergent Tracheostomy (surgical procedure)
- McGill Forceps (for nasotracheal intubation only, which is not indicated for ICU patients)

References: Adapted from Difficult Airway Lecture by David Fishman, MD and airway lecture by Joseph Esherick, MD
Failed intubation alone is not a crisis if the lungs can still be ventilated. Failed ventilation is an emergency. The priority is to oxygenate the lungs. Don’t forget about an oral airway to move the tongue out of the way during ambu-bagging. It often takes 2 hands to adequately hold the facemask with a good seal to the patient’s face. Get help!

Confirmation of Endotracheal Tube/Tracheostomy Placement

- The use of capnography to detect end-tidal carbon dioxide is the only reliable method of confirming ETT placement
  - False-positive results may occur initially when exhaled gases enter the esophagus during mask ventilation or when the patient is generating carbon dioxide in the gastrointestinal tract, for example, recent ingestion of carbonated beverages or bicarbonate-based antacids
  - False-negative (ETT in the trachea but no CO₂ detected) may occur when pulmonary blood flow is minimal, for example, during cardiac arrest with poor cardiopulmonary resuscitation or with intubation-induced bronchospasm
- Visualizing the trachea or carina through a fiberoptic bronchoscope or Glide-scope will also confirm correct placement of the ETT or tracheostomy tube
- Bilateral breath sounds, presence of condensed water vapor in the ET tube, chest wall movements with ventilation attempts, and direct visualization of the tube passing through the cords may be falsely positive are not adequate evidence for correct Endotracheal Tube placement

Replacement of Endotracheal Tube That Has Become Dislodged or Needs Changing

- Cook Endotracheal Tube Exchanger is a long yellow or blue tube which can be advanced through an existing ET Tube into the trachea, holding position for advancing or removal of the Endotracheal tube and replacement with another via the Seldinger technique. Using the “Jet Insufflator”, the patient can also be oxygenated (but not well ventilated) through this tube. Be sure patient is sedated and paralyzed for tube exchange. Also have intubation equipment available for tube exchange.
- Do NOT attempt tube exchange through the Eschman stylette (it may be too short)

**Ventilator Management**

**Indications for Ventilatory Support**
- Management of Respiratory Distress
  - Decrease physical effort (work) of breathing
  - Relieve Respiratory Muscle Fatigue or Apnea
  - Assist with Secretion Management
- Improve Gas Exchange and Acid-Base Status
  - Reverse Hypoxemia
  - Reverse Hypercapnea
  - Manage Metabolic Acidosis
- Allow Chest-Wall, Airway, or Lung Healing
  - Post-surgical
  - Post-trauma
  - Post Inhalational Injury
- Improve Pulmonary/Airway Dynamics
  - Treatment and Prevention of Atelectasis
  - Prevention of Further Lung Injury
  - Alter Compliance – V/Q Relationships

**Functions of the Ventilator**
- Mechanical Ventilation – the patient has inadequate inclination or ability to ventilate
- Oxygen Delivery – the patient requires efficient delivery of high concentrations of oxygen.
- PEEP (Positive End Expiratory Pressure) – The patient requires the benefits of PEEP that cannot be provided by less-invasive means.
- Airway access or protection – The patient has inadequate reflexes (e.g. sedation, stroke) to ensure airway patency or prevent aspiration.

**Goals of Ventilator Management**

*To achieve the following goals without causing harm to the patient is the goal of ventilator management:*

**Acid-Base Goals:**
- Normal pH (see discussion on Acid-Base, page 96)

**Oxygenation Goals:**
- $\text{PaO}_2 > 60 \text{ mm Hg}$ ($\geq 70 \text{ mm Hg}$ is reasonable for all except CO$_2$ retainers, where the goal should be 60 mm Hg, or an O$_2$ Sat of 90-93%)
  - Consider keeping $\text{PaO}_2 > 75$ in head trauma patients
  - Consider $\text{FiO}_2 = 100\%$ for 12 hours post Necrotizing Soft Tissue Infection surgery

**Ventilation Goals:**
- Normal pH

**Problems/Harm Caused by Ventilator Therapy**

**Excessive PEEP**
- Decreases preload, potentially causing hypotension and/or elevated ICP
- Consider PEEP of 0 in patients with high intracranial pressure

**Excessive Tidal Volume**
- “Volu-trauma” increases risk of death
- $\text{Vt=Initial Tidal Volume=6-8 ml/kg predicted body weight (PBW)}$ (see “Initial Ventilator Settings”)

**Excessive Pressure**
- Plateau Pressure $> 30 \text{ cm H2O}$
- Causes pneumothorax/ barotrauma
Excessive FiO₂>60% (0.6) for prolonged periods of time
- Causes free radical formation, oxygen toxicity
- Increasing PEEP at a ratio of 5:1 (FiO₂:PEEP) can be helpful to improve oxygenation

Excessive Duration of Ventilator
- increases risk of infection, particularly past 5 days
- increases risk of muscle atrophy
  - Within 72 hours of mechanical ventilation without spontaneous breathing, there is a >50%-biopsy proven atrophy of the diaphragm compared to controls [N Engl J Med 2008; 358: 1327-35.]

Inadequate Ventilation
- PCO₂>80-100 or pH<7.20 to 7.15 causes refractory hypotension, acidosis, obtundation (see Severe Acidosis, Page 100)
- “Permissive hypercapnea” as a way to avoid harming the patient up to the above goals may be tolerated if the patient does not have elevated intracranial pressure.

Excessive Respiratory Rate
- Respiratory Rate generally>36 can cause decreased expiratory time, inadequate exhalation, buildup of auto-PEEP
- Rates much lower than this may still cause auto-PEEP buildup in patients with significant obstructive pulmonary disease or wheeze (see Acute Asthma, Page 71)

Ventilator Modes
Pressure-Regulated Volume Control (PRVC): Usual initial ventilator mode at VCMC. Delivers a preset volume (with limitation on the amount of pressure) at a preset rate. Initiation of spontaneous breaths by the patient will deliver additional full volume breaths. Used for limited patient effort or heavy sedation. May cause patient-ventilator dyssynchrony. PRVC is a form of Assist Control (AC), as are Pressure Control and Volume Control
Pressure Control (PC): Delivers a preset pressure for a preset time to the patient, leading to variable tidal volumes (if lung compliance improves, may yield very high tidal volumes; worsening lung compliance may cause small tidal volumes). Used for patients with excessively high pressures on other modes.
Volume Control (VC): See PRVC, but without the limitation on pressure. May improve patient-ventilator dyssynchrony that may be seen with PRVC, but can cause excessively high pressures.
Synchronous Intermittent Mechanical Ventilation (SIMV): Delivers a preset rate with preset Tidal Volume to the patient. Initiation of spontaneous breaths by the patient will be aided by a set level of pressure support. May be used if some respiratory effort or patient-ventilator dyssynchrony on AC.
Continuous Positive Airway Pressure (CPAP): CPAP (or PEEP) is supplemented with Pressure Support. Used for patients who are awake, those with significant ventilator dyssynchrony, and in ventilator weaning. May lead to increased work of breathing over other ventilation modes.
Airway Pressure Release Ventilation (APRV): Delivers high PEEP with very brief release of pressure to PEEP=0. Comfortable mode for patients who may (rather, should) breathe over the PEEP. Used for refractory hypoxia, to recruit alveoli. Will initially decrease minute ventilation and may worsen hypercarbia. ICU Attending consultation required. Usual initial settings: Pressure high 30, Pressure low 0, Time high 4 (4-5) seconds, Time low 0.6 (0.3-0.6) seconds. See page 56 for further discussion
Oscillatory Ventilation: Used for refractory hypoxia. Pulmonology consult required.
Initial Ventilator Settings and Ventilator Management

Modes of Ventilation
- **Assist Control (AC)** if very limited patient effort or heavy sedation (i.e. PRVC)
- **SIMV** if some respiratory effort or patient-ventilator dyssynchrony on AC

Initial settings for Oxygenation
- Initial FiO\textsubscript{2} 0.8-1.0, adjust according to Oxygen Saturation
- Initial PEEP 5 cmH\textsubscript{2}O, adjust according to FiO\textsubscript{2} (ARDSNet PEEP-FiO\textsubscript{2} algorithm:)

<table>
<thead>
<tr>
<th>FiO\textsubscript{2}</th>
<th>0.3</th>
<th>0.4</th>
<th>0.4</th>
<th>0.5</th>
<th>0.5</th>
<th>0.6</th>
<th>0.7</th>
<th>0.7</th>
<th>0.8</th>
<th>0.9</th>
<th>0.9</th>
<th>1.0</th>
<th>1.0</th>
<th>1.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEEP*</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>8</td>
<td>8</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>12</td>
<td>14</td>
<td>14</td>
<td>16</td>
<td>18</td>
<td>18</td>
</tr>
</tbody>
</table>

- Aim for PaO\textsubscript{2} ≥ 60 mmHg and Oxygen Saturation ≥90%
- Aim to titrate FiO\textsubscript{2} ≤ 0.6

Initial Settings for Ventilation
- Tidal volume: 6-8 mL/kg ideal body weight (IBW) = “Lung protective ventilation”
  - “Lung protective Ventilation” indicated for ARDS/acute lung injury or severe sepsis
  - IBW for men (kg) = 50 + [2.3 x (height in inches – 60)]
  - IBW for women (kg) = 45.5 + [2.3 x (height in inches – 60)]
- Ventilator rate: 12-16/minute, adjust based on PaCO\textsubscript{2} and pH
  - Consider initial rate of 20-24/minute in acute respiratory distress syndrome (ARDS) or in severely acidic patients (pH<7.2 to 7.1)
  - Can increase rate to 36 breaths/minute if necessary
- Keep plateau pressure ≤30 cmH\textsubscript{2}O
- Allow ‘permissive hypercapnea’ if necessary as long as patient has no elevated ICP
- May use sodium bicarbonate drip if necessary to keep pH > 7.15

Additional ventilator settings
- Triggering sensitivity: adjust to minimize patient effort
- I:E ratio: initially 1:2, decrease inspiratory time (may also need to decrease respiratory rate) for severe bronchospasm; can increase inspiratory time for refractory hypoxia
- Pressure support in SIMV mode: adjust between 6-20 cmH\textsubscript{2}O, titrate to patient comfort

Monitoring During Mechanical Ventilation
- Continuous cardiopulmonary monitor
- Ventilator: tidal volume, minute volume, airway pressures, serial arterial blood gases
- End-tidal carbon dioxide (ET\textsubscript{CO}\textsubscript{2}) monitors desirable for ventilator weaning

Ventilator Management General Guidelines and Adjustments
- To be made in conjunction with the respiratory therapist only
- Adjust ventilation (PaCO\textsubscript{2}) by changing minute volume = tidal volume x respiratory rate
- Ventilate to pH, not to PaCO\textsubscript{2}
- Improving oxygenation: increase FiO\textsubscript{2}, PEEP or inspiratory time (if refractory hypoxia)
- Any changes in ventilator settings should be accompanied both by a written order as well as a one-line Progress Note as to the reason for the change
- As a general rule, changes on the ventilator take a minimum of 20 minutes (usually closer to 1 hour) to achieve steady state
- Weaning of PEEP should be made in increments of 2 cm H\textsubscript{2}O per 2 hours at most
- Avoid paralytics if possible
- Continuous sedation titrated to patient comfort
- Daily interruption of continuous sedation and assess readiness to extubate daily

Adapted with permission from Joseph Esherick, MD.
### Ventilator alarms: Differential Diagnosis

<table>
<thead>
<tr>
<th>Alarm</th>
<th>Potential causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Pressure</td>
<td>Patient-specific: Patient-ventilator dyssynchrony; stiff lungs (ARDS, CHF), extrinsic compression on lungs (restrictive lung disease, obesity, tension pneumothorax); excessive tidal volume; bronchospasm Tube/ circuit specific: biting tube, kinked tube, condensation (water) in tubing</td>
</tr>
<tr>
<td>Low Pressure</td>
<td>Break in the circuit; loss of airway (total or partial extubation); ET tube or tracheostomy cuff leak</td>
</tr>
<tr>
<td>Apnea/ Low Respiratory Rate Alarm</td>
<td>Respiratory arrest; oversedation; loss of airway (total or partial extubation)</td>
</tr>
<tr>
<td>High Tidal Volume, Minute Ventilation, or Respiratory Rate</td>
<td>Agitation, anxiety, pain; impending brain herniation; severe acidosis Excess condensation in tubing (false reading)</td>
</tr>
<tr>
<td>Low Tidal Volume or Minute Ventilation</td>
<td>While on controlled mechanical ventilation: ET tube or tracheostomy cuff leak; break in the circuit While on CPAP: Oversedation; neuromuscular weakness or muscle fatigue</td>
</tr>
<tr>
<td>PEEP Alarm (high or low)</td>
<td>Measured PEEP outside of the set limit</td>
</tr>
</tbody>
</table>

Note: Pressure, Respiratory Rate, Minute Ventilation and PEEP alarms (high and low) are all set manually by the Respiratory Therapist.

### Respiratory Therapy Interventions for Vented and Non-Vented Patients

| Monitoring | • O2 Sat Monitoring:  
• End Tidal CO2 Monitoring: monitors ventilation, either intubated or non-intubated; rises anywhere from 5-240 seconds prior to oxygen saturation going down |
| Oxygen Delivery Methods | • Nasal Cannula – up to 6 liters per minute (39% FiO2)  
• High flow Nasal Cannula – up to 15 liters per minute (~60% FiO2)  
• Simple Mask – variable oxygen delivery (6 L/min up to 12 L/min)  
• Oxymask – variable oxygen delivery; higher FiO2 than simple mask  
• Vapotherm – considered to have some PEEP; high flow (up to 40 L), up to 100% FiO2  
• Non-rebreather – considered to have between 90% and 100% FiO2 |
| Incentive spirometer | • Encourages deep breathing/ respiratory muscle use  
• To be used in all non-intubated hospitalized patients at risk for atelectasis (i.e. all) |
| EZ-Pap | • Positive pressure (expiratory resistance) via mouthpiece, mask or direct tracheostomy connection in patients not on ventilator to provide PEEP  
• Usually with albuterol/ipratropium if no contraindications; saline if contraindications  
• Useful for treatment of atelectasis |
| Meta-neb | • Oscillatory treatments designed to mobilize secretions  
• Positive pressure (EZ Pap) with internal oscillatory percussion (50/50 each) via mouthpiece, mask, or direct tracheostomy connection  
• May also attach directly to a ventilator for internal oscillatory percussion only (vented patients already have PEEP) |
| IPPB | (Intermittent positive pressure breaths): Hyperinflation (‘blowing the lungs open’) via mouthpiece, mask or direct tracheostomy connection; used less often than EZ Pap |
| CPAP/BiPap | See “Non-Invasive Ventilation” (page 63) |
| Interventions to Mobilize Secretions | • Theravest  
• Metanebs as above  
• Cough assist and chest physiotherapy felt to be less effective |
| Interventions for Wheeze | • MDI with spacer; MDI teaching very beneficial for patients prior to discharge  
• Nebulizers via ventilator or via hand held nebulizer or mask (see page 71) |

Reference: Tom Adelman, Respiratory Therapy
Advanced Interventions for Severe Lung Disease/ Severe Hypoxia

Airway Pressure Release Ventilation (APRV)

Description:
- Delivers high PEEP with very brief release of pressure to PEEP=0. A synonym may be “Bi-Level Ventilation” or “BiVent” (though they are not 100% synonymous).
- Relies on diffusion of gases across alveoli (oxygen and carbon dioxide both)

Indications:
- Institution dependent:
  - At VCMC, used for refractory hypoxia (to recruit alveoli) and ARDS with poor lung compliance.
    - ICU Attending consultation required to start on this mode.
  - At Shock Trauma in Maryland, APRV is the usual mode of ventilation for the majority of trauma patients to prevent ARDS

Contraindications:
- Severe academia (controversial)
- Severe obstructive lung disease (controversial)
- Elevated Intracranial Pressure (controversial)

Potential Benefits:
- Comfortable mode for patients who may (rather, should) breathe over the PEEP (Phigh), potentially leading to less ventilator-patient dysynchrony by allowing patients to control their own spontaneous respiratory rate and tidal volume \( \rightarrow \) less sedation needed \( \rightarrow \) potentially less delirium, less neuromuscular blocking agents, less ventilator days
- Recruits alveoli more so than conventional ventilation
- May decrease rates of ARDS by less ‘open and shut’ stress on alveoli, ‘atelectotrauma’

Potential Drawbacks:
- Any ‘break in the circuit’ (release of pressure) (i.e. transitioning from one ventilator to a transport ventilator; occasionally suctioning with a suction catheter that leads to a break in the circuit), may lead to rapid and severe de-recruitment of alveoli and worsening gas exchange
- Increases overall mean airway pressure \( \rightarrow \) decreases venous return \( \rightarrow \) may cause hypotension.
- May initially decrease minute ventilation \( \rightarrow \) worsens hypercarbia
- No proven mortality benefit in ARDS (in humans; evidence of improved mortality in ARDS in animal models) – by allowing patient to control their tidal volumes, patients may exceed the 4-6 ml/kg IBW tidal volumes that has been shown to improve mortality

Initial Settings:
- Ordered via “BiVent” mode on Servo ventilator.
- Initial settings: Pressure high 30, Pressure low 0, Time high 4 (4-5) seconds, Time low 0.6 (0.3-0.6) seconds, pressure support 0.
  - Ideal Time low is when the expiratory flow rate is 70-80% of the max expiratory flow rate; may be difficult to quantify, and may vary breath by breath; usually 0.4 to 0.6 seconds

Weaning from APRV:
- Monitor Respiratory Rate, Tidal volume, and PaCO2 at least daily, and after changing settings
- Weaning usually only begins when FiO2 has reached 40% or lower
- Wean by “Drop and Stretch” together
  - “Drop” P high (high pressure) by 2 cm H2O each step (i.e. 1st step down to 28 cm H2O)
  - “Stretch” out T high (high time) by ½ second each time (i.e. 1st step up to 4.5 seconds from 4 seconds)
  - Usually done q 8-12 hours depending on the patient’s tolerance from an oxygenation standpoint
- As the patient tolerates drop and stretch, may consider adding pressure support, to have a Phigh max of no more than 30 cm H2O
May transition straight to CPAP, or may convert to conventional mechanical ventilation (i.e. PRVC) when P high approaches 18-20 cm H2O
  - Goal should be to try to maintain approximately the same mean airway pressure on transition
  - On transition, Tlow is eliminated which does not cause issues or problems

Evidence behind Prone Positioning in ARDS:
Recent “PROSEVA” (“Proning Severe ARDS Patients”) study investigator trial reported in New England Journal of Medicine (2013)

- Multi-center prospective randomized controlled trial of 466 patients, randomized to at least 16 hours of prone positioning vs. remaining supine (237 prone, 229 supine)

- Inclusion criteria:
  - Endotracheal intubation and mechanical ventilation for ARDS for less than 36 hours
  - Severe ARDS (defined as PaO2:FiO2 ratio of < 150 mm Hg) for a minimum of 12-24 hours
  - FiO2 ≥ 0.6, PRRP ≥ 5 cm H2O, and a Vt ~ 6 ml/kg predicted body weight

- Contraindications and/or exclusion criteria from Prone Positioning “PROSEVA” study
  - Intracranial pressure > 30 mm Hg or cerebral perfusion pressure < 60 mm Hg
  - Massive hemoptysis requiring immediate surgical or interventional radiology procedure
  - Tracheal surgery or sternotomy during the previous 15 days
  - Deep venous thrombosis treated for less than 2 days
  - Cardiac pacemaker inserted in last 2 days
  - Unstable spine, femur or pelvic fractures
  - Mean arterial pressure lower than 65 mm Hg
  - Pregnant women
  - Single anterior chest tube with air leaks
  - Lung transplantation
  - Burns on > 20% of the body surface
  - Underlying disease with a life expectancy of < 1 year
  - Non-invasive ventilation delivered for more than 24 hours before inclusion

- Mortality improved in prone positioning vs. supine (16% vs. 32.8% 28 day mortality respectively; 23.6% vs. 41% 90 day mortality respectively) (p<0.001)
  - Higher incidence of cardiac arrest in supine group; otherwise no difference in incidence of complications between groups

VCMC investigating rental of the “Roto Prone” bed from KCI
- The above inclusion criteria would include many patients; VCMC likely to have a higher threshold for use of this bed
- Above study used conventional ventilation and did NOT use APRV
- Average patient requires the Roto Prone bed for 4.4 days
- Weight limit: 350 lb. (159 kg); Height limit 6’ 6” (78”)

References: Lecture by Nader Habashi, One Legacy, September 2013; http://www.draeger.com/sites/en_us/Pages/Hospital/APRV-Webinar.aspx?navID=1219 (most impressive demonstration is at 14:35)
DRAFT of Prone Position Policy

Policy Statements:
1. An attending level ICU physician order is required for the initiation, maintenance and discontinuance of Prone Positioning.
2. Frequency and duration of prone positioning will be determined by the attending ICU physician.
3. Prone positioning requires a collaborative effort between Respiratory Care and Nursing, with a care ratio of 1:1.
4. All patients that require prone positioning will be placed on “Rotoprone” bed.
5. Patients on prone positioning will be ordered on post-pyloric feeding. (**via Tiger Tube**)
6. A healthcare provider who has the ability to intubate must be available during patient pronation in the event of accidental intubation or airway emergency.
7. Specific criteria must be met in order for the patient to qualify for prone positioning.
8. Patients will be considered “responders” if they exhibit an increase of at least 10mmHg PaO2 within an hour of prone positioning and “non-responders” if no improvements occur within an hour of pronation.
9. If patient is classified as “non-responder”, consider recruitment maneuvers or an increase in PEEP prior to discontinuing prone position.
10. Patients will be assessed for skin integrity every 2-4 hours and as needed.
11. The need for prone positioning will be reassessed every 24 hours.
12. Patient must have arterial line in place.

Indications:
1. Severe ARDS with P:F ratio < 100
2. Mechanical ventilation < 36 hours (beyond 36 hours is a relative contraindication)

Contraindications:
Contraindications are relative and risk/benefit ratio must be assessed by the physician. Relative contraindications include:
1. Weight ≥ 350 lbs/ 159 kg or <88 lbs/ 40 kg
2. Height > 6’6” or < 4’6”
3. Shock, persistent mean arterial pressure < 55 mmHg
4. Acute bleeding, hemorrhagic shock or massive hemoptysis
5. Spinal instability
6. Pregnancy
7. Increased intracranial pressure > 30 mmHg
8. Recent tracheostomy (<1 week) or sternal surgery (<1 month)
9. Recent abdominal or thoracic surgery requiring frequent evaluation, wound dressing changes or potential for wound dehiscence due to positional stress (<2 weeks)
10. Facial or skull fractures
11. Peritonitis/ severe ascites
12. Bilateral thoracostomy tubes
13. Open abdominal wounds
Procedure:
1. Explain procedure to patient and/or family members.
2. Assess placement of endotracheal tube, including position on lip/teeth and distal tip on most recent chest x-ray (should be recorded in RT record).
3. Ensure that mechanical ventilator is set up with active humidification prior to pronation.
4. Ensure that a closed inline suction catheter is in place.
5. Ensure patency of post-pyloric feeding tube prior to patient pronation.
6. Hold tube feeding for at least 60 minutes prior to patient pronation.
7. Ensure that fecal management system is intact and patent (as appropriate).
8. Remove EKG patches from chest and have a new set ready to place on patient’s back.
9. Check all lines and tubes for adequate length.
10. Ensure that all lines will not tangle or kink during turn. Place appropriate swivel devices onto mechanical ventilator circuit to prevent excess torquing.
11. Disconnect all unnecessary IV’s.
12. Ensure all central line dressings are secured and that all central lines and arterial lines are sutured in place.
13. Change any dressings on the anterior aspect of the patient.
14. Empty drainage bags.
15. Ensure prescribed RASS (usually -4 to -5) and Train of Four (usually 2 of 4) (if applicable) goals are achieved.
16. Prior to resecuring endotracheal tube, apply non-alcohol based barrier wipe to patient skin.
17. Resecure endotracheal tube with cloth tape or Elastoplast. Do not use Anchorfast or bite block.
18. Perform full patient-ventilator assessment and obtain baseline ABG and 12 lead EKG prior to pronation.
19. Hyperoxygenate patient for at least 5 minutes prior to pronation.
20. Suction endotracheal/ tracheostomy tube and oropharynx thoroughly prior to pronation.
21. Have a minimum of 5 staff (RT, primary RN and other trained staff) available ready at the bedside prior to turn.
22. Turn patient towards the ventilator during pronation to lessen risk of accidental extubation.
23. Attach EKG patches and leads to patient’s back.
25. Unless contraindicated, place Rotoprone bed in reverse Trendelenberg position at 10-20° to decrease possibility of periorbital and conjunctival edema.
26. Reassess position of all lines and tubes and recalibrate vascular pressure transducers as necessary.
27. Document patient response to prone positioning within 30 minutes.
28. Perform another full patient-ventilator assessment and re-obtain an ABG after 1 hour.
29. Inform physician of patient response to prone positioning, whether a patient is a “responder” or a “non-responder”.
30. Frequently assess the security of the endotracheal tube and integrity of patient’s skin.

Patient Care Provided for Pronated Patients:
1. Patient Care While Prone
a. Maintain patency of tubes and lines
b. Assess posterior aspect of patient
c. Change any dressings as necessary on the posterior aspect of the patient
d. Oral care per protocol
e. Baseline posterior 12-lead EKG
f. Inspect the face hourly and assess for any skin breakdown

2. Patient Care Provided While Supine
   a. Maintain patency of tubes and lines
   b. Sedation vacation if able
   c. Full assessment of the anterior aspect of the patient and neurological status
   d. Obtain chest x-rays if ordered
   e. Change any dressings as necessary on the anterior aspect of the patient
   f. Resecure lines and change IV tubings per unit policy

3. Ongoing Monitoring For Pronated Patients
   a. Vital signs and assessments per policy
   b. ABG as ordered
   c. RASS and Train of Four goals maintained as ordered
   d. If feeding, maintain patency of GI access
   e. Maintain IV drips and other monitoring as ordered

Criteria for Prone Positioning Discontinuation:
1. Continued improvement in patient oxygenation with PaO2/FiO2 ratio ≥ 150 mmHg on FiO2 ≤ 60% and PEEP ≤ 10 mmHg maintained for at least 4 hours after the end of the last prone session.
2. Significant decline in oxygenation while in prone position
3. Endotracheal tube dislodgement or accidental extubation
4. Cardiac arrest
5. Patient’s family wishes to discontinue treatment

Documentation:
Document specific criteria for assessment and reassessment and should include:
1. Vital signs and other assessments per policy
2. Areas of skin breakdown
3. Development of the above mentioned complications

Weaning and Liberation from Mechanical Ventilators

**Patient is ready for a Spontaneous Breathing Trial if they meet the following criteria:**

- Awake, cooperative and follows commands
- Good gag reflex
- Strong cough
- Minimal secretions
- Hemodynamically stable off vasopressors (may be on dobutamine ≤ 5 mcg/kg/min)
- The underlying disease state leading to intubation has resolved
- Hemoglobin ≥ 8 gram/dL
- Spontaneous breathing on PEEP < 8 cm H2O
- PaO2/FiO2 ratio ≥ 150-200 (or SaO2≥ 90% with FiO2 ≤ 0.4)
- Systemic pH ≥ 7.25
- Minute ventilation < 15 Liters/ minute
- Rapid Shallow Breathing Index (‘SBI’) < 105 (for 2-3 minutes on CPAP, PEEP 5, PSV 0, FiO2 ≤ 0.4)  
  \( RSBI = \text{Respiratory Rate/Tidal Volume in Liters} \)

**Spontaneous Breathing Trial (SBT)**

- Settings: T-piece or CPAP, PEEP 5 cm H2O and Pressure Support 5-8 cm H2O
- Duration: 30-120 minute trial
- Patient passes SBT if:
  - Respiratory Rate ≤ 35 / min
  - Heart rate < 140 / min and no increase > 25 / min
  - SBP > 90 and < 180; no increase > 40
  - SaO2≥90% or PaO2≥60 mm Hg on FiO2≤ 0.4
  - VT≥ 4 ml/kg predicted body weight, or ≥ 325 ml (in adults)
  - PaCO2 increase < 10 mm Hg
  - Absence of apnea > 60 seconds, agitation, diaphoresis, or increased work of breathing

**Reasons to pass SBT but NOT extubate:**
- Fluid overload
- Patient too weak
- Oversedation
- Unstable/ Unsafe/ Swollen airway
- Secretions
- Altered Mental Status
- Awaiting Procedure

**Resume Mechanical Ventilation**

- Search for causes of failure
  - Malnutrition → weakness
  - Electrolyte abnormalities
  - Cardiopulmonary disease
  - Mucus plugging
  - Fluid overload
  - Oversedation
  - Neurological dysfunction
  - Underlying disease necessitating mechanical ventilation has not sufficiently resolved
- Resume non-fatiguing mode of ventilation

**Daily ventilator weaning**

- PEEP weaning
  - Wean PEEP to 5-8 cm H2O as tolerated
- Pressure support weaning
  - Pressure support 6-20 cm H2O to keep respiratory rate < 30 minute
  - Gradually wean pressure support by 2-4 cm H2O as tolerated
  - If patient is unable to tolerate pressure support ventilation, use a backup rate with a comfortable mode of ventilation
- Daily paired sedative/ ventilator weaning has been demonstrated to reduce the number of days of ventilatory support needed, duration of hospitalization, and mortality.

**Consider "Cuff Leak Test"**

See page 62

**Extubate if successful SBT**
Post-Extubation Laryngeal Edema (PELE)

Clinical Presentation:
- Post-extubation stridor (often inspiratory) is the hallmark clinical manifestation
- Direct laryngoscopic visualization is the gold standard for diagnosis
- One of the primary causes of post-extubation respiratory distress
- Incidence estimated at 3-30% in all intubated ICU patients
- Of patients experiencing PELE, reintubation rates are described as anywhere from 1-5% to up to 50% at 72 hours

Risk Factors:
- Female
- Trauma to upper airway anatomy
- Age > 70 years, or in pediatrics
- Mechanical ventilation for > 6 days
- Patients with an endotracheal tube size: laryngeal diameter > 45%

Diagnosis:
- “Cuff-Leak Volume” is measured by deflating the endotracheal tube cuff and measuring the difference between inspired and expired tidal volumes
  - Positive test = either < 24% of inspired volume or an absolute value of less than 130 ml (some sources list less than 110 ml)
  - With a positive test, ~20-25% of patients will develop clinical Post Extubation Stridor
  - Significant debate about the utility of the Cuff Leak Test in ICU patients, with 75-80% of patients with a positive test having no Post-Extubation Stridor and perhaps unnecessarily delaying extubation

Treatment:
- Steroids
  - For low-risk patients (all-comers), steroids do not decrease incidence of Post Extubation Stridor
  - For high-risk patients with positive Cuff Leak Test, 3 placebo-controlled trials revealed a decrease in rates of Post-Extubation Stridor and reintubation
    - Relative Risk of PELE and Post-Extubation Stridor with use of steroids = 0.67
    - Relative Risk of reintubation with use of steroids = 0.54
  - Optimal type of steroid, dose, duration, and waiting time before extubation have not completely been determined
    - Type of steroid: dexamethasone 5 mg IV q 6 hours x 4 doses, methylprednisolone 80 mg divided q 3 hours x 12 hours and methylprednisolone 40 mg divided q 6 hours x 24 hours were all effective
    - It is generally accepted that a dose of methylprednisolone of at least 80 mg, with waiting time at least 12 hours prior to extubation

Non-invasive ventilation

Potential indications for Non-invasive Positive Pressure Ventilation (NPPV)
- Moderate-severe COPD exacerbations
- Severe CHF exacerbations
- Acute hypoxemic respiratory failure
- Acute respiratory failure in immunocompromised patients
- Prevention of post-extubation respiratory failure in patients with COPD exacerbation

Contraindications for NPPV
- Inability to take off mask in case of vomiting (i.e. depressed level of consciousness, severe encephalopathy, neuromuscular weakness, etc.)
- Risk of aspiration or inability to protect airway
- Upper airway obstruction
- Hemodynamic instability or life-threatening arrhythmia
- Recent GI, facial or oropharyngeal surgery
- Facial deformities or anatomic abnormalities precluding a tight mask application
- Severe claustrophobia

Technique
- Slowly acclimate patient to NPPV
- Initiate BiPAP with iPAP 10 cmH2O/ePAP 4-5 cmH2O
- Increase iPAP titrated to tidal volume (Vt) = 5-7 mg/kg predicted body weight
- Increase ePAP and wean FiO2 to maintain a SaO2≥90%
- Avoid iPAP≥25 cmH2O and caution with iPAP>20 cmH2O (causes gastric distension)
- Check an ABG after 1-2 hours to assess efficacy

Monitoring Patients on NPPV
- Continuous cardiac monitoring and oximetry
- Observe for decreased work of breathing, agitation, dyspnea and improved comfort
- Monitor for ventilator-patient dyssynchrony and for significant air leaks

Predictors of Failure for NPPV
- Poor cooperation and poor fitting or intolerance of face mask
- Low body mass index≤23
- Presence of ARDS or Simplified Acute Physiology Score II (SAPS II) score>35
- Initial pH<7.2 or initial PaCO2>90 mmHg
- Minimal improvement after 1 hour of NPPV

Complications of Noninvasive Positive Pressure Ventilation

<table>
<thead>
<tr>
<th>Minor Complications</th>
<th>Major Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasal or sinus congestion</td>
<td>Severe gastric distension</td>
</tr>
<tr>
<td>Sinus or ear pain</td>
<td>Pulmonary aspiration</td>
</tr>
<tr>
<td>Conjunctival irritation</td>
<td>Pneumothorax</td>
</tr>
<tr>
<td>Pressure sore on nasal bridge or cheeks</td>
<td>Pressure ulcers on nasal bridge or face</td>
</tr>
<tr>
<td>Mild-moderate gastric distension</td>
<td>Hypotension</td>
</tr>
</tbody>
</table>

Acute Respiratory Distress Syndrome (ARDS)

Criteria: Acute onset of:
- Bilateral patchy alveolar infiltrates
- PCWP≤18 mmHg (or no clinical evidence for increased left atrial pressure)
  - 1/3-1/2 of pts have a PCWP>18 mmHg; PaO₂/FiO₂ may vary with PEEP
- “P:F Ratio” (PaO₂/FiO₂) ≤ 200
  - Acute lung injury (ALI): same criteria as above, except the PaO₂/FiO₂ = 201-300

Etiology
- Common: pneumonia, sepsis, aspiration pneumonitis, severe multi-trauma with shock and multiple transfusions
- Uncommon: drowning, pancreatitis, trauma, pulmonary contusion, inhalation injury, DIC, drug overdose, fat embolus, transfusion of blood products (more blood products ➔ higher risk), cardiopulmonary bypass, reperfusion pulmonary injury after lung transplantation or embolectomy

Treatment
- Lung protective ventilation with tidal volumes = 6-8 mL/kg predicted body weight
  - See “Mechanical Ventilation” section, page 54, for FiO₂:PEEP ratios suggested for ARDS
- Maintain Plateau Pressures (Pplat)≤30 cmH₂O
  - Check Pplat (0.5 second inspiratory pause) at least q 4 hours and after each change in PEEP or Tidal Volume (VT)
  - If Pplat>30, decrease VT by 1ml/kg steps (minimum = 4ml/kg Predicted Body Weight (PBW))
  - If Pplat<25 cmH₂O and VT<6ml/kg, increase VT by 1ml/kg until Pplat>25 or VT=6ml/kg
- Conservative fluid strategy preferred if patient is normotensive and non-oliguric
- Methylprednisolone 1 mg/kg IV daily may be beneficial in early, severe ARDS
  - ‘Meduri protocol’: 1mg/kg bolus followed by 1mg/kg/day continuous drip over 24 hours from day 1 through day 14, 0.5mg/kg/day continuous drip from day 15-21, 0.25mg/kg/day drip from day 22-25 and 0.125mg/kg/day from day 26 to 28; if the patient is extubated between day 1 and 14, the protocol is advanced to day 15; given in early ARDS (within 72 hours (up to 5 days) of diagnosis of ARDS, reduction in mortality, duration of ventilation, ICU stay)
- “Permissive hypercapnea” may be allowed if no concern for elevated intracranial pressure as long as the PCO₂ < 80 and pH > 7.2 (below recommendations for keeping pH>7.3 are from ARDSNet)
  - If pH<7.3, increase respiratory rate until pH>7.3 or PCO₂<25 (maximum RR=35)
  - If pH 7.15-7.3, increase respiratory rate to 35
  - If pH remains <7.15, VT may be increased in 1ml/kg increments until pH>7.15
    - Pplat target of 30 may be exceeded
    - Consider IV infusion of Sodium Bicarbonate
- Prone positioning may be of benefit in refractory cases; technically very difficult to perform
- Airway Pressure Release Ventilation may be of benefit in refractory cases
- Oscillatory ventilation may be of benefit in refractory cases. 1 oscillatory ventilator has been purchased at VCMC. Pulmonary consultation required
- Nitric Oxide may be of benefit in refractory cases (not available at VCMC)
- Supportive Care
  - Nutritional support (consider Oxepa)

Prognosis
- 31% mortality rate quoted with maximal medical therapy and protective lung ventilation

Ventilator Associated Pneumonia (VAP)/ Hospital-acquired Pneumonia (HAP)/ Healthcare-Associated Pneumonia (HCAP)

Definitions
- **HAP**: pneumonia that occurs 48 hours or more after admission
- **VAP**: pneumonia that arises more than 48-72 hours after endotracheal intubation
  - VAP occurs in 9-27% of all intubated patients
  - Risk of VAP is highest early in the course of ventilation (3%/day risk in the first 5 days of ventilation, 2%/day risk from days 5-10 of ventilation, 1%/day risk after day 10)
- **HCAP**: pneumonia that arises in a patient with one or more of the following risk factors:
  - Hospitalization for 2 days or more in the preceding 90 days
  - Residence in a nursing home or extended care facility
  - Home infusion therapy (including antibiotics, chemotherapy) within 30 days
  - Chronic dialysis within 30 days
  - Home wound care within 30 days
  - Attended a hospital clinic within 30 days
  - Family member with multi-drug resistant pathogen
- “**Early-onset**” pneumonia occurs within 4 days of admission (HAP) or intubation (VAP)
  - Better prognosis, more likely to be caused by a sensitive bacteria (e.g. Moraxella catarrhalis, Haemophilus influenza, Strep pneumonia)
- “**Late-onset**” pneumonia occurs ≥ 5 days after admission (HAP) or intubation (VAP)
  - More likely to be caused by a multi-drug resistant (MDR) organism (e.g. multi-drug resistant (MDR) enteric gram (-) rods [Pseudomonas aeroginosa, Acinetobacter, Enterobacter-Klebsiella group], Methicillin-resistant Staphylococcus aureus)

Risk Factors for Multi-Drug Resistant (MDR) Pathogens in VAP/HAP/HCAP
- Antimicrobial therapy in last 90 days
- Current hospitalization of 5 days or more
- High frequency of antibiotic resistance in the community or in the specific hospital unit
- Presence of risk factors for HCAP above
- Immunosuppressive disease and/or therapy

Modifiable Risk Factors / Prevention of VAP
- Increased risk of VAP with reintubation, nasotracheal intubation (vs. orotracheal intubation), enteral feeding (particularly when the patient is not semi-recumbent at 30-45°), transfusion
- Decreased risk of VAP with:
  - non-invasive ventilation (not intubating the patient in the first place)
  - shorter duration of ventilation (assess for readiness to extubate daily)
  - hospital staff using alcohol-based hand cleansing
  - continuous aspiration of subglottic secretions via special endotracheal tube
  - ET Tube cuff pressure >20 cm H2O to prevent bacterial passage to the lungs
  - post-pyloric feeding versus gastric feeding
  - semi-recumbent positioning (30-45°)
  - chlorhexidine oral cleansing
  - selective gut decontamination (but increases risk of multi-drug resistant organisms, thus should be restricted to the first 96 hours of intubation in trauma patients only)
  - in some groups, prior antibiotic use decreases risk of VAP but increases risk of multi-drug resistant pathogens, particularly with longer duration of antibiotic use
  - restrictive transfusion trigger policy
  - leukodepleted PRBCs (vs. non-leukodepleted) (all PRBCs at VCMC are leukodepleted)
  - trend towards reduced VAP with sucralfate versus H2-blockers or proton pump inhibitors (but increased ulcer bleeding)
CDC Nomenclature for Ventilator Associated Pneumonia was changed to the following (2013):

**Ventilator Associated Events:**

<table>
<thead>
<tr>
<th>Step 1</th>
<th>Ventilator Associated Condition (VAC) (&gt;= 1 required)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patient has a baseline period of stability or improvement on the ventilator, defined by ≥ 2 calendar days of stable or decreasing daily minimum FiO2 or PEEP values, prior to:</td>
</tr>
<tr>
<td></td>
<td>Daily minimum FiO2 increase ≥0.2 (20 points) x 2 consecutive days (after 2+ days of stable or decreasing daily minimum values)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Step 2</th>
<th>Infection-related Ventilator Associated Complication (IVAC) = VAC + below</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Temperature &gt; 38º C or &lt;36º C -OR- White Blood Cell count ≥ 12,000 or ≤ 4,000 cells/mm³</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Step 3</th>
<th>Possible Ventilator Associated Pneumonia (meets criteria for VAC and IVAC, and:)</th>
<th>Probable Ventilator Associated Pneumonia (meets criteria for VAC and IVAC, and:)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Purulent respiratory secretions ¥ (defined as secretions from the lungs, bronchi, or trachea that contain &gt;25 neutrophils and &lt;10 squamous epithelial cells per low power field, or equivalent semi-quantitative results) -OR- One of the following ¥ (qualitative, semi-quantitative, or quantitative):</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Positive culture of sputum^</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Positive culture of endotracheal aspirate^</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Positive culture of bronchoalveolar lavage^</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Positive culture of lung tissue^</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Positive culture of protected specimen brushing^</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Purulent respiratory secretions ¥ AND one of the following (meeting definition of purulent secretions to the left):</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Positive endotracheal aspirate ≥ 10⁵ CFU/mL or equivalent semi-quantitative</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Positive culture of bronchoalveolar lavage ≥ 10⁴ CFU/mL or equivalent semi-quantitative result</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Positive culture of lung tissue ≥ 10⁴ CFU/g or equivalent semi-quantitative result</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Positive culture of protected specimen brushing ≥ 10³ CFU/mL or equivalent semi-quantitative result -OR-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>One of the following results ¥ (without requirement for purulent respiratory secretions), as outlined in protocol</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Positive pleural fluid culture</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Positive lung histopathology</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Positive diagnostic test for Legionella spp.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Positive diagnostic test for viral pathogens (i.e. influenza, RSV, adenovirus, others)</td>
<td></td>
</tr>
</tbody>
</table>

¥: Excludes normal respiratory/oral flora and mixed respiratory/oral flora, candida species or yeast identified, coagulase negative Staphylococcus, Enterococcus

¥: Collected after 2 days of mechanical ventilation and within +/- 2 days of onset of increase in FiO2 or PEEP

Abbreviations: CFU, colony forming units; RSV, respiratory syncytial virus


[Return to Table of Contents]
Management of Suspected Ventilator-Associated Pneumonia

### Suspected Ventilator-associated pneumonia
- See page 65

#### Work-up:
- blood culture x 2; “semi-quantitative” culture and gram stain of lower respiratory tract (endotracheal aspirate, bronchoalveolar lavage (BAL) or protected specimen brush sample (called “Mini BAL”)

#### Early onset (<48-96 hours in hospital) AND no risk factors for Multi-Drug Resistant (MDR) Pathogens (page 65)

#### Late-onset: ≥5 days OR presence of risk factors for MDR bacteria

### Empiric antibiotic options
- **Antipseudomonal β-lactam ≡**
  - Piperacillin-tazobactam
  - Ceftazidime or cefepime
  - Imipenem or meropenem (2nd line)
- PLUS fluoroquinolone or aminoglycoside
  - Levofoxacin or ciprofloxacin
  - Amikacin, gentamicin or tobramycin (once daily dosing preferred over q8 hour dosing)
- PLUS MRSA agent
  - Vancomycin (VancoTrough 15-20 mcg/mL)
  - Linezolid (2nd-line at VCMC)

### Empiric antibiotic options
- Ceftriaxone + Azithromycin
- Levofloxacin or moxifloxacin
- Ampicillin/sulbactam
- Ertapenem (this medication is not preferable at VCMC)

### De-escalate antibiotics based on culture results within 48-72 hours
- If clinically improved, cultures negative & Clinical Pulmonary Infection Score (CPIS) † ≥ 6 or less at 72 hours, consider D/C antibiotics
- If cultures negative and clinical worsening at 72 hrs, search for other pathogens, sites of infection or consider noninfectious disease processes

### Duration of treatment:
- VAP in immunocompetent, nonneutropenic pts with good clinical response: 7-8 days
- VAP caused by Non-fermenting Gram (-) rod (Acinetobacter spcc., Flavobacterium spcc., Pseudomonas aeruginosa, Burkholderia cepacia, Burkholderia pseudomallei, Stenotrophomonas maltophilia):
  - 15 days
  - Unclear if ongoing dual therapy superior to monotherapy once susceptibilities are known (may be safe to switch to monotherapy after 5-7 days)

### Clinical Pulmonary Infection Score (CPIS) †

- **Temperature:**
  - 36.5-38.4= 0 points
  - 38.5-38.9 or 36-36.5 = 1 point
  - >39 or <36 = 2 points

- **Leukocytosis:**
  - 4,000-11,000 = 0 points
  - <4,000 or >11,000 = 1 point
  - Absolute Band Count > 500 = + 1

- **Tracheal Secretions:**
  - Rare = 0 points
  - Abundant = 1 point
  - Abundant and Purulent = 2 points

- **PaO2/FiO2 mmHg**
  - >240 or ARDS = 0 points
  - <240 and no ARDS = 2 points

- **Chest Radiograph**
  - No Infiltrate = 0 points
  - Diffuse or Patchy Infiltrates = 1 point
  - Localized Infiltrate = 2 points

- **Tracheal Aspirate culture**
  - negative = 0 points
  - positive = 2 points

- **CPIS Score > 6** is 60% sensitive and 59% specific for the diagnosis of VAP.

### Reference:

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Borrowed with permission from Joseph Esherick, MD.
Community-Acquired Pneumonia (CAP)

Definitions
- Constellation of clinical findings (symptomatology, laboratory data, and radiographic findings) indicating infection of the lower respiratory tract; AND
- The patient does not meet the definition for Healthcare Acquired Pneumonia (HCAP), Hospital-Acquired Pneumonia (HAP), or Ventilator-Associated Pneumonia (VAP) (see page 65)
- Usual etiologies of Inpatient (non-ICU) CAP: S. pneumoniae, M. pneumoniae, C. pneumoniae, H. influenzae, Legionella species, aspiration or oral contents, respiratory viruses
- Usual etiologies of Severe CAP: S. pneumoniae, Methicillin Sensitive Staph aureus (MSSA) and Methicillin Resistant Staph aureus (MRSA), Legionella species, Gram-negative bacilli, Haemophilus influenzae, Pseudomonas (see page 69 for Pseudomonas Risk Factors)

Workup
- Chemistries, Liver Function Tests, Renal Panel, CBC with differential, Pulse Oximetry
- C-reactive Protein
  - Level $>10$mg/dL has a Positive Likelihood Ratio of 50 for bacterial pneumonia
  - Level $<1$mg/dL has a Negative Likelihood Ratio of 0.27 for bacterial pneumonia
- Chest X-ray
  - may be normal in up to $1/3$ of patients who are eventually diagnosed with CAP
  - more likely to be falsely negative in neutropenia or dehydration
- Blood cultures x 2
  - Rate of bacteremia only 6-9%; half of positive blood cultures are contaminants
  - Blood culture results in change in antibiotic therapy in 0.25 to .04% of patients
  - Still recommended, particularly for ICU patients
- Sputum Culture: adequate specimen obtained in only 22% of cases
  - “Q score” is obtained by totaling the points for the sputum Gram stain characteristics:

<table>
<thead>
<tr>
<th>Characteristic ↓</th>
<th>Points →</th>
<th>-2</th>
<th>-1</th>
<th>0</th>
<th>+1</th>
<th>+2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Squamous epithelial cells</td>
<td>$\geq 10$ cells/LPF</td>
<td>0-9 cells/LPF</td>
<td>Absent</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WBCs</td>
<td>$&lt;10$ WBC/LPF</td>
<td>10-24 WBC/LPF</td>
<td>$\geq 25$ WBC/LPF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mucus</td>
<td>Absent</td>
<td>Present</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

A Q score of 2+ or 3+ is considered a very good specimen; repeat specimen is automatically ordered for squames $>10$

- HIV Test recommended for those ages 15-45
- Consider Legionella pneumophila and Strep pneumonia urinary antigens in severe CAP cases

Assessment of Pneumonia Severity/ Site of Care of Patients with CAP
- Numerous scoring systems available; superiority of one system over another has not been established
- “Severe” Community Acquired Pneumonia: $\geq 1$ Major Criteria OR $\geq 3$ Minor Criteria
  - Major Criteria: Invasive mechanical ventilation, septic shock with the need for vasopressors
  - Minor Criteria: Respiratory rate $\geq 30$ breaths/min, PaO2/FiO2 ratio $\leq 250$, Multi-lobar infiltrates, Confusion/disorientation, Uremia (BUN level $\geq 20$ mg/dL), Leukopenia (WBC count $< 4000$ cells/mm3), Thrombocytopenia (platelet count $< 100,000$ cells/mm3), Hypothermia (core temperature $< 36^\circ$C), Hypotension requiring aggressive fluid resuscitation [may also consider hypoglycemia (in nondiabetic patients), acute alcoholism/ alcoholic withdrawal, hyponatremia, unexplained metabolic acidosis or elevated lactate level, cirrhosis, and asplenia]
  - Strong consideration to management in ICU if the patient meets criteria for “severe pneumonia”
- CURB-65 Criteria
  - 1 point each for Confusion, Uremia (BUN$>20$mg/dL), Respiratory rate $\geq 30$, Blood pressure $<90/60$, age $\geq 65$ years
  - A score of 0-1 may be considered for outpatient therapy; a score of 2 treated as an inpatient; a score of $\geq 3$ should be considered for ICU management
• Assessment of Pneumonia Severity/ Site of Care of Patients with CAP (continued)

**Pneumonia Severity Index (PSI)**

<table>
<thead>
<tr>
<th>Age</th>
<th>Physical Exam findings</th>
<th>Laboratory or Radiographic Finding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male: Years of Age</td>
<td>Altered Mental Status = 20</td>
<td>Arterial pH &lt; 7.35 = 30</td>
</tr>
<tr>
<td>Female: Years of Age - 10</td>
<td>Respiratory Rate &gt;30 = 20</td>
<td>BUN &gt; 30 = 20</td>
</tr>
<tr>
<td>Nursing Home Resident = 10</td>
<td>Systolic Blood Pressure &lt;90 = 20</td>
<td>Sodium &lt; 130 = 20</td>
</tr>
<tr>
<td></td>
<td>Temperature &lt; 35 or &gt;40 = 15</td>
<td>Glucose &gt; 250 = 10</td>
</tr>
<tr>
<td></td>
<td>Pulse &gt; 125 = 10</td>
<td>Hematocrit &lt; 30 = 10</td>
</tr>
</tbody>
</table>

**Comorbid Illnesses**

- Neoplastic disease = 30
- Liver Disease = 20
- Congestive Heart Failure = 10
- Cerebrovascular Disease = 10
- Renal Disease = 10

**Recommendations:**

- Hospitalization Recommended for score > 91 (class IV-V)
- Brief admission or observation for score 71-90 (class III)

**Mortality Rates:**

- Class I or II (<= 70 points)= 0.1-0.6%
- Class III (71-90 points) = 0.9%
- Class IV (91-130 points) = 9.3%
- Class V (>130 points) = 27%


• Also consider hospitalization for unstable comorbid conditions, poor psychosocial circumstances, failed outpatient therapy, inability to take oral medication, active substance abuse

**Empiric Treatment of Suspected CAP**

<table>
<thead>
<tr>
<th>Category</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitalized, Non-ICU</td>
<td>Beta Lactam* AND [Macrolide¥ OR Doxycycline (2nd line)], -OR- Respiratory Fluoroquinolone ζ</td>
</tr>
<tr>
<td>ICU Patient without Pseudomonas Risk Factors†</td>
<td>Beta Lactam* AND [Macrolide¥ OR Doxycycline (2nd line)], -OR- Beta Lactam* AND Respiratory Fluoroquinoloneζ ADD Vancomycin or Linezolid for MRSA Risk Factors‡</td>
</tr>
<tr>
<td>If Documented Beta Lactam Allergy: Quinolone +/- Clindamycin</td>
<td></td>
</tr>
<tr>
<td>ICU Patient with Pseudomonas Risk Factors†</td>
<td>Antipseudomonal Agent ∫ AND either ciprofloxacin or levofloxacin, OR Antipseudomonal Agent ∫ AND Aminoglycoside AND [antipseudomonal Quinolone = OR Macrolide ¥ ] Add Vancomycin or Linezolid for MRSA Risk Factors‡</td>
</tr>
<tr>
<td>If Documented Mild Beta Lactam Allergy: Ceftazidime or Cefepime IV + Antipseudomonal Quinolone = or IV Aminoglycoside</td>
<td></td>
</tr>
<tr>
<td>If Documented Anaphylactic Beta Lactam Allergy: Meropenem IV or Aztreonam IV + Antipseudomonal Quinolone = or IV Aminoglycoside</td>
<td></td>
</tr>
</tbody>
</table>

* ceftriaxone, cefotaxime, ampicillin/sulbactam, or ertapenem
¥ azithromycin or clarithromycin
ζ levofloxacin, moxifloxacin, gatifloxacin, gemifloxacin
† Residence in a long-term care facility, underlying cardiopulmonary disease, multiple medical comorbidities, recent antibiotics for >7 days or hospitalization for at least 48 hours in the past month, structural lung disease (severe COPD, cystic fibrosis, or bronchiectasis), malnutrition, immunosuppressive illness, or chronic prednisone use of >10mg/day.
∫ Piperacillin-tazobactam, cefepime, ceftazidime, aztreonam, imipenem (2nd line) or meropenem (2nd line)
‡ Residence in a long-term care facility, history of intravenous drug use, post-influenza, sickle cell disease, or history of MRSA = levofloxacin, gatifloxacin, moxifloxacin
Risk Factors for Penicillin and Drug-resistant Pneumococci
- Age>65, Beta lactam therapy in last 90 days, Alcoholism, Immunosuppressive illness, multiple medical co-morbidities, exposure to infected child in day care center

Duration of Antibiotic Therapy
- Switch from IV to oral therapy when the patient is clinically stable
  - Signs of clinical stability: Temperature ≤37.8°C, heart rate ≤100 beats/min, respiratory rate ≤24 breaths/min, systolic blood pressure ≥90 mm Hg, arterial oxygen saturation ≥90% or pO2 ≥ 60 mm Hg on room air, ability to maintain oral intake, normal mental status
- Patients should be treated for at least 5 days (usual duration 7-10 days), for at least 48 to 72 hours beyond their last fever, and should have no more than 1 sign of clinical instability when therapy is stopped
- ‘Short-duration’ (5 days) of therapy may be suboptimal for patients with bacteremic S. aureus pneumonia (because of the risk of associated endocarditis and deep-seated infection), for those with meningitis or endocarditis complicating pneumonia, and for those infected with other, less common pathogens (e.g., Burkholderia pseudomallei or endemic fungi).

Etiologies of Non-Resolving Pneumonia

<table>
<thead>
<tr>
<th>Failure to Improve</th>
<th>Deterioration or Progression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early (72 h of treatment): Normal</td>
<td>Early (≤ 72 h of treatment)</td>
</tr>
<tr>
<td>Delayed:</td>
<td>Delayed</td>
</tr>
<tr>
<td>- Resistant organism</td>
<td>- Nosocomial superinfection:</td>
</tr>
<tr>
<td>- Parapneumonic effusion/ empyema</td>
<td>o Nosocomial pneumonia</td>
</tr>
<tr>
<td>- Nosocomial superinfection:</td>
<td>o Extrapulmonary</td>
</tr>
<tr>
<td>Nosocomial pneumonia,</td>
<td>- Exacerbation of comorbid illness</td>
</tr>
<tr>
<td>Extrapulmonary</td>
<td>- Intercurrent noninfectious disease</td>
</tr>
<tr>
<td>- Noninfectious</td>
<td>o PE</td>
</tr>
<tr>
<td>- Complication of pneumonia (e.g., BOOP)</td>
<td>o Myocardial infarction</td>
</tr>
<tr>
<td>- Misdiagnosis: PE, CHF, vasculitis</td>
<td>o Renal failure</td>
</tr>
<tr>
<td>- Drug fever</td>
<td></td>
</tr>
</tbody>
</table>

Core Measures for Pneumonia (specific to CAP, generalizable to all pneumonia)
- ABG or Pulse Oximetry within 24 hours of Admission
- Blood cultures drawn before antibiotics are given
- Blood cultures within first 24 hours in all patients admitted to ICU
- Antibiotics given within 6 hours of arrival
- Correct Antibiotic for Admitted Patients
- Pneumococcal and Influenza Screening/Vaccination
- Smoking Cessation Advice/Counseling

Acute Asthma/Status Asthmaticus

Evaluation

- Consider spirometry, with FEV₁ < 25% concerning for severe asthma and warranting further workup and observation
- Pulse oximetry, ABG, Chest X-Ray, CBC, Chemistries, +/- EKG

Treatment

- Oxygen: goal O₂ Sat ≥ 92% (humidification is likely to be of benefit)
- Bronchodilators
  - Beta2-agonist: Albuterol as intermittent (2.5-5 mg nebulized q 2 hours, q 1 hour prn) or continuous (10 mg over 1 hour “Hart” neb); low-dose Levalbuterol may cause less tachycardia
  - Anticholinergics: Atrovent 0.5 mg nebulized q 6 hours
- Steroids
  - Methylprednisolone 160 mg daily in 4 divided doses is adequate for most patients
  - Usually take 6-24 hours to take effect
- Non-invasive Positive Pressure Ventilation (NPPV) may be considered as an alternative to intubation

Adjunctive Treatments (not routinely recommended):

- Magnesium IV 2 grams IV over 20 minutes may be beneficial to a subgroup of patients with severely compromised FEV₁ (<30%, or <60% after 1 hour of therapy)
- Subcutaneous Epinephrine 0.3-0.5 ml of 1:1000 concentration subcutaneous q 20 minutes to a maximum of 3 doses
- Theophylline: narrow therapeutic index and high toxicity; only recommended for refractory cases
- Antibiotics: recommended only if concern for pneumonia or bronchitis (fever + purulent sputum)
- Heliox: Not routinely recommended

Specifics of Mechanical Ventilation in Asthma Exacerbations

- Indicated with refractory hypoxemia (PaO₂ < 60 mmHg), persistent hypercapnia (PaCO₂ > 55-77 mmHg), increasing hypercapnia despite aggressive treatment (PaCO₂ > 5 mmHg/h), signs of exhaustion despite bronchodilator therapy, worsening of mental status, hemodynamic instability, coma, apnea, or progressive deterioration despite aggressive medical therapy
- Ventilation may be very challenging, with severe obstruction of the airways increasing the risk of auto-PEEP buildup with subsequent very high risk for elevated peak pressures and pneumothorax
- Adequate time needs to be allowed for the patient to fully exhale before initiating the next breath
  - Using a stethoscope to determine when the breath has ended may be very beneficial in initial ventilator management
  - Consider bagging the patient and NOT attaching them to the ventilator in severe cases
- Propofol and Ketamine may reduce bronchospasm if intubation is warranted
- Halothane and enflurane (inhalational anesthetics) are bronchodilators and may be considered for refractory cases
- AVOID paralytics for risk of myopathy (consider cis-atracurium if paralysis is required)

Prognosis

- Severe asthma may have a mortality rate as high as 22%
- Risk factors for death in severe asthma include history of mechanical ventilation, increasing use of nebulizers, history of ICU admission, increased use of oral steroids, increased use of oral theophylline, history of hospital admission, 2 or more hospitalizations in the past year, history of sudden severe exacerbations, presence of significant cardiovascular disease or other medical condition, poor perception of dyspnea, mental illness, illicit drug use, low socioeconomic status

COPD Exacerbations

Evaluation
- Pulse oximetry, ABG, Chest X-Ray, EKG, CBC, Chemistries
- Assess for Purulent Sputum

Treatment
- Oxygen used VERY cautiously, to keep $O_2$ Sat 89-91% or $PaO_2$ at 60mmHg (no higher)
- Bronchodilators
  - Beta2-agonist: Albuterol as intermittent (2.5-5mg nebulized q 2 hours, q 1 hour prn) or continuous (10mg over 1 hour “Hart” nebul)
  - Anticholinergics: Atrovent 0.5mg nebulized q 6 hours
- Steroids
  - Methylprednisolone 30-40mg IV daily recommended in GOLD
- Antibiotics: only if increased sputum purulence AND increased dyspnea or increased sputum volume
  - Oral or occasionally IV, to cover Strep pneumonia, H. flu, and Moraxella spcc.
- Consider Non-Invasive Positive-Pressure Ventilation (NPPV)
- Supportive Care
  - Monitor fluid status and nutrition
  - Consider subcutaneous heparin
  - Identify and treat associated medical conditions (e.g. CHF, Arrhythmias)
  - Closely monitor condition of the patient

Indications for ICU Admission in COPD Exacerbations
- Severe dyspnea that responds inadequately to initial emergency therapy
- Changes in mental status (confusion, lethargy, coma)
- Persistent or worsening hypoxemia ($PaO_2 < 40$ mmHg), and/or severe/worsening hypercapnia ($PaCO_2 > 60$ mmHg), and/or severe/worsening respiratory acidosis ($pH < 7.25$) despite supplemental oxygen and noninvasive ventilation
- Need for mechanical ventilation
- Hemodynamic instability—need for vasopressors

Indications for Mechanical Ventilation in COPD Exacerbations
- Unable to tolerate NPPV or NPPV failure (direct physician bedside observation is often indicated in early moments of NPPV use to assess patient tolerance)
- Severe dyspnea with use of accessory muscles and paradoxical abdominal motion.
- Respiratory frequency > 35 breaths per minute
- Life-threatening hypoxemia
- Severe acidosis ($pH < 7.25$) and/or hypercapnia ($PaCO_2 > 60$ mm Hg)
- Respiratory arrest
- Somnolence, impaired mental status
- Cardiovascular complications (hypotension, shock)
- Other complications (metabolic abnormalities, sepsis, pneumonia, pulmonary embolism, barotrauma, massive pleural effusion)
- NOTE: Patients with severe COPD Exacerbations requiring intubation should be met with informed consent; such patients are extremely difficult to get off the ventilator and may be facing tracheostomy and prolonged ventilator rehabilitation

COPD Exacerbation not responding to usual medical therapy
- Consider other etiologies of hypoxia/hypercarbia (CDSPIES: Cardiac, Drugs, Secretions, Pneumothorax, Infection, Embolism, Splinting, Spasm)

Tracheostomy

This writeup incorporates the VCMC/Santa Paula Hospital Tracheostomy Guideline, 2012, available through the VCMC Medical Staff Office website link to Clinical Practice Guidelines.

Indications for Tracheostomy:
- Prolonged Ventilatory Support Needed
- Difficult Airway
- Attempts to wean from mechanical ventilation unsuccessful for 14-21 days
  - Subglottic Stenosis is more common with prolonged intubation past 14 days
- Relief of Upper Airway Obstruction
- Severe Sleep Apnea
- Pulmonary Secretion Clearance
- “Early tracheostomy”: when duration of ventilator-dependence is estimated to be >14 days,
  - tracheostomy may be considered as early as 48 hours (usually considered at 5-7 days)

Benefits of Tracheostomy:
- Tracheostomy in general
  - Earlier mobilization of the patient with physical therapy
  - Decrease in airway resistance vs. an endotracheal tube, decreasing work of breathing
  - Duration of ventilation
  - Risk of Ventilator-Associated Pneumonia
  - Sedation necessary is much less vs. endotracheal tube
  - If the patient disconnects from the ventilator, it is no longer a medical emergency—the patient just gets reconnected to the ventilator
- “Early tracheostomy”
  - Cochrane review of early tracheostomy suggests decreased duration of mechanical ventilation and decreased ICU stay in patients receiving tracheostomy at <1 week
  - 1 study also suggests decreased mortality

Drawbacks of Tracheostomy:
- Difficulty swallowing (video swallow evaluation generally indicated prior to initiating oral feeding)
- Risk of the surgical procedure (bleeding, infection, loss of the airway most commonly; less commonly: fistulas, tracheal stenosis/tracheomalacia, pneumothorax, pneumonia, cellulites, false placement of cannula, cardiopulmonary arrest, death)

Percutaneous tracheostomy (Ciaglia Technique: “Blue Rhino”) versus Surgical Tracheostomy:
- May be less bleeding risk with Percutaneous Tracheostomy
- Percutaneous tracheostomy is relatively contraindicated in morbid obesity, repeated tracheostomy, high PEEP, severe coagulopathy, and unusual neck anatomy

Post-op Care:
- After a tracheostomy, the patient will be managed in the ICU or DOU for at least the first 24 hours.
- Obturator at bedside at all times.
- Extra same type & size trach tube at bedside at all times along with clean Velcro trach ties.
- Keep cuff inflated while on a ventilator. Check cuff daily for appropriate pressure (~20cm water pressure to prevent tracheal necrosis).
- Suction trach as needed. Initially will require more frequent suctioning along with pulmonary toilet.
- Change and clean inner cannula daily. If lots of secretions and debris, inner cannula may need to be changed or cleaned more frequently.
Post-op Care (continued):
- Bleeding around trach site is common and usual during initial post-op period. However, contact operating service if brisk bright red blood bleeding or oozing resulting in saturated dressing within minutes.
- During this period, the tracheostomy is not to be changed or removed except by service performing the procedure or qualified physician who will perform first trach change.
- The cuff should be deflated after 24 hours in non-ventilated patients.
- Humidified air once off ventilator.
- Tracheostomy care should be taught to patient by nursing staff and RT when patient is off ventilator. This includes self-suctioning.
- Arrangements should be initiated on POD 1 for home suction machine, trach supplies, and home health visit if patient is anticipated to be discharged home with tracheostomy.
- Patient may be transferred from DOU or ICU when able to demonstrate self-suctioning and does not require frequent suctioning by staff.

First Tracheostomy Change:
- The first tracheostomy change is usually done between day 4 and 7. A thin patient who has a secure Bjork flap may get an earlier tracheostomy change than an obese patient. Stay sutures may be removed at this time. The timing of trach change to be determined by operating service.
- Recommended that first trach change will be performed by operating service or by qualified physician after discussing with operating service.
- If a well formed tract is noted at time of first trach change, RT/RN may perform all future trach changes unless otherwise instructed by operating service.
- Trach Care instruction for patient and family including:
  - How to remove and replace entire trach tube (outer and inner cannulas).
  - Cleaning of trach stoma.
  - Daily cleaning of inner cannula.
  - At least weekly cleaning of outer cannula.
- A Passy-Muir valve trial can be initiated.

Passy-Muir Speaking Valve:
- One-way valve which allows the patient to exhale around their tracheostomy and speak

```
+-----------------+------------------------------------------+-----------------------------+
| Suction patient, deflate cuff | Stop trial, inflate cuff | Consider ENT Consult for correct tube size/airway obstruction |
| Stable Vital Signs? | | |
| Air around the deflated cuff? | No | |
| Yes | Stop trial, remove valve, inflate cuff, consider later trial |
| Voicing with finger occlusion? | HR, RR, O₂Sat ok? |
| No | Continue trial 5-10 minutes, Establish schedule for future use |
| Yes | |
| Place Passy-Muir valve in-line | |
```
Tracheostomy Decannulation Protocol:

- Process of safely removing tracheostomy tube.
  - Initial indication for tracheostomy placement must be resolved.
  - Downsized to a size 4 shiley.
  - Monitor overnight after downsizing. Notify physician if difficulty with breathing.
  - If patient tolerates downsizing, attempt finger occlusion. If tolerates finger occlusion then capping trial.
  - Physician will write order in chart for capping trial.

- Capping trial protocol: Patient must be monitored on pulse ox for at least 10 minutes with nurse in the room who will cap the trach.
  - After 10 minutes, nurse or RT will need to demonstrate to patient how to uncap trach. Patient must be able to demonstrate how to uncap trach.
  - If patient unable to uncap trach, then consider transferring to monitor bed, or DOU depending on a case by case basis.
  - Trach should not be uncapped for routine suctioning or trach care during capping protocol unless patient is complaining of shortness of breath or in distress.
  - Physician to be notified if trach is uncapped.

- If patient tolerates capping overnight, the trach tube can be removed.
  - Occlusive dressing will be placed over the stoma. Encourage the patient to cover the stomal dressing when coughing and talking to facilitate site closure. Stoma dressing should be changed as often as necessary to maintain a clean, dry dressing.
  - Following decannulation, a tracheostomy tube of the appropriate size should be readily available for reinsertion if the patient develops respiratory distress.
  - Patient to be monitored overnight.

Discharge:

- If discharging with trach:
  - Arrange for home suction machine, trach supplies, and may require home health follow-up.
  - Patient and family must be taught routine trach care and hygiene which needs to be continually taught during the hospitalization.
  - Teach how to manage mucus plug.
  - Arrange follow up with operating service.
  - Trach sutures must be removed prior to discharge.

- If decannulated:
  - Arrange follow up with operating service.
  - Dressing supplies.
  - Return precaution for respiratory distress.

GASTROENTEROLOGY

Cirrhosis and its Complications

Pathophysiology
- Cirrhotics have higher levels of endotoxin, TNF-α, Interleukin-6, and other pro-inflammatory cytokines than non-cirrhotic patients.
- Cirrhotics have less activated Protein C than non-cirrhotics.
- Infection in cirrhotic patients increases the risk of bleeding (and rebleeding) due to:
  - increased sinusoidal pressure
  - altered hemostasis
  - increased nitric oxide production which alters platelet aggregation
  - chronically decreased levels of coagulation factors VII, X, V and II, increasing the risk of severe coagulation abnormalities with DIC and sepsis
  - increased levels of endogenous heparin-like substances in the face of infection

Complications: Cirrhosis and Infection
- Approximately 30-50% of cirrhotics admitted to the hospital are admitted for some form of infection or sepsis.
- Once admitted, 15-35% of cirrhotic patients develop nosocomial infections (compared with 5-7% of the general population).
- The main sites of infection in cirrhosis include ascites, urinary tract, lungs, and blood.
- The most common bacterial organism is *E. coli*, followed by *Staph aureus, Enterococcus faecalis, Strep pneumonia, Pseudomonas aeruginosa*, and *Staph epidermidis*.

Complications: Cirrhosis and Sepsis
- Retrospective study of 100 consecutive patients with Child’s C Cirrhosis, creatinine>1.3, and mechanically ventilated in a Medical ICU revealed a survival rate at 72 hours of 2% (1988).
- Subsequent studies from 1998-2001 of all MICU admissions with cirrhosis: 43-49% mortality rate seen.
- Conventional signs and symptoms of infection are often lacking in cirrhotics, even in severe sepsis. A high index of suspicion for infection is necessary in cirrhotics, when they are unwell or present with non-specific complaints.
- All surgery in cirrhotic patients is high-risk for post-operative infection (or bleeding or hepatorenal), not only in the immediate post-operative period but often weeks to months later.
- Anecdotally, cirrhotic patients seem to tolerate encephalopathy from sepsis better than non-cirrhotic patients, and can be mentating up until the point of circulatory collapse and death.
- Anecdotally, serum lactate levels correlate much better with sepsis than blood pressure or pulse.
- It is very reasonable to consider serial labs, including serial serum lactate levels, to evaluate cirrhotic patients admitted with non-specific complaints, particularly in the post-operative setting and particularly with low blood pressures.

Complications: Cirrhosis, Sepsis, and Adrenal Insufficiency
- In one recent series, 51% of cirrhotic patients with severe sepsis (based on Cosyntropin Stimulation Testing) qualified as adrenally insufficient.
- The patients with adrenal insufficiency had a hospital mortality rate of 80.7% versus an 36.7% mortality rate in those with normal adrenal function.
Complications: Spontaneous Bacterial Peritonitis (SBP)

- Bleeding (particularly variceal bleeding) in cirrhotic patients is associated with a very high incidence of Spontaneous Bacterial Peritonitis (SBP) (30% incidence in Child’s C cirrhosis vs. 8% in Child’s B and 3% in Child’s A)
- All patients with variceal bleeding should be given antibiotic treatment
- All patients with presumed infection should undergo paracentesis to rule out Spontaneous Bacterial Peritonitis
  - Primary SBP: ≥ 250 polymorphonuclear cells in ascites fluid
  - Secondary SBP (from bowel perforation, cholecystitis, cholangitis, etc.): ↑ concern if ascitic fluid WBC count > 10,000/μL, glucose< 50 mg/dL, LDH>1000 U/L, protein>1g/dL, alkaline phosphatase> 240 U/L, carcinoembryonic antigen (CEA)>5 ng/mL, or polymicrobial gram stain or culture growth

SBP Treatment
- Cefotaxime 2 grams IV q8 hours or Ceftriaxone 2 grams IV daily; or
- Trimethoprim/Sulfamethoxazole DS 1 tab po bid x 7 days; or
- Ciprofloxacin 500 mg po bid to complete 7 days (norfloxacin off the market)
- Use of Albumin along with Cefotaxime in one study of 126 patients with SBP (1999, study has not been repeated) showed improved mortality and less renal failure when patients were given albumin 1.5 g/kg IV on day 1 and albumin 1 g/kg IV on day 3; another observational study showed improved only in high risk patients with high albumin or high creatinine. Further studies needed but reasonable treatment option.

SBP Prognosis: With proper treatment with a 3rd generation cephalosporin, recovery from SBP is at least 80-90%, and 30-day survival is at least 80%, even when sepsis is present

SBP Prophylaxis
- Indicated as an outpatient with prior history of SBP, history of variceal bleeding, ascites total protein < 1.5 g/dL, serum Tbili > 2.5 mg/dL, Child’s Pugh score ≥10, serum sodium <130, or creatinine > 1.2 mg/dL.
- Options include TMP/SMX DS 1 tab daily; ciprofloxacin 500 mg daily

Gastrointestinal Bleeding (see also: Bleeding in Liver and Kidney Disease, Upper GI Bleeding)

Management of Gastroesophageal Variceal Bleeds
- Octreotide 50 mcg IV bolus, then infuse at 50 mcg/hr x 3-5 days for variceal bleeds
- Antibiotic prophylaxis x 7 d: ↓ risk of SBP or variceal rebleeding
- Endoscopic variceal ligation (EVL) or sclerotherapy if ligation not possible
  - Serial EVL every 3 weeks until varices are obliterated
- Beta-blockers: propranolol or nadolol titrated to decrease resting heart rate 25%
- Nitrates: isosorbide mononitrate 30 mg PO daily; added to serial EVL and β-blockers
- Transjugular intrahepatic portosystemic shunt (TIPS) for gastric varices or recurrent esophageal variceal bleeds.

Complications: Cirrhosis and Hepatorenal Syndrome

- Diagnosis of exclusion (must rule out prerenal azotemia); serum creatinine >1.5 mg/dL or CrCl<40 mL/min and urinary indices mimic prerenal azotemia (UNa<10 mEq/L)
- No sustained renal improvement after fluid challenge and stopping diuretics
- Therapy options: midodrine 7.5-15 mg PO tid AND octreotide 100-200 mcg subcut tid; OR norepinephrine 0.5-3 mg/hr infusion; duration of treatment is 5-15 d until creatinine<1.5 mg/dL (terlipressin is alternative to norepinephrine but unavailable in US)
  - Add albumin 1 gm/kg IV on day 1, then 20-40 grams IV daily
### Child-Turcotte-Pugh Cirrhosis Classification

<table>
<thead>
<tr>
<th>Points:</th>
<th>1 point</th>
<th>2 points</th>
<th>3 points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin/Nutrition</td>
<td>&gt;3.5/good</td>
<td>2.8-3.5/good</td>
<td>&lt;2.8/Poor</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>&lt;2</td>
<td>2-3</td>
<td>&gt;3</td>
</tr>
<tr>
<td>INR</td>
<td>&lt;=1.7</td>
<td>1.8-2.24</td>
<td>&gt;2.25</td>
</tr>
<tr>
<td>Ascites</td>
<td>None</td>
<td>Controlled</td>
<td>Uncontrolled</td>
</tr>
<tr>
<td>Encephalopathy</td>
<td>None</td>
<td>Stage 1-2</td>
<td>Stage 3-4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Encephalopathy</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1</td>
<td>alert, euphoria or depression, mild confusion, slurred speech, disordered sleep, + asterix</td>
</tr>
<tr>
<td>Stage 2</td>
<td>lethargy, moderate confusion, + asterix</td>
</tr>
<tr>
<td>Stage 3</td>
<td>marked confusion, incoherent speech, sleeping but arousable</td>
</tr>
<tr>
<td>Stage 4</td>
<td>coma</td>
</tr>
</tbody>
</table>

### Surgical Mortality and Child-Turcotte-Pugh Class

<table>
<thead>
<tr>
<th>Surgery</th>
<th>Child’s A</th>
<th>Child’s B</th>
<th>Child’s C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-emergency abdominal surgery</td>
<td>10%</td>
<td>30%</td>
<td>82%</td>
</tr>
<tr>
<td>Emergent abdominal surgery</td>
<td>22%</td>
<td>38%</td>
<td>100%</td>
</tr>
<tr>
<td>Elective cardiac surgery</td>
<td>0%</td>
<td>50%</td>
<td>100%</td>
</tr>
</tbody>
</table>

### MELD Score

The MELD score is calculated using the following formula:

\[
\text{MELD Score} = 0.957 \times \log(\text{creatinine mg/dL}) + 0.378 \times \log(\text{bilirubin mg/dL}) + 1.120 \times \log(\text{INR}) + 0.643.
\]

Multiply the score by 10 and round to the nearest whole number. Laboratory values less than 1.0 are set to 1.0 for the purposes of the MELD score calculation. For candidates on dialysis, defined as having 2 or more dialysis treatments within the prior week; or candidates who have received 24 hours of CVVHD within the prior week, will have their serum creatinine level automatically set to 4.0 mg/dL. MELD Score calculators are available online.

A MELD Score of 6 will qualify a patient for getting on the transplant list. A MELD Score of >15 is considered a candidate for liver transplantation.

### Mortality and MELD Score and Mortality in Selected Clinical Scenarios

**Surgery:**
- For elective abdominal operations, 90-day mortality rate is: 10% if MELD score ≤ 8; 25% if MELD score 9-16; and 50% if MELD score > 16.
- 30-day mortality for non-transplant surgery increases 1% per point for MELD scores between 6 and 20 and 2% per point for scores above 20.
- Recommend no surgery for MELD score > 15; consider surgery with close monitoring for MELD score 10-15; proceed with surgery for MELD score <10.

**Sepsis Unrelated to Spontaneous Bacterial Peritonitis (SBP):**
- Three-month survival was greater than 90 percent in patients with MELD <20 compared with approximately 60 percent in those with MELD ≥20.
Hepatorenal Syndrome, Type 2:
- MELD score of ≥20 was associated with 3 month transplant-free survival compared with 11 month median survival in those with a lower score.

Acute Variceal hemorrhage:
- Poorer prognosis with a MELD score ≥ 15 in one study
- Another study demonstrated that patients with MELD ≥18 who require four or more units of blood transfusion are at substantially increased risk of death in the setting of acute variceal hemorrhage compared with patients with lower MELD and lower transfusion requirement.

Trauma:
A retrospective study of 285 trauma patients with presumed cirrhosis who were evaluated at a single level-1 trauma center from 2003 to 2009 revealed the following:
- The Injury Severity Score (ISS) (see page 208) and the MELD score were significant predictors of increased mortality in the setting of trauma, with the ISS explaining 48 percent of the variation in mortality and the MELD score contributing an additional 7 percent to the variation.
- Trauma patients who died had a slightly higher MELD score compared with those who survived (14 versus 11, p<0.001)
- For each one-point increase in MELD score, the odds for mortality increased by 18 percent.

Upper Gastrointestinal Bleeding (UGIB)

Etiologies
- Peptic ulcer disease (30-50%); varices (10-30%); gastritis (10-15%); Mallory-Weiss tear (10-20%); esophagitis (5-10%); angiodysplasia (5%); and malignancy (2%)

Initial Management (see page 77 for management of varices)
- Aggressive IV fluid resuscitation with isotonic saline or PRBC transfusions
- Platelet transfusion for platelet<50K/µL
- Correct coagulopathy with FFP +/- Vitamin K (until PTT normalizes in cirrhotic patients)
- Proton pump inhibitors IV bid or as continuous infusion
  - Continue PO bid x 4-8 weeks for peptic ulcer disease
  - Assess for H. pylori infection and treat if present

Prognosis
- Pre-endoscopy Clinical Predictors of Poor Outcome with UGIB: Age>60; cirrhosis; renal failure; cardiopulmonary disease; SBP<100 mmHg; concurrent sepsis; APACHE II score≥11; presence of hematemesis, hematochezia, bright red nasogastric aspirate; or presence of coagulopathy, thrombocytopenia or Hgb≤8 gm/dL
- Endoscopic Findings as Predictors of Outcome for Peptic Ulcers

<table>
<thead>
<tr>
<th>Findings</th>
<th>Rebleeding risk</th>
<th>Surgery needed</th>
<th>Mortality risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clean base</td>
<td>5%</td>
<td>0.5%</td>
<td>2%</td>
</tr>
<tr>
<td>Flat spot</td>
<td>10%</td>
<td>6%</td>
<td>3%</td>
</tr>
<tr>
<td>Adherent clot</td>
<td>22%</td>
<td>10%</td>
<td>7%</td>
</tr>
<tr>
<td>Visible vessel</td>
<td>43%</td>
<td>34%</td>
<td>11%</td>
</tr>
<tr>
<td>Bleeding vessel</td>
<td>55%</td>
<td>35%</td>
<td>11%</td>
</tr>
</tbody>
</table>

- Rockall Scoring System for Upper Gastrointestinal Bleeds

<table>
<thead>
<tr>
<th>Score</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>&lt;60</td>
<td>60-79</td>
<td>≥80</td>
<td></td>
</tr>
<tr>
<td>Vitals</td>
<td>HR&lt;100</td>
<td>HR≥100</td>
<td>SBP&lt;100</td>
<td></td>
</tr>
<tr>
<td>Co-morbidities</td>
<td>None</td>
<td>Chronic heart or lung disease</td>
<td>Renal or liver failure; metastatic CA</td>
<td></td>
</tr>
<tr>
<td>Endoscopic findings</td>
<td>Mallory Weiss tear or No lesion/ no SRH</td>
<td>All other diagnoses</td>
<td>Malignant lesion of upper GI tract</td>
<td></td>
</tr>
<tr>
<td>SRH</td>
<td>Clean base or dark spot on ulcer base</td>
<td>Adherent clot, visible or bleeding vessel</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Duration of Inpatient Observation
- None for Mallory-Weiss tears, gastritis, esophagitis or clean ulcer base;
- 1 day for red spot on ulcer
- 1-2 days for adherent clots
- 3 days for visible or bleeding vessels treated endoscopically

Lower Gastrointestinal Bleeding (LGIB)

**Etiologies**
- diverticulosis; angiodysplasia; infectious or ischemic colitis; inflammatory bowel disease; hemorrhoids; upper GI bleed; or malignancy

**Risk Factors (RFs) of Poor LGIB Outcomes**
- SBP≤115 mmHg; HR≥100; syncope; nontender abdominal exam; hematochezia during first 4h of evaluation; history of ASA use; initial Hct≤35%; & >2 active medical comorbidities
- Risk of severe bleeding: low (0 RFs;<10%); medium (1-3 RFs; 45%); high (>3 RFs; 80%)

**Suggested Evaluation of Acute Lower Gastrointestinal Bleeding (LGIB)**


**Management of Lower Gastrointestinal Bleeding**
- Bowel rest and aggressive fluid resuscitation with isotonic saline or PRBC transfusions
- FFP for coagulopathy if INR>1.5 or PTT elevated>1.5x normal
- Platelet transfusion if platelets<50K/µL
- Treatment of uncontrollable LGIB: angiography with selective embolization versus surgery

Acute Mesenteric Ischemia

Etiologies
- Cardioembolism (50%): most commonly affects the superior mesenteric artery (SMA)
- Nonocclusive mesenteric ischemia (25%): shock, post-MI, low cardiac output, severe aortic insufficiency, sepsis, hemodialysis, vasopressors, or post-cardiac or abdominal surgery
- Mesenteric vein thrombosis (10%): hypercoagulable states, abdominal trauma, pregnancy, cancer, low flow states, or portal hypertension
- Mesenteric artery thrombosis (10%): SMA affected > inferior mesenteric artery (IMA)
- Focal small bowel ischemia (5%): vasculitis, small vessel embolism, or incarcerated hernias

Clinical Presentation
- Sudden onset of severe, colicky abdominal pain out of proportion to exam; associated with abdominal distension, nausea, vomiting, anorexia; +/- GI bleeding if right colon affected
- “Intestinal angina” (postprandial abd. pain) suggests chronic mesenteric arterial stenosis
- Exam: abdominal distension with minimal tenderness; peritonitis suggests infarcted bowel.

Work-up
- Lab abnormalities: leukocytosis +/- ↑ amylase, CK, and LDH; ↑ lactate is a late finding
- ECG, cardiac monitoring and 2D-Echocardiogram: evaluates for cardioembolic event
- Imaging: KUB normal in mild cases; severe cases: bowel distension, ileus, “thumbprinting”
  - CT scan with PO/IV contrast: identifies intestinal distension, bowel wall thickening, and mesenteric vein thrombosis; pneumatosis intestinalis is a late finding
  - CT angiogram: more sensitive than CT scan for mesenteric arterial thrombosis/stenosis

Treatment
- NPO with bowel rest, volume resuscitation, and discontinue any contributing medications
- NGT decompression to low intermittent suction for severe ileus with abdominal distension
- Antibiotics indicated for signs of intra-abdominal sepsis or bowel infarction
- Acute heparinization if acute mesenteric arterial/venous thrombosis or cardioembolic event
- Options for refractory mesenteric arterial thrombosis or embolism: catheter-directed thrombolysis; surgical embolectomy; or SMA revascularization for SMA thrombosis
- Consider selective mesenteric arteriography with intra-arterial papaverine infusion for nonocclusive mesenteric ischemia
- Indications for surgery: bowel infarction, perforation, or refractory intra-abdominal sepsis

Ischemic Colitis

Etiologies
- Shock; acute IMA thrombosis; low cardiac output states, cholesterol emboli; colonic obstruction; hypercoagulable states; vasculitis; aortic, colonic or cardiac surgery; sickle cell disease; abdominal trauma; aortic dissection; post-MI; or vasoconstrictive meds
- Medications: Alosetron, amphetamines, antihypertensives, cocaine, danazol, digoxin, diuretics, estrogens, NSAIDS, OCPs, pseudoephedrine, psychotropic drugs, and triptans

Clinical presentation
- Acute onset of crampy, LLQ abdominal pain, anorexia, nausea, vomiting, an urge to defecate, and often passage of red/maroon stool
- Exam: focal LLQ tenderness, distension, & ileus; peritonitis suggests bowel infarction

Diagnostic Studies
- Stool for guaiac testing, culture, +/- C. difficile toxin to rule out infectious colitis
- Abnormal labs: none in mild cases; ↑ WBC, LDH, amylase, and lactate (late) in severe cases
- ECG, cardiac monitoring & 2D-Echo: finds source of cardioembolism in up to 40% of cases
- Imaging: plain x-rays demonstrate bowel distension +/- air-fluid levels
  - CT scan with PO/IV/rectal contrast demonstrates same findings as in mesenteric ischemia
  - CT angiogram of limited utility as arterial thrombosis or embolism essentially never seen
- Colonoscopy diagnostic modality of choice once patient stable: locates segmental ischemia

Treatment
- NPO with bowel rest, aggressive IV hydration, and discontinuation of offending meds
- Broad-spectrum antibiotics for moderate-severe cases
- NGT decompression with low intermittent suction for severe ileus and distension
- Indications for surgery: peritonitis, persistent intra-abdominal sepsis, symptomatic colonic strictures, persistent symptoms >2-3 weeks, or chronic protein-losing enteropathy

Bowel Obstruction

Etiology
- Causes of small bowel obstruction (SBO): adhesions (50-70%); incarcerated hernia (15-30%); volvulus; cancer; intussusception; Crohn’s disease; or stricture (radiation or prior anastomosis)
- Causes of large bowel obstruction (LBO): cancer, complicated diverticulitis, and volvulus are most common; intussusception, foreign body, ischemic colitis, and strictures are less common
- Cancer is the most common cause of large bowel obstruction in elderly patients

Clinical Manifestations of Bowel Obstruction
- Diffuse, colicky pain with abdominal distension, nausea and vomiting
- No flatus or bowel movements in complete SBO/LBO; these are ↓ but present in partial SBO

Evaluation and Management of Bowel Obstruction

<table>
<thead>
<tr>
<th>Colon distended on radiographic</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Large bowel obstruction (LBO)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Partial LBO</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NGT decompression</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aggressive IV fluid resuscitation</td>
<td></td>
<td></td>
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<tr>
<td>Correct electrolytes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serial exams and x-ray studies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urgent operation if signs of peritonitis, sepsis, or perforation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consider operation for recurrent partial SBO</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete LBO</td>
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<td></td>
</tr>
<tr>
<td>Surgical consultation</td>
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<td></td>
</tr>
<tr>
<td>CT scan abdomen if not already done</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NGT decompression</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aggressive IV fluid resuscitation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Correct electrolytes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sigmoidoscopy if volvulus suspected</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urgent operation for other causes</td>
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<td></td>
</tr>
<tr>
<td>Small bowel with signs of obstruction on radiographic imaging*?</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Complete SBO</td>
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<td></td>
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<tr>
<td>Partial or early SBO</td>
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</tr>
<tr>
<td>NGT decompression</td>
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<td></td>
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<tr>
<td>Aggressive IV fluid resuscitation</td>
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<tr>
<td>Correct electrolytes</td>
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<td>Serial exams and x-ray studies</td>
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<tr>
<td>Urgent operation</td>
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<tr>
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<td></td>
<td></td>
</tr>
<tr>
<td>Consider operation for recurrent partial SBO</td>
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</tr>
</tbody>
</table>

Colonic Pseudo-obstruction (Ogilvie’s syndrome)
- Occurs in bedbound, hospitalized elderly patients
- Treatment: rectal tube or colonoscopic decompression and frequent repositioning
  - Laparotomy and operative decompression if conservative measures unsuccessful or if patient develops worsening abdominal tenderness, fever or peritonitis

Toxic megacolon
- Complication of inflammatory bowel disease or *C. difficile* colitis
- Treatment is laparotomy with colectomy and ileostomy & treatment of underlying condition

Borrowed with permission from Joseph Esherick, MD.
Gastroenterology: Acute Pancreatitis

Acute Pancreatitis

High-Risk Pancreatitis
- ≥ 4 admission risk factors
- Admission Ranson’s score ≥ 3
- CT severity index ≥ 7

No
- Continue supportive medical therapy
- IVF to maintain euvolemia
- Clears when abdominal pain resolves

Yes
- Admit to ICU
- Imipenem 500 mg IV q6h
- Surgical consult

Treatment after 1st 24 hours
- Enteral feeds via Dobbhoff tube
- Contrast-enhanced abdominal CT using pancreatic protocol
- Early ERCP with sphincterotomy for severe gallstone pancreatitis with persistent biliary obstruction
- Tight glucose control: 80-110

< 30% pancreatic necrosis
- Continue supportive medical therapy
- Repeat CT scan with possible CT-guided aspiration if clinical condition worsens

≥ 30% pancreatic necrosis
- Imipenem 500 mg IV q6h
- Surgical consult
- No improvement at 72 hrs or
- Signs of sepsis

CT-guided aspiration
- Infection present
- Early pancreatic necrosectomy if patient unstable
- Consider delayed necrosectomy ≥ 14 days if clinically stable
- Sterile
- Supportive medical therapy
- Antibiotics for 5-7 days based on clinical response and CRP trend

Admission Risk Factors
- BMI > 30
- Age > 55 years†
- Systolic BP < 90 mmHg
- Glucose > 200 mg/dL†
- LDH > 350 IU/L†
- AST > 250 IU/L†
- WBC > 16,000†
- Creatinine > 2 mg/dL (or UO < 0.5 mL/kg/hr after rehydration)
- PaO₂ ≤ 60 mmHg
- Elevated hemidiaphragms or significant pleural effusion(s)
- Hct>43% (♂) or ≥40% (♀)
- GI bleeding > 500 mL/24h

High-Risk Features ≤ 48 h
- Apache II score not decreasing
- CRP ≥ 15 mg/dL at 48h
- Hct decreases > 10%†
- BUN increases > 5 mg/dL†
- Calcium < 8 mg/dL†
- PaO₂ ≤ 60 mmHg†
- Base deficit > 4 MEq/L†
- Fluid sequestration > 6 L†

† = Ranson’s Criteria

Diagnostic Approach
- History and Exam
- CXR
- Labs: CBCD, Amylase +/- lipase, Chem 7, Mg, Ca, Phos, liver panel, PT, PTT, LDH
- Calculate Apache II score
- Abdominal UTZ (1st 24h)
  - GI/surgery consults if gallstones/CBD dilated
- ABG if hypoxic or low serum bicarbonate

Treatment First 24 hours
- Isotonic fluids until hemodynamically stable
- Aggressive IVF to maintain adequate UO > 0.5 mL/kg/hr
- Oxygen for SaO₂ ≥ 94%
- NPO
- Morphine or fentanyl (if hypotensive) for analgesia
- HOB elevated 30°
- DVT prophylaxis
- GI ulcer prophylaxis
- Incentive spirometry
- Chemsticks q6-8h
- Daily labs: CBC, chem 7, Calcium, LFTs & CRP (in ICU)

CT Severity Index = CT Grade + % Necrosis of Pancreas
CT Grade: CT Grade A (0 points) = Normal pancreas; CT Grade B (1 point) = enlarged pancreas; CT Grade C (2 points) = pancreatic and/or peripancreatic inflammation; CT Grade D (3 points) = a single peripancreatic fluid collection; CT Grade E (4 points) = at least 2 peripancreatic collections and/or retroperitoneal air
% Necrosis: No necrosis, 0 points; <30% necrosis, 2 points; 30-50% necrosis, 4 points; >50% necrosis, 6 points

Stress Ulcer Prophylaxis

(**Note: This does not apply to those with overt current Upper GI Bleeding, who are to be treated for that bleeding with Proton Pump Inhibitors and/or other modalities. Patients with a history of GERD who are admitted on acid suppressive therapy may also be continued on that therapy.)

Purpose:
1. To identify those at risk for stress ulceration
2. To establish a standardized approach to preventing the development of stress ulceration
3. To minimize the over-use of acid suppressing medications, which have been shown in the literature to increase the risk of infections including Clostridium difficile colitis and community-acquired and ventilator-associated pneumonias. Up to 60% of prescriptions for proton pump inhibitors in the hospital are not indicated.

Risk Factors:

Major Risk Factors (risk of Clinically Significant Bleeding (CSB†) estimated to be 3.7%)
- Mechanical Ventilation
- Coagulopathy (plt<50,000, INR>1.5 or pTT > 2 times the upper limit of normal)
- Shock of any etiology
- Severe Burns (particularly with Body Surface Area >35%)
- Severe Head Trauma (Glasgow Coma Scale <=10 at any time)
- Elevated Intracranial Pressure
- Acute Hepatic Failure
- Spinal Cord Injury

Minor Risk Factors (<0.1% developed CSB† without major risk factors)
- Multi-Trauma (injury severity score > 16)
- Acute Coronary Syndrome
- Acute Renal Failure
- Prior History of UGI Bleeding within 1 year of admission
- Surgery/Post-Surgical Status
- Glucocorticoid or NSAID use (>250mg/day hydrocortisone or equivalent)

Treatment:
- Patients with at least 1 major risk factor or at least 2 minor risk factors should be treated with once daily proton pump inhibitor, esomeprazole.
- Patients with 1 minor risk factor or less may be treated with sucralfate. It is also reasonable not to treat those patients and to solely observe them.
**Note: As sucralfate interferes with gastric absorption of most enterally administered medications, it should be administered at least 1 hour after or 2 hours before other enteral medications.**

Treatment Cessation:
- Acid suppressive medications should be discontinued for all patients on discharge from the ICU unless a) they had developed stress ulceration during their ICU stay or b) if they were on acid suppressive therapy as an outpatient
- Daily re-evaluation of risk factor presence should be ascertained, and acid suppressive therapy discontinued when risk factors have resolved.

†CSB = Clinically Significant Bleeding (CSB) is defined as overt bleeding complicated by the following in 24 hours:
(1) ↓SBP>=20mmHg, (2) ↑HR>=beats/min, (3) ↓Hb>=2g/dL, (4) transfusion without appropriate ↑ in Hb

RENAL

Acute Kidney Injury (AKI)

Definition
- Deterioration of renal function over a period of hours to days, resulting in the failure of the kidney to excrete nitrogenous waste products and maintain fluid and electrolyte homeostasis
- Diagnosis by serum creatinine alone has significant shortcomings
  - Lack of steady-state concentrations in the ICU (i.e. oliguric patient with normal SCr, septic patient with AKI but improving urine output will have worse and better renal function than calculated, respectively)
  - Lack of sensitivity, often underestimating the degree of AKI in critically ill patients
- There is no standardized definition of laboratory abnormalities seen with acute renal failure, though a large number of classifications do exist (upwards of 30+ classifications)
  - RIFLE Classification: (Risk, Injury, Failure, Loss, End Stage)
  - Acute Kidney Injury Network (AKIN): Stage 1-3

<table>
<thead>
<tr>
<th>Increasing severity of AKI</th>
<th>RIFLE</th>
<th>SCr criteria</th>
<th>UOP criteria</th>
<th>AKIN</th>
<th>SCr criteria</th>
<th>UOP criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>R</td>
<td>↑ 1.5 x baseline</td>
<td>&lt;0.5 ml/kg/h x 6h</td>
<td>Stage 1</td>
<td>↑ 1.5-2x baseline, or ↑ 0.3 mg/dL</td>
<td>&lt;0.5 ml/kg/h x 8h</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>↑ 2x baseline</td>
<td>&lt;0.5 ml/kg/h x 12h</td>
<td>Stage 2</td>
<td>↑ 2-3x baseline</td>
<td>&lt;0.5 ml/kg/h x 12h</td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>↑ 3x baseline, or ≥4 mg/dL with an acute rise of ≥ 0.5 mg/dL</td>
<td>&lt;0.5 ml/kg/h x 24h or anuria x 12 h</td>
<td>Stage 3</td>
<td>↑ 3x baseline, or ≥4 mg/dL with an acute rise of ≥ 0.5 mg/dL</td>
<td>&lt;0.5 ml/kg/h x 24h or anuria x 12 h</td>
<td></td>
</tr>
<tr>
<td>L</td>
<td>Persistent loss of kidney function &gt; 4 weeks</td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>E</td>
<td>Persistent loss of kidney function &gt; 3 months</td>
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</tbody>
</table>

Epidemiology
- Estimated to occur in 36-67% of critically ill patients (depending on definition of AKI)
  - Sepsis causes up to 50% of AKI in the ICU

Etiology
- Usually multi-factorial in the critically ill patient (combination of hypovolemia, sepsis, medications, and hemodynamic compromise)
- Also multi-factorial in the critically ill trauma patient (hemorrhagic shock, abdominal compartment syndrome, rhabdomyolysis) – up to 31% of trauma patients experience AKI
- Causes should be differentiated into Prerenal vs. Intrinsic Renal vs. Post-Renal Causes
  - Prerenal (70% of community-acquired cases, vs. 40% of hospital-acquired cases)
    - May be rapidly reversible if treated quickly
    - In the face of sepsis, sustained prerenal azotemia often leads to acute tubular necrosis
    - Medical conditions implicated: CHF, cirrhosis, peri-operative fluid shifts
  - Intrinsic Renal
    - Acute Tubular Necrosis (ATN): Oliguric (<400ml urine/day) vs. Non-oliguric (>400ml urine/day)
      - Toxic effect (35% of cases): Aminoglycosides, vancomycin, NSAIDs, ACE inhibitors, acyclovir, IV contrast for radiologic procedures, chemotherapeutics
      - Ischemia (50% of cases)
- Sepsis (moderate sepsis: 19% incidence of AKI; severe sepsis: 23% incidence of AKI; septic shock with bacteremia: 51% incidence of AKI)
- Hypovolemic shock (dehydration, hemorrhage)
- Decreased Effective Intravascular Volume: CHF, cirrhosis, nephrosis
- Medications: Cyclosporine, tacrolimus, amphotericin B, medications above
- Large-vessel renal vascular disease: renal artery thrombosis/embolism, renal artery stenosis
- Small-vessel renal vascular disease: vasculitis, atheroembolism, HUS, malignant hypertension, scleroderma, pre-eclampsia, sickle cell, hypercalcemia
  - Non-oliguric carries a better prognosis, with only 25% needing long-term dialysis;
  - oliguric ATN reflects a more profound insult and carries a poorer prognosis
  - Interstitial Nephritis (penicillins)
  - Acute Glomerulonephritis
  - Post-Renal
    - Prostatic hypertrophy, other causes of urinary retention and large bladder
    - Urinary obstruction from Tumor or Stone
    - Severe vesico-ureteral reflux

**Workup**
- Urinalysis with Microscopy (sent to lab, do not rely on ED microscopy), checking for urine sediment
- Fractional Excretion of Sodium (<1 consistent with prerenal even in the face of diuretics)
- In the face of diuretics, check Fractional Excretion of Urea (<35 consistent with prerenal)
- Consider further workup as warranted: CPK, HIV, Hepatitis C Antibody, Urinary eosinophils, Complement levels, ANA, dsDNA, ASO Titre, post-void residual +/- renal ultrasound

**Prevention/ Treatment:**
- As AKI in ICU is often multi-factorial, secondary prevention of further injury is important
  - Remove the offending agent/treat the underlying cause
  - Recognize and manage underlying conditions: diabetes, chronic kidney disease, hypertension, liver or cardiac dysfunction
  - Achieve euvoema as quickly as possible
  - Avoid hyperglycemia
  - Avoid nephrotoxins (aminoglycosides, vancomycin, acyclovir, ACE inhibitors, NSAIDs, chemotherapy (platinum), amphotericin, diuretics, vasopressors, IV contrast)
  - Prevention of contrast-induced nephropathy
    - N-acetylcysteine
      - Effective at 600mg po bid dosing; MORE effective at 1200mg po bid dosing
      - Must be given for the 24 hours prior to the administration of contrast and continued for the 24 hours after the administration of contrast
    - Bicarbonate Therapy (conflicting data as to if normal saline is as effective as bicarb)
      - Administer as 3 Amps of Sodium Bicarbonate in 1 Liter of D5W, at a rate of 3ml/kg per hour for the one hour prior to the administration of contrast, and 1ml/kg per hour for the 6 hours following the administration of contrast
      - If dextrose is to be avoided for concern for hyperglycemia, may use 1.5 Amps of Sodium Bicarbonate in 1 Liter 0.45% saline
    - Use of low-volume non-ionic low-osmolar or iso-osmolar contrast
- Consider ‘Renal Replacement Therapy’ (hemodialysis) when indicated, with the following absolute indications for dialysis:
  - AEIOU: Acidosis, Electrolytes (e.g. refractory hyperkalemia), Intoxications, Overload, Uremia
  - Conflicting evidence of benefit of Continuous Veno-Venous Hemodiafiltration (CVVHDF) vs. conventional hemodialysis

The Estimation of Effective Intravascular Volume

Estimation of effective intravascular volume is a clinical task that must take numerous clinical and other data into account to make correct assessments and subsequent adjustments to therapy. Volume status is often dynamically changing from minute to minute and hour to hour. Correct interpretation of the data, the pursuit of more data when the answer isn’t clear, and continuous re-evaluation of therapies and responses to therapies are critical to proper patient care.

You will be often asked to evaluate this in the face of a number of clinical scenarios; decreased urine output is the most common in the ICU. As a general rule, the brain is perfused preferentially over any other organ, and can be perfused with a systolic blood pressure as low as 60 (is your patient mentating?). Adequate urine output often takes a mean arterial pressure of 65, but intrinsic renal injury, ATN, and post-renal obstruction may impact how much urine the kidneys can make.

DATA SUGGESTING INTRAVASCULAR DEPLETION:

**History:**
Pneumonia or other source of infection
Vomiting, diarrhea, paracentesis, or other volume loss

**Physical Exam:**
Poor skin turgor
Orthostatic hypotension
Dry mucus membranes
Sunken eyes/fontanelle
Hypotension, Tachycardia †

**Labs/Studies:**
BUN:creatinine > 20:1 †
High urine specific gravity †
Hemoconcentration
FeNa <1 (even in the face of diuretics) †
Markers of infection: Rising WBC, toxic granulations, left shift, elevated CRP
BNP <100 or NT-pro BNP<350 rules out overload † (but does not rule in hypovolemia)

**Fluid balance** negative with worsening clinical status (over prior hours to weeks)

**Invasive Hemodynamics (if needed):**
CVP<3-5 is suggestive but not diagnostic (not reliable, esp. with high PEEP) †
PCWP<8-12

DATA SUGGESTING INTRAVASCULAR OVERLOAD:

**History:**
History of heart failure, low ejection fraction
Recent transfusion, particularly of PRBCs

**Physical Exam:**
JVD
S3 Gallop
Rales, Peripheral Edema
Hepatojugular reflex
Moist mucus membranes
Usually normal pulse and BP, but may have hypotension, tachycardia if in cardiogenic shock †

**Labs/Studies:**
BNP>500 and NT-pro BNP>1000 to 1200 are strongly suggestive of overload (but NOT RELIABLE IN THE ICU) †
CXR with perihilar congestion, cephalization (supine film unreliable) †

**Fluid balance** positive with worsening clinical status (over prior hours to weeks)

**Invasive Hemodynamics (if needed):**
CVP > 16-18 is suggestive but not diagnostic †
PCWP >18 is the gold standard, but not reliable with MR or pulmonary hypertension

† = Results are unreliable in critically ill patients
‡ = May be present in either significant hypo-volemia or significant hyper-volemia

Return to Table of Contents
Clear volume depletion

“Fluid Challenge”: Begin with a bolus of NS (consider 250ml in elderly, 500ml in others)

Re-evaluate fluid status after the bolus, which may include checking response to Blood pressure, urine output, physical exam, BUN/creatinine response…

Not improved/worse

Either a) you guessed wrong and they’re overloaded, or b) they need more fluid.

Re-evaluate your data, get more labs, call your attending

Improved

Bolus with NS; consider Albumin only in cirrhotics with albumin level <2 or in those with recent paracentesis.

Clear volume overload

Begin with 20mg Lasix IV in Lasix-naïve patients, may start higher depending on how severe the overload is and how high the blood pressure is.

Re-evaluate fluid status after the Lasix, which may include checking response to BLOOD pressure, urine output, physical exam, BUN/creatinine response…

Not improved/worse

Either a) you guessed wrong and they’re dry or b) you need to give more diuretic.

Re-evaluate your data, get more labs, call your attending.

Improved

Diurese until clinically euolemic, then diurese 500ml-1000ml per day

Determine the patient’s most pressing problem

e.g. elevated creatinine with concern for hepatorenal; low BP; extreme tachycardia (>130), etc.

Give fluid, following labs and other parameters very closely

Improved

Determine the patient’s most pressing problem

e.g. oxygenation or ventilation problem; wound healing in the face of interstitial edema, etc.

If no problem ‘wins out’ consider more invasive monitoring with your attending.

Diurese, following labs and other parameters very closely
“More information” Regarding Volume Status (discuss with your Attending)

Echocardiogram:
- Useful for assessing the presence of systolic heart failure
- Useful for assessing the presence of diastolic heart failure (high risk for fluid overload with relatively small changes in volume—give fluids gingerly!)
- Useful for assessing the presence of significant valvular abnormalities
- Useful for assessing the presence of pulmonary hypertension (estimated by degree of Tricuspid Regurgitation)

More Data About Preload:
- CVP: Not a good marker of volume status unless very low (<5) or very high (>~18)
- Ultrasound of the IVC as a surrogate of CVP

<table>
<thead>
<tr>
<th>IVC Size</th>
<th>Respiratory Change</th>
<th>Estimated CVP</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1.5 cm</td>
<td>Total Collapse</td>
<td>0-5 mm Hg</td>
</tr>
<tr>
<td>1.5-2.5 cm</td>
<td>&gt;50% Collapse</td>
<td>5-10 mm Hg</td>
</tr>
<tr>
<td>1.5-2.5 cm</td>
<td>&lt;50% Collapse</td>
<td>11-15 mm Hg</td>
</tr>
<tr>
<td>&gt;2.5 cm</td>
<td>&lt;50% Collapse</td>
<td>16-20 mm Hg</td>
</tr>
<tr>
<td>&gt;2.5 cm</td>
<td>No change</td>
<td>&gt;20 mm Hg</td>
</tr>
</tbody>
</table>

- Arterial Line with Cardiac Index
  - Normally 2.5-4; <2.0 is consistent with cardiogenic shock
  - Often quite elevated in Septic Shock (in the 3.5 to 6 range)

- Stroke Volume Variability (“SVV”)
  - A variability of >12% conveys a Positive Predictive Value of 94% and a Negative Predictive Value of 96% for estimating “fluid responsiveness”
  - Patient must be on controlled mechanical ventilation to measure this

More Data about Perfusion of Tissues:
- Lactic Acid, serially
  - All values > 2 are abnormal
  - A lactate of >3.5 on admission conveys a 57% mortality rate, with the exception of trauma patients (high lactate in trauma = not adequately resuscitated)
  - A rise in serum lactate, as well as a failure to return to normal by 48 hours, is associated with a 74% mortality

- Arterial Blood Gases, serially

- SvO₂ (Mixed Venous Oxygen Saturation) Monitor Triple Lumen Catheter
  - Normally 70- (~82-85)
  - Too low signifies inadequate O₂ delivery or too high consumption by tissues
  - Too high signifies shunting or inability of tissues to utilize oxygen

More Data about Both Preload and Perfusion of Tissues:
- SvO₂ Saturation Monitor Triple Lumen Catheter + Cardiac Index Arterial Line
- Swan-Ganz Catheter (see page 25)
  - Often most helpful in patients with renal failure who are going to surgery, where massive fluid shifts are to be expected
  - May also be helpful in ARDS with renal failure, though studies have not borne this out.

AGAIN: ALWAYS MONITOR RESPONSE to THERAPIES and ADJUST ACCORDINGLY!

## Renal: Volume Status

### Fluids

<table>
<thead>
<tr>
<th>Fluid Type</th>
<th>Fluid Components</th>
<th>Indications</th>
<th>Advantages</th>
<th>Disadvantages</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Saline (0.9% NaCl) (per Liter)</td>
<td>154 mEq of Sodium Chloride pH=5.5, Osm=308mOsm/L</td>
<td>Fluid Resuscitation</td>
<td>Inexpensive</td>
<td>Worsens third-spacing in cirrhotics</td>
<td>Preferred for volume resuscitation</td>
</tr>
<tr>
<td>Lactated Ringers (per Liter)</td>
<td>130 mEq Sodium 109 mEq Chloride 28 mEq Lactate 4 mEq Potassium 3 mEq Calcium pH=6.6, Osm=273mOsm/L</td>
<td>Fluid Resuscitation</td>
<td>Inexpensive</td>
<td>Worsens third-spacing in cirrhotics</td>
<td>Generally preferred in trauma patients Does not improve survival in current form versus normal saline</td>
</tr>
<tr>
<td>D5W (per Liter)</td>
<td>50 grams of glucose Water</td>
<td>Hypernatremia</td>
<td>Dilutes sodium level</td>
<td>Diffuses across all membranes</td>
<td>AVOID in elevated intracranial pressure</td>
</tr>
<tr>
<td>Hypertonic Saline (3%) (per Liter)</td>
<td>513 mEq of Sodium Chloride</td>
<td>Management of ↑ intra-cranial pressure</td>
<td>Volume expansion</td>
<td>Overcorrection of Na level!!!</td>
<td>AVOID in hyponatremia unless patient is seizing!!</td>
</tr>
</tbody>
</table>

### Crystalloids

<table>
<thead>
<tr>
<th>Fluid Type</th>
<th>Fluid Components</th>
<th>Indications</th>
<th>Advantages</th>
<th>Disadvantages</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Packed Red Blood Cells (PRBCs) (1 Unit = ~350ml) $258/Unit</td>
<td>RBCs and WBCs, no plasma Hct of 60 to 70</td>
<td>Severe anemia, hemoglobin &lt; 7 Septic patients not achieving SvO₂ goal</td>
<td>Corrects severe anemia</td>
<td>↑ risk of fluid overload ↑ Risk of infection, thrombosis</td>
<td>1 Unit PRBCs should raise hemoglobin by 1 point</td>
</tr>
<tr>
<td>Fresh Frozen Plasma (1 Unit = ~225ml)</td>
<td>Plasma components</td>
<td>Bleeding + INR &gt; 1.5</td>
<td>Corrects INR &gt; 1.5</td>
<td>Volume expansion</td>
<td>1 Unit raises coagulation factors 5-8%</td>
</tr>
<tr>
<td>Albumin</td>
<td>100ml 25% = 25 grams ($80) 500ml 5% = 25 grams ($66)</td>
<td>Volume expansion in severely hypoalbuminemic patients</td>
<td>Trend towards improvement in mortality in sepsis *</td>
<td>Causes greater drop in hemoglobin than Crystalloids; viral transmission risk</td>
<td>Avoid in Head Trauma patients (increased mortality*)</td>
</tr>
<tr>
<td>Platelets (1 Pheresis Unit = 5-6 platelet concentrates = ~300ml)</td>
<td>1 Pheresis Unit</td>
<td>Various indications/ cut-offs</td>
<td></td>
<td>$585 per pheresis unit</td>
<td>Avoid in TTP, ITP, DIC</td>
</tr>
<tr>
<td>Cryoprecipitate (1 Unit = 15ml diluted with 10ml saline or FFP)</td>
<td>Factor VIII (80 Units), Fibrinogen (150mg), vWF</td>
<td>Hypofibrinogenemia in DIC, Factor VIII</td>
<td></td>
<td>$490 for pooled unit (=6-10 units) or $73 for individual units</td>
<td>Use in DIC with Fibrinogen level &lt;150</td>
</tr>
<tr>
<td>Hetastarch (1 Liter)</td>
<td>Synthetic sugar</td>
<td>Lower infection risk vs. Albumin</td>
<td></td>
<td>↑ Risk of bleeding, anaphylaxis</td>
<td>Not often used because of side effects</td>
</tr>
</tbody>
</table>

### Abbreviations: vWF, von Willebrand’s Factor

*Based on SAFE Trial [N Engl J Med 2004; 350: 2247-5.}
Nutritional Support for the Critically Ill Adult

This summary lists the key nutrition factors specific to adult ICU patients. These guidelines do not apply to pediatric or non-critically ill patients.

- **If the GI tract is functional – use ENTERAL support before resorting to parenteral nutrition support**
  - Enteral nutrition compared to parenteral nutrition is associated with a significant reduction in the number of infectious complications in critically ill. (Canadian guidelines)

- **Start tube feedings within 24-48 hours of injury or ICU admission**
  - Early enteral nutrition is associated with a trend towards reduction in mortality and reduction of infectious complications in critically ill. (Canadian guidelines 2007)
  - EXCEPTION: Hold feeds in patients with significant hemodynamic compromise, or on high-dose inotropic support or large-volume resuscitation needed to maintain perfusion until the patient is fully resuscitated and/or stable (ASPEN guidelines, 2009)

- **Estimate CALORIE REQUIREMENTS**
  - 20-25 kcal/kg/d during the initial acute phase of critical illness, calories “in excess of 20-25 kcal/kg BW/day may be associated with a less favorable outcome.” (ASPEN)
  - Advance to 25-30 kcal/kg/d during the anabolic / recovery phase (ASPEN 2006)
  - Obese: if previously well nourished and BMI >30, should not exceed 60-70% of target energy requirements: initiate feeds at 10-14 kcal/kg/day of actual body weight or 22-25 kcal/kg ideal body weight (ASPEN 2009)
  - CNS medications, such as vecuronium, versed, fentanyl, pentobarbital, propofol, have been shown to decrease metabolic rate from 6-33%. (J Am Diet Assoc 2005)
  - Avoid overfeeding in: hyperglycemia, fatty liver, hypertriglyceridemia, immune suppression, inflammatory response, increased CO2, azotemia.

- **Estimate PROTEIN needs**
  - 1.5 – 2 g/kg/day of protein (for obese, ≥ 2 g/kg ideal body weight for BMI 30-40 and ≥ 2.5 g/kg ideal body weight for BMI >40 (ASPEN 2009))

- **When to use PARENTERAL support**
  - If patient with malnutrition or catabolic state is unable to tolerate enteral diet for 5 or more days.
  - If fail to tolerate 50% of enteral feeding goal rate by post-trauma day 7 (EAST 2003)

- **Consider Glucose and Lipid limitations for Critically Ill patients on TPN**
  - Permissive underfeeding at ~20 calories/kg ideal wt/day (McClave, DNS 2007)
  - Propofol contributes lipid and calories (1.1cal or 0.1 gm lipid/ml)

- **MONITOR Nutrition Support**
  - Albumin / PreAlbumin – negative acute phase reactants, questionable value as indicators of nutritional status in critically ill. Prealbumin increased with renal failure, steroids, acute ETOH intoxication; Decreased with inflammation, end stage liver disease, burns, malignancy, zinc deficiency. Consider trending with CRP.
  - Nitrogen balance = nitrogen intake (g protein/6.25 or appropriate conversion) minus nitrogen losses (UUN excretion in g + 3-5 gm “fudge factor”)
  - Feeding should be stable at goal rate for at least 2-3 days prior to collection.
• MONITOR Nutrition Support (continued)
  o Tube Feedings – Also monitor the following:
    ▪ Abdominal distention
    ▪ NGT drainage of 1200 ml/day is approximate cut-off for initiation of gastric feeds.
    ▪ Nausea, vomiting, cramping, abdominal discomfort
    ▪ Residuals POORLY correlate with feeding intolerance. At VCMC, it is preferred to not hold feedings due to residuals < 500 ml unless other symptoms are present.
    ▪ Stool frequency, volume, consistency
    ▪ Body weight – update at minimum of 1x/week
    ▪ Hypotension or hemodynamic instability – If initiating or increasing dose of pressors hold TF. May be ok to feed if stable dose of pressors for 24-48 h or decreasing doses. Hold feeds for any sign of intolerance while on pressors: increased NG output, abdominal distention or pain, cessation of flatus, stool. Fiber free, gastric feeds recommended. (McClave DNS conference 2007)
    ▪ Consider Small Bowel Feedings rather than TPN if: lack of accessible stomach, gastric outlet obstruction, gastric intolerance, pancreatitis (if patient does not tolerate gastric feeds first), significant risk for gastric aspiration – although patient position and oropharygeal care are more significant aspiration risks.

• How to ADVANCE Tube Feedings
  o Start tube feeding rate at 20-30 ml/hr
  o Advance 10-25 ml every 6-24 hours as tolerated
  o Consider the slower end of advancement range for patients who have
    ▪ Not been fed for >7 days or otherwise at risk for refeeding syndrome
    ▪ Been on long-term TPN
    ▪ Significant bowel resection
    ▪ Impaired gastric emptying
    ▪ Bowel wall edema, multiple bowel re-explorations, open abdominal cavity
    ▪ Been placed on a calorie dense or high osmolality formula e.g. 2CalHN or Nepro
    ▪ Gut hypoperfusion, hypotension or hemodynamic instability.

• Refeeding Syndrome
  o Definition: potentially dangerous or fatal fluid and electrolyte shifts that occur in patients receiving artificial refeeding, whether enterally or parenterally
  o Usually causes hypophosphatemia, but may also cause hypomagnesemia, hypokalemia, thiamine deficiency, fluid and sodium abnormalities, and changes in glucose, protein and fat metabolism
  o Clinical conditions at high-risk for refeeding syndrome: anorexia, chronic alcoholism, active cancer, elderly, uncontrolled diabetes, chronic malnutrition (marasmus, prolonged fasting or low-energy diet, morbid obesity with profound weight loss, high stress patient unfed for >7 days), malabsorption (inflammatory bowel disease, chronic pancreatitis, cystic fibrosis, short bowel syndrome), long-term antacid use (binds phosphorus), long-term diuretic use.
  o Major criteria for risk for refeeding (1 or more of the following): Body Mass Index (BMI)<16kg/m², Unintentional weight loss >15% in past 3-6 months, little or no nutritional intake for > 10 days, or low levels of phosphorus, magnesium, or potassium prior to feeding
  o Minor criteria for risk for refeeding (2 or more of the following): BMI < 18.5, Unintentional weight loss >10% in past 3-6 months, little or no nutritional intake for > 5 days, history of alcohol or drug abuse, medication use (insulin, chemotherapy, antacids, or diuretics)
  o Treatment: prior to starting feeding, begin thiamine 200-300mg po daily + multivitamins
  o Begin feeding at ≤50% of calculated energy needs; slowly advance over 4-7 days up to full feeds
  o Frequent checks of phosphorus, magnesium, potassium levels and repletion as needed

Borrowed with permission from Patty Manpearl, RD.
<table>
<thead>
<tr>
<th>FORMULA</th>
<th>FIBER-SOURCE HN</th>
<th>REPLETE</th>
<th>IMPACT PEPTIDE 1.5</th>
<th>OXEP A</th>
<th>PEPTAMEN AF</th>
<th>PEPTAMEN BARIATRIC</th>
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<table>
<thead>
<tr>
<th>Calories</th>
<th>Protein</th>
<th>Carbs</th>
<th>mOsm</th>
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<tbody>
<tr>
<td>1200 cal/L</td>
<td>54 g/L</td>
<td>160 g/L</td>
<td>490</td>
</tr>
<tr>
<td>1000 cal/L</td>
<td>54 g/L</td>
<td>160 g/L</td>
<td>490</td>
</tr>
<tr>
<td>1500 cal/L</td>
<td>94 g/L</td>
<td>140 g/L</td>
<td>510</td>
</tr>
<tr>
<td>62.7g/L</td>
<td>140 g/L</td>
<td>510</td>
<td></td>
</tr>
<tr>
<td>107 g/L</td>
<td>107 g/L</td>
<td>535</td>
<td></td>
</tr>
<tr>
<td>1200 cal/L</td>
<td>76 g/L</td>
<td>107 g/L</td>
<td>390</td>
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<tr>
<td>1000 cal/L</td>
<td>93.2g/L</td>
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<table>
<thead>
<tr>
<th>FORMULA</th>
<th>DIABETI-SOURCE AC</th>
<th>VIVONEX RTF</th>
<th>BOOST PLUS</th>
<th>BOOST GLUCOSE CONTROL</th>
<th>NUTREN 2.0</th>
<th>NOVASOURCE RENAL</th>
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</table>

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<tbody>
<tr>
<td>1200 cal/L</td>
<td>60 g/L</td>
<td>100 g/L</td>
<td>450</td>
</tr>
<tr>
<td>1000 cal/L</td>
<td>50 g/L</td>
<td>176 g/L</td>
<td>630</td>
</tr>
<tr>
<td>355.5 cal/ 237 mL</td>
<td>14 g/ 237 mL</td>
<td>45 g/ 237 mL</td>
<td>670</td>
</tr>
<tr>
<td>251 calories/ 237 mL</td>
<td>14 g/237 mL</td>
<td>23 g/237 mL</td>
<td>400</td>
</tr>
<tr>
<td>2000 cal/L</td>
<td>80 g/L</td>
<td>196 g/L</td>
<td>745</td>
</tr>
<tr>
<td>2000 cal/L</td>
<td>90.7 g/L</td>
<td>183 g/L</td>
<td>800</td>
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<table>
<thead>
<tr>
<th>PRODUCT</th>
<th>BOOST BREEZE</th>
<th>BOOST VHC</th>
<th>GLUTASOLVE</th>
<th>JUVEN</th>
<th>BOOST PUDDING</th>
<th>UNJURY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uses/Features</td>
<td>Replaces Ensure Active. Clear liquid, no fiber. Nutritionally incomplete.</td>
<td>Replaces Hi-Cal. Very high calorie for low appetite or high calorie needs (i.e. CF). No fiber.</td>
<td>L glutamine. Recommended in ICU Trauma. Mix 22.5 g packet w/ 60-120 mL warm H2O</td>
<td>Arginine, glutamine, beta-hydroxy-beta-methylbutyrate. Surgical wound healing aid. Oral or TF flush. Mix w/ 8 oz. water.</td>
<td>Lactose free. Appropriate for dysphagia.</td>
<td>Protein powder for TF flush or addition to foods. Mix 1 packet with ~120ml warm water for flush.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Calories</th>
<th>Protein</th>
<th>Carbs</th>
</tr>
</thead>
<tbody>
<tr>
<td>251 calories/ 237 mL</td>
<td>9 g/ 237 mL</td>
<td>54 g/ serving</td>
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<tr>
<td>533 calories/ 237 mL</td>
<td>22 grams/ 237 mL</td>
<td>46 g/ serving</td>
</tr>
<tr>
<td>90 cal/ packet</td>
<td>15 g L glutamine</td>
<td>7 g L-arginine, 7 g L-glutamine/ packet</td>
</tr>
<tr>
<td>78 cal/packet</td>
<td>7 g/5 oz can</td>
<td>33 g/serving</td>
</tr>
<tr>
<td>240 cal/5 oz can</td>
<td>20g/pkt</td>
<td>4 g/packet flavored</td>
</tr>
</tbody>
</table>
Blood Gases and Art Lines

Indications for ordering an ABG:

- **When there are concerns about VENTILATION** (or, is your patient breathing enough?):
  - Not awake enough to breathe:
    - Obtunded COPD patient (due to hypercarbia)
    - To verify no hypercarbia in a patient with altered mental status/obtundation
  - Breathing too fast/concern for poor gas exchange or muscle fatigue:
    - Anxious asthmatic/COPDer breathing fast
    - Septic patient breathing fast with concern for “tiring out”
  - **NOTE**: ABGs must be interpreted in the context of the patient. An ABG of 7.40/42/72 is a very good ABG for someone not in distress and sleepy, but is a TERRIBLE ABG indicative of impending respiratory failure in an asthmatic or COPDer breathing 45 a minute with accessory muscle use.

- **When there are concerns about OXYGENATION** when O₂ Sat doesn’t suffice: (it usually does suffice; see 40/50/60/70/80/90 rule below):
  - Concern for Carbon Monoxide Intoxication (carboxyhemoglobinemia) or Methemoglobinemia (e.g. Benzocaine intoxication, congenital)
  - On day of discharge to verify PO₂ < 60, for the patient to qualify for home oxygen
  - To determine the A-a gradient (?) (NOTE: normal A-a gradient does NOT rule out pulmonary embolism)
  - In most cases, you may follow oxygen saturations instead of relying on the PaO₂. The 40/50/60 70/80/90 rule is generally a good estimate of the PaO₂:
    
    | PaO₂ | O₂ Saturation (SaO₂) |
    |------|----------------------|
    | 40   | 70                   |
    | 50   | 80                   |
    | 60   | 90                   |

- **When there are concerns about ACID-BASE BALANCE**:
  - Sepsis
  - DKA
  - Poly-drug overdose
  - Increased anion gap or decreased bicarbonate on chemistries without obvious cause
  - To assess “adequacy of resuscitation” in shock (Lactic Acid may be substituted for ABGs)

- **Miscellaneous**:
  - After intubation in all patients
  - To monitor progression of disease or response to therapy in vented ICU patients or COPD patients on BiPap/after other interventions.
  - For rapid (<10 minutes) assessment of sodium, potassium, chloride, ionized calcium (“ABG Plus”)
  - During the “Apnea Test” to determine brain death
  - To assess for candidacy for extubation as one of many criteria (ABG not required in every patient)
When NOT to get an ABG:
- Oxygenation alone, for the most part, can be assessed by Oxygen Saturation in most cases.
  **NOTE:** Keep in mind that you maintain your O₂ Sat while you get hypercarbic and then stop breathing. O₂ Sats go down very far into respiratory failure.
- “Routine” management of vented patients in the ICU-- Not every intubated patient needs an ABG everyday if they are stable
- If you will be performing an indicated procedure regardless of the result (i.e. if the patient needs to be tubed, tube them and get an ABG afterwards)

Indications for Arterial Line Placement:
- Anticipating the need for multiple (e.g. >4) ABG draws during the hospital stay
- Need to monitor blood pressure on a second-by-second basis (shock of any etiology especially if on pressors; head trauma when ICP is measured continuously, severely hypertensive on antihypertensive drip (i.e. nitroprusside (Nipride), etc.)

Arterial Line Placement Tips:
- Please drape widely for all lines, including arterial lines
- Site selection: Radial, Brachial (ultrasound guidance) preferred to Femoral
- If the patient is awake, premedicate the insertion site with a small quantity of Lidocaine intradermally with a 29 gauge tuberculin syringe, taking care not to obscure landmarks.
- Try to place art lines in the ICU only (e.g. not in the ER)
- Arterial lines need to come out prior to the patient leaving ICU

A-a Gradient:
- Tells you whether oxygen is appropriately getting into the blood through the lungs or not
- A = Alveolar (or, the partial pressure of oxygen that you’re breathing)
- a = arterial (or, the partial pressure of oxygen getting into your blood stream)
- At sea level on room air, Alveolar O₂ should be 150 – (PaCO₂/0.8). The A-a gradient is calculated by subtracting the MEASURED arterial O₂ from this value.
- “Normal” = (Age/4) + 4
  - 28 year olds should have an A-a gradient of 11; 80 year olds should have an A-a gradient of 24)
  - A-a gradient goes up as your FiO₂ goes up (that’s normal)
  - NOTE: A “normal” A-a gradient still does not rule out pulmonary embolism.
- Abnormal A-a gradient
  - Indicative of some sort of Ventilation-Perfusion (V-Q) mismatch
Acid Base Interpretation: A step-wise algorithmic approach

1. Acidemic or alkalemic? (normal pH 7.40 +/- 0.05)

2. Is the primary problem metabolic or respiratory?
   - acidosis: pCO₂ > 40 Respiratory; HCO₃ <24 Metabolic
   - alkalosis: pCO₂ <40 Respiratory; HCO₃ >24 Metabolic

3. If respiratory, is the problem acute or chronic?
   - Acute Problem: Expected change in pH = -0.008 (pCO₂-40)
   - Chronic Problem: Expected change in pH = -0.003(pCO₂-40)

   This can also be calculated by looking at expected change in HCO₃.
   - Acute acidosis: Expected change in HCO₃ = 0.10 x (change in pCO₂)
   - Chronic acidosis: Expected change in HCO₃ = 0.35 x (change in pCO₂)
   - Acute alkalosis: Expected change in HCO₃ = 0.30 x (change in pCO₂)
   - Chronic alkalosis: Expected change in HCO₃ = 0.50 x (change in pCO₂)

4. If metabolic acidosis, gap or non-gap?
   - Simplified anion gap = Na-Cl-HCO₃
   - True anion gap reflects the principle that all positive and negative charges in body fluids must be equal.
     *anions: proteins (ie albumin), phos, sulfates, organic acids i.e. lactic acidosis, ketoacidosis, etc.
     *cations: K+, Li, Mg++, Ca++. hypergammaglobulinemia (ie MM)
   - theoretically, changes in these ions change the normal gap. For example, for each 1 g/dL decline in serum albumin, the AG decreases by 2.5 mmoll. Therefore a gap of 12 in a hypoalbuminemic patient would represent an AG acidosis. However, some clinicians feel this correction is unlikely to be of true clinical importance.

5. If metabolic, adequate compensation? (Winter's formula)
   - acidosis: expected pCO₂ = 8 + (1.5 *HCO₃) +/- 2
   - alkalosis: expected pCO₂ = 0.9*HCO₃ + 15+/-5 OR change in pCO₂ = 0.6(change HCO₃)

6. If Anion Gap (AG) acidosis, is there a mixed acid-base disorder? (“delta delta”)
   - (calculated AG-12) + HCO₃ = corrected HCO₃
     * > 26 primary metabolic alkalosis
     * <22 non-gap metabolic acidosis

7. Is there an increased osmolal gap? (normal<10 mosm/kg)
   - osmolal gap = [2*Na + glucose/18 + BUN/2.8 + Ethanol/4.6] – Measured Serum Osmolality
     * increased osmolal gap (>10) with etoh, ketones, lactate, mannitol, ethylene glycol, methanol, propylene glycol, isopropanol (isopropanol and propylene glycol cause no gap acidosis)

NOTE: The body will NOT compensate to get back to a pH of 7.40; if you get back to 7.40, there is another (a “concomitant”) disorder.

NOTE: Base deficit is another number used in place of ABG Interpretation. Its value incorporates both respiratory and metabolic issues into one number. It is often followed in trauma or surgical patients to assess adequacy of resuscitation.

   Base Excess > 3 signifies a significant alkalosis
   Base Deficit < -3 (more negative) signifies a significant acidosis
Assessment and Treatment of Acid-Base Disorders

Metabolic Acidosis, Differential Diagnosis and Treatment:

**High Anion Gap Acidosis Differential Diagnosis List**

- Mudpiles (or MudpileRs)
- M-methanol
- U-uremic
- D-diabetic keto-acidosis or other ketosis: alcoholic ketosis (EtOH, methanol, ethylene glycol), starvation ketosis
- P-paraldehyde, perforin
- I-inh, infection, iron, inborn error of metabolism including pyruvate metabolism
- L-lactic acidosis (sepsis, trauma, seizures)
- E-ethylene glycol, ethanol
- R-rhabdomyolysis
- S-salicylate

Other rarer causes include organic acidosis (i.e. chronic acetaminophen overdose).

**Normal Anion Gap Acidosis Differential Diagnosis List**

- Renal Tubular Acidosis
- Uremic Acidosis (early)
- Intestinal loss of bicarbonate or organic acid ions (diarrhea, pancreatic fistula)
- Ureteroenterostomy
- Drugs:
  - Acetazolamide
  - Sulfamylon
  - Cholestyramine
  - Acidifying agents: NH4Cl, oral CaCl2, arginine-HCl, lysine-HCl
  - Aldactone (in pts. w/cirrhosis)
- Rapid IV Hydration
- Correction of respiratory alkalosis
- Hyperalimentation
- diarrhea
- pancreatoenteric fistula

\[
\text{Urine anion gap} = [\text{Na}] + [\text{K}] - [\text{Cl}]
\]

If urine anion gap is a negative number, the kidney is getting rid of ammonia and the cause of the non-gap acidosis is intestinal loss of bicarbonate.

If urine anion gap is a positive number, then the kidneys are not acidifying the urine in the face of an acidosis, and thus they have a renal cause of their non-gap acidosis.
**Metabolic Acidosis Treatment:**
- Correct the underlying cause, to a goal pH 7.40 (7.21-7.49 is tolerable)
  - Note: In trauma patients, tissue hypoperfusion and lactic acidosis (usually from under-resuscitation and/or bleeding) is the #1 reason for acidosis until proven otherwise
- Bicarbonate Therapy
  - May be considered for a pH<7.2 to 7.1
  - Each Amp of Na-HCO₃ contains 50 mEq of Sodium and 50 mEq of bicarbonate; thus, 2 Amps in 1 Liter ½ NS or 3 Amps in D5W will approximate 177mEq or 150mEq respectively
  - Adverse Effects:
    - Sodium load (expands volume)
    - May worsen CO₂ levels and overall acidosis
- Using the Ventilator to your advantage
  - In the face of an acidosis with a pH<7.2 or 7.1, the patient may be hyperventilated (increasing respiratory rate and/or tidal volume) to give them a concomitant and compensatory respiratory alkalosis and raise the pH. General rules to help avoid adverse reactions from the ventilator can be found under “Ventilator Management”

<table>
<thead>
<tr>
<th>Sequelea of Severe Acidosis (pH&lt;7.2 to 7.1)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cardiovascular</strong></td>
</tr>
<tr>
<td>o Decreased contractility</td>
</tr>
<tr>
<td>o Centralized blood volume</td>
</tr>
<tr>
<td>o Decreased cardiac output and BP</td>
</tr>
<tr>
<td>o Increased arrhythmias</td>
</tr>
<tr>
<td>o Decreased responsiveness to catecholamines</td>
</tr>
<tr>
<td><strong>Respiratory</strong></td>
</tr>
<tr>
<td>o Hyperventilation</td>
</tr>
<tr>
<td>o Respiratory muscle fatigue</td>
</tr>
<tr>
<td>o Dyspnea</td>
</tr>
<tr>
<td><strong>Metabolic</strong></td>
</tr>
<tr>
<td>o Increased metabolic demands</td>
</tr>
<tr>
<td>o Hyperkalemia (H-K exchange)</td>
</tr>
<tr>
<td>o Insulin Resistance</td>
</tr>
<tr>
<td><strong>Obtundation, Coma</strong></td>
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<table>
<thead>
<tr>
<th>Sequelea of Severe Alkalosis (pH&gt;7.5)</th>
</tr>
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<tbody>
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</tr>
<tr>
<td>o Arteriolar constriction</td>
</tr>
<tr>
<td>o Decreased coronary blood flow</td>
</tr>
<tr>
<td>o Decreased angina threshold</td>
</tr>
<tr>
<td>o Predisposition to arrhythmias</td>
</tr>
<tr>
<td><strong>Respiratory</strong></td>
</tr>
<tr>
<td>o Hypoventilation</td>
</tr>
<tr>
<td><strong>Metabolic</strong></td>
</tr>
<tr>
<td>o Stimulation of organic acid production</td>
</tr>
<tr>
<td>o Hypokalemia (H-K)</td>
</tr>
<tr>
<td>o Decreased ionized Ca</td>
</tr>
<tr>
<td>o Hypo Mg, Hypo Phos</td>
</tr>
<tr>
<td><strong>Cerebral</strong></td>
</tr>
<tr>
<td>o Reduced blood flow</td>
</tr>
<tr>
<td>o Tetany, seizures, lethargy, delirium, stupor</td>
</tr>
</tbody>
</table>
Metabolic Alkalosis Differential Diagnosis List

- Chloride Responsive (Urine Chloride<10mmol/L) (Usually Volume Depletion)
  - GI (vomiting, gastric drainage, villous adenoma of colon, chloride diarrhea)
  - Diuretics
  - rapid correction of chronic hypercapnia
  - cystic fibrosis
  - laxative abuse

- Chloride Unresponsive (Urine Chloride>20mmol/L)
  - Excess mineralocorticoid activity
    - primary hyperaldosteronism
    - Cushing's disease
    - Licorice
    - ectopic ACTH production
    - secondary hyperaldosteronism [renovascular disease, malignant HTN, CHF with diuretic therapy, cirrhosis with diuretic therapy]
  - Profound Hypokalemia
  - Bartter's syndrome
  - Renal failure

- Unclassified
  - Alkali Administration
  - Milk-Alkali Syndrome
  - Non-parathyroid hypercalcemia
  - Massive transfusion
  - Glucose ingestion s/p starvation
  - Large doses Carbenicillin or Penicillin
  - Recovery from organic acidosis
  - Antacids and exchange resins in renal failure

Bartter's Syndrome:

- VERY rare syndrome characterized by:
  - normotension
  - hypokalemia with renal potassium loss
  - saline-resistant metabolic alkalosis
  - high urine chloride
  - high levels of renin and aldosterone

- may be confused with surreptitious vomiting, laxative abuse, diuretic abuse

- Treatment
  - NSAIDs, Amiloride

Metabolic Alkalosis Treatment:

- Correct the underlying cause, to a goal pH 7.40 (7.21-7.49 is tolerable)
- For Chloride Responsive, consider fluid challenge or cessation of diuretics
- For Chloride Unresponsive, may consider Acetazolamide if severe and not volume depleted.
Respiratory Acidosis Differential Diagnosis

**CDSPIES:**
- Cardiac (CHF)
- Drugs (sedatives, narcotics)
- Spasm (asthma, COPD, bronchospasm)
- Pneumothorax
- Infection
- Embolism (Pulmonary Embolism)
- Secretions, Splinting

(CDSPIES is also the differential for reversible causes of decreased PO2)

Other causes of respiratory acidosis or decreased PO2 include:
- Muscle weakness/deconditioning, severe neuromuscular disorders, myopathies, chest wall disorders, oversedation, brainstem stroke, traumatic brain injury, intracranial hemorrhage, C-spine injury, bronchiectasis, obesity-hypoventilation syndrome, aspiration pneumonitis, interstitial lung disease, severe pulmonary hypertension, pulmonary fibrosis

Respiratory Acidosis Treatment:
- Treat the underlying cause
- For patients with CO2 retention, consider BiPap (see “Non-Invasive Ventilation” Section)

Respiratory Alkalosis Differential Diagnosis

- Differential list is enormous
- The most important causes include
  - EARLY SEPSIS
  - Pain, Anxiety, Agitation
  - Hepatic Failure or Cirrhosis
  - Salicylate Toxicity
  - Pulmonary Embolism

- Note: Respiratory Alkalosis is normal in high altitudes and in pregnancy

Respiratory Alkalosis Treatment
- Treat the Underlying Cause

Essentials of Understanding Sodium Management

**DOGMA #1:**
Determine the volume status first.
Volume is determined by the total amount (in milliEquivalents) of sodium present in the body (plasma + extra-cellular space).
Volume status has very little to do with water!

Hypovolemia = ‘too little’ sodium in the patient’s body
Euvolemic = ‘the right amount’ of sodium in the patient’s body
Hypervolemia = ‘too much’ sodium is present in the patient’s body

**DOGMA #2:**
Next, look at the sodium level.
The sodium **level** is a dilution. It tells you about the relative amount of water in the body.

Hyponatremia = ‘too much’ water (the sodium determined in step 1 is diluted out)
Normal sodium level = ‘the correct amount’ of water for the amount of sodium you determined in step 1
Hypernatremia = ‘too little’ water (the sodium determined in step 1 is concentrated)

**RULE #3:**
Never use Thiazide Diuretics in someone who is hyponatremic (think about it: the reason why thiazides are first choice with hypertension is that they selectively diurese more sodium than they do water, worsening hyponatremia)

**RULE #4:**
People can be “total body overloaded but intravascularly depleted” or “total body overloaded but intravascularly euvolemic”, often in cases of decreased oncotic pressure in the vascular space (malnutrition, liver disease, etc.) or increased leakiness of capillaries (sepsis, capillary leak syndrome). Based on Dogmas 1 and 2, you do want to treat the volume overload (reduce the total body sodium) with Lasix +/- Aldactone, but you can only do that to the point where you start to get symptomatic from hypovolemia (orthostatic and dizzy, or prerenal with azotemia). If someone is already looking prerenal, you often have to give volume in the face of knowing that you will make the total body overload worse. Colloid (blood, FFP, platelets, albumin, Hetastarch) stays in the vascular space for a short time. Albumin has not been shown to improve overall outcomes and should be avoided. FFP should only be given if indicated for active bleeding or pre-procedure correction of INR down to 1.5 or less, not for its use as a colloid only.

**RULE #5:**
Never give a hypotonic solution (e.g. ½ NS, D5W or LR) to a person who is hyponatremic—it will make their hyponatremia worse.

**RULE #6:**
Rule out hypothyroidism for all patients with hyponatremia. Also for hyponatremic patients, consider ruling out adrenal insufficiency with a cosyntropin stimulation test, particularly in the face of hyperkalemia and hypoglycemia.
Management of Sodium Problems

1. The most efficacious way to treat sodium/water problems is to consider Volume Status (amount of sodium in the body) as one problem and Sodium Level (a dilution, the amount of water in the body) as a distinct and separate problem.

2. Treatment of Volume Status generally takes precedence
   a. Hypovolemia: need to replete SODIUM (always isotonic fluid, i.e. Normal Saline)
   b. Hypervolemia:
      i. generally treated with diuretics except for the case of “intravascular depletion with total body overload”.
         1. Loop diuretics will generally lead to excretion of hypotonic urine (~½ NS), thereby usually making the serum sodium level rise
         2. Thiazide diuretics excrete hypertonic urine, making the serum sodium level fall; chlorothiazide IV is prohibitively expensive; oral chlorothiazide 500-1000 mg daily to BID is a reasonable alternative, though less effective than loop diuretics for diuresis.
      ii. Removal of volume (sodium and water) with dialysis, paracentesis or thoracentesis is another option for treatment of hypervolemia

3. Treatment of Sodium Level is of paramount importance when severely high (>150) or severely low (<120)
   a. Rate of change in serum sodium is of PARAMOUNT IMPORTANCE
      i. MAXIMUM allowable rate of change is 8 to 10 mEq per 24 hours (and 18 mEq in 48 hours) when the hyponatremia is chronic ≈ > 48 hour duration
   ii. If the patient is correcting too quickly, reversal of that correction may be achieved in the following manner:
      1. Hyponatremia correcting too quickly needs to be corrected by the administration of a certain quantity of water; the “Water Deficit” formula may be helpful in this situation
         a. In very rare cases, administration of water does not slow the rate of rise in a serum sodium level; in these cases, the patient usually is excreting very dilute urine at a high rate; very cautious administration of DDAVP (i.e. 1 mcg IV x 1) may be given, with close observation of the patient’s sodium levels, urine output, and mental status (water intoxication and cerebral edema are most severe side effects). Blood sugar should also be watched closely on high rates of D5W.
   b. Hyponatremia:
      Asymptomatic:
         i. Water restriction is effective for all patients who are euvoletic or hypervolemic (see 2.a. for hypovolemia treatment)
         ii. The strictest water restriction is 800ml of water in 1 day; 1.5 Liters per day is reasonable for most patients.
   Symptomatic:
         i. Seizures are the only real indication for hypertonic saline; all other cases are to be treated as “asymptomatic”
         ii. There is very high risk for fluid overload and overcorrection of sodium level with hypertonic saline administration
c. Hypernatremia
   i. Water repletion (either via D5W through the IV or through water intake/NG tube) is effective for all patients
   ii. The “Water Deficit” formula is extremely accurate for the amount of water that needs to be replaced:
       \[ \frac{\text{body water}}{100} \times \text{Weight in kg} \times \frac{\text{Plasma Na} - \text{Goal Na}}{\text{Goal Na}} \]
   iii. % of weight that is body water may be estimated as follows, as muscle mass declines with age:
       - 60% of weight in young males; 50% of weight in older males
       - 50% of weight in young females; 45% of weight in older females
   d. ICU Admission should be considered for all patients who are symptomatically hyponatremic (e.g. seizures), and for any Sodium level <115.

3. Urine Sodium and Urine Osmolality may be helpful in some cases of hyponatremia to differentiate water intoxication from the Syndrome of Inappropriate Antidiuretic Hormone (SIADH).
4. For management of Diabetes Insipidus, see “Brain Injury and Intracranial Pressure (ICP) Management” (see page 211)
5. For treatment of SIADH refractory to fluid restriction and treatment of the underlying cause, demeclocycline may be indicated.

**Diagnostic Algorithm for Hyponatremia**

- Hyperglycemia
- Mannitol infusion
- Parenteral nutrition
- Contrast infusion

- Hypovolemic
  - Urine Na < 20 mEq/L
  - GI Losses
  - Pulmonary losses
  - Skin losses
  - Fluid sequestration (‘third space’): (i.e. burns, pancreatitis)

- Hypovolemic
  - Urine Na ≥ 20 mEq/L
  - Diuretics
  - Adrenal insufficiency
  - Osmotic diuresis
  - Salt-wasting nephropathy
  - Cerebral salt wasting

- Evolemic
  - Urine Na < 20 mEq/L & Urine osm <100 mOsm/L
  - Psychogenic polydipsia
  - Beer potomania
  - Reset osmostat
  - Tea-and-toast diet
  - Na+-free irrigation

- Evolemic
  - Urine Na ≥ 20 mEq/L & Urine osm ≥ 100 mOsm/L
  - SIADH
  - Hypothyroid
  - Acute Renal Failure
  - Adrenal Insufficiency

- Hypervolemic
  - End Stage Renal Disease/
  - Nephrotic Syndrome
  - Cirrhosis
  - Congestive Heart Failure

# Hyperkalemia Treatment (Mnemonic = “C BIG K DROP”)

<table>
<thead>
<tr>
<th>Mnemonic = “C BIG K DROP”</th>
<th>Drug</th>
<th>Dose</th>
<th>Onset</th>
<th>Duration</th>
<th>K+ Decrease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Treatment:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Calcium gluconate</td>
<td>10ml of 10% solution</td>
<td>Few minutes</td>
<td>30-90 minutes</td>
<td>NA</td>
</tr>
<tr>
<td>Temporary Treatment:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>IV Bicarbonate</td>
<td>3 Amps Bicarb in 1 Liter D5W</td>
<td>Immediate</td>
<td>Caution: causes volume overload</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Insulin + Glucose</td>
<td>10 Units regular IV + D50 1 Amp (50 grams)</td>
<td>15-30 minutes</td>
<td>“several hours”</td>
<td>0.5-1.5mmol/L</td>
</tr>
<tr>
<td></td>
<td>Beta-2 Agonists</td>
<td>Nebulizer</td>
<td>30 minutes</td>
<td>2-4 hours</td>
<td>0.5-1.5mmol/L</td>
</tr>
<tr>
<td>Permanent Treatment:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Kayexalate</td>
<td>60 grams x 1, then 15 grams q4 h until stool</td>
<td>1-2 hours</td>
<td>4-6 hours</td>
<td>0.5-1 mmol/L</td>
</tr>
<tr>
<td></td>
<td>Diuretics, Loop</td>
<td>Furosemide 40mg IV</td>
<td>1-2 hours</td>
<td>Combination enhances potassium excretion</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diuretics, Loop + thiazide</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dialysis</td>
<td></td>
<td>Immediate</td>
<td>Lasting</td>
<td>As much as needed</td>
</tr>
</tbody>
</table>

---

## Hypercalcemia

### Etiologies
- Hyperparathyroidism or malignancy in the vast majority of cases

### Clinical Manifestations
- Bones, stones, groans, psychiatric overtones

### Treatment (indicated when serum calcium≥14mg/dL)
- Normal Saline to rapid correction of hypovolemia
- Lasix (with Normal Saline, to keep urine output 100-200ml/hour, avoiding intravascular depletion)
- Calcitonin +/- Hydrocortisone
- Bisphosphonates (zoledronic acid more effective than pamidronate)

## Hypocalcemia

### Etiologies
- Alkalosis, Blood Transfusions, Cardiopulmonary Bypass, Drugs (Aminoglycosides, Cimetidine, Heparin, Theophylline), Fat Embolism, Magnesium Depletion, Pancreatitis, Renal Insufficiency, Sepsis, Hypoparathyroidism (leading cause in outpatients)

### Clinical Manifestations
- Hyperreflexia, Tetany, Seizures if severe; Chvostek’s Sign, Trousseau’s Sign
- Hypotension, Decreased Cardiac Output, Ventricular Ectopy

### Calcium Replacement
- Calcium Chloride 10% solution contains 27 mg (1.36 mEq)/ml elemental calcium (give through large central vein if possible due to high osmolality) (1 ampule = 10 ml=270 mg)
- Calcium Gluconate 10% solution contains 9mg (0.46 mEq)/ml elemental calcium (1 ampule = 10 ml)
- A bolus of 200mg elemental calcium (diluted in 100 ml NS) over 10 minutes should raise the total serum calcium by 1 mg/dL, but it will then fall after 30 minutes; consider calcium infusion

---

References: Marino ICU Book, 2nd Edition. Hyperkalemia treatment borrowed with permission from Tony Valdini, MD
Data for Transfusion in Critical Illness: TRICC Trial

- Randomized 838 anemic ICU patients to a restrictive transfusion strategy (hemoglobin (Hb) 7-9) vs. a liberal transfusion strategy (Hb>10)
- Restrictive transfusion strategy overall Mortality 18.7% vs. Liberal transfusion strategy Mortality 23.3% (p = 0.11)
- In patients with “significant cardiac disease” (e.g. Acute MI, Unstable Angina), restrictive strategy Mortality 20.5% vs. liberal strategy 22.9% (p = 0.69)

### Variable | Transfusion Trigger | Goal
--- | --- | ---
Generally Critically Ill (no acute bleeding) | Hb 7 g/dL | Hb 7-9 g/dL
Critically Ill with Septic Shock (<6 hours) | Hb 8-10 g/dL | Hb 10 g/dL
Critically Ill with Septic Shock (>6 hours) | Hb 7 g/dL | Hb 7-9 g/dL
Critically Ill with Chronic Cardiac Disease | Hb 7 g/dL | Hb 7-9 g/dL
Critically Ill with Acute Cardiac Disease (e.g. ACS, MI) | Hb 8-10 g/dL | Hb 10 g/dL

NOTE: This does NOT apply to patients with acute bleeding. Goals for acutely bleeding patients include hemodynamic stability and/or hemoglobin ≥8 to 10 g/dL.

### Recommendations in the Non Critically-Ill

| Variable | Transfusion Trigger | Goal |
--- | --- | ---
Hospitalized Hemodynamically Stable Patients | Hb 7 g/dL | Hb 7-9 g/dL
Post-operative surgical patients | Hb 8 g/dL | Hb 8-10 g/dL
Cancer patients on chemotherapy (bone marrow unlikely to produce RBCs) | Hb 8 g/dL | Hb 8-10 g/dL
Symptomatic patients – chest pain, orthostatic hypotension, unresponsive tachycardia, CHF: | Consider Hb 8 g/dL | Hb 8-10 g/dL

### Blood transfusion in Trauma

- For all Tier 1 Traumas, 2 units of O-negative blood are brought to the ED by the lab
  - To be used only for severe life-threatening hemorrhage not expected to respond to crystalloid resuscitation, and before type-specific or cross-matched blood available; requires ‘Emergency Release’ to be signed
  - Consider O, Rho(D) positive (O-positive) blood for males and sterile or post-menopausal women
  - Risks: 1.3% of all patients will have clinically significant antibody other than anti-D, and 70% of these will be women; risk of delayed hemolytic transfusion reaction
- Uncross-matched ABO, Rh(D) compatible blood
  - Available 10 minutes after sample received in the blood bank
  - Requires ‘Emergency Release’ to be signed
  - Indications: hypotension with Hct<25 or ongoing obvious bleeding, or need for immediate laparotomy/thoracotomy, prior to availability of cross-matched blood
- Type and cross-matched blood
  - 4 units available 45 minutes after sample received in blood bank
- Consider Autotransfuser for chest tubes with exsanguinating hemorrhage
  - Contraindicated if contamination of blood (i.e. bowel injury with diaphragmatic injury)
Risks of Transfusion (listed in order of severity)

- Acute Hemolytic Reactions (1:30,000-50,000 transfusions) (1:600,000 fatal)
  - Destruction of donor RBCs by pre-formed recipient antibodies
    - IgM anti-A and anti-B fix complement \( \rightarrow \) rapid intravascular hemolysis
    - May occasionally be associated with minor RBC antigens—Kell, Duffy
  - Clinical presentation: Classic triad of fever, flank pain and red or brown urine
    - Severity is rate and dose related
    - May also see: chills, hypotension, uncontrollable bleeding, tachycardia, constricting chest pain, warmth over infused vein, pain in lumbar region, hemoglobinuria, hyperbilirubinemia
    - Most patients initially have only fever, chills and nausea within 10-30 minutes
    - Anesthetized or comatose patients may have only oozing from venipuncture sites, dark urine, and hypotension and shock
  - Majority (60-80%) caused by clerical error
  - For every suspected transfusion reaction, the following process should be followed:
    1. Stop transfusion but leave IV access
    2. Begin normal saline
    3. From other arm, draw sample for direct antiglobulin test (or Coomb’s) and plasma free hemoglobin
    4. Save urine sample for hemoglobin testing
    5. Alert blood bank
    6. Check for clerical error
  - Treatment of Acute Hemolytic Transfusion Reaction
    - Generous fluid replacement (normal saline, mannitol)
      - Goal urine output > 100 ml/hour (may consider Lasix also)
    - Consider heparin infusion (i.e. 10 units/kg/hour) for high risk of DIC (heparin drip may prevent DIC)
    - Supportive care (hyperkalemia \( \rightarrow \) dialysis; hypotension \( \rightarrow \) pressors)
  - Prognosis: 50% mortality rate depending on circumstances

- Delayed hemolytic transfusion reaction (1:1000 transfusions)
  - Alloantibodies to minor red cell antigens
  - Most common in previously transfused patients and multiparous women
  - Clinical presentation: Symptoms begin 5-10 days after transfusion—fatigue, back pain, dark urine, low hemoglobin
    - Direct antigen test may be negative; check retic count, urine hemosiderin, indirect bilirubin, haptoglobin
    - Try to identify RBC antigen to avoid with future transfusions
  - Usually mild (extravascular hemolysis) but occasionally severe; up to 10% of deaths from transfusion

- Anaphylaxis (1:20,000-50,000) (see page 163)
  - MEDICAL EMERGENCY: Hypotension and respiratory distress without fever
  - Occurs within a few seconds to a few minutes after initiation of a treatment that contains plasma
  - Caused by anti-IgA antibodies in IgA deficient recipient (1:300-500 people)
- Prevent by using IgA deficient blood products or ‘ultra-washed’ RBCs or platelets

**Transfusion-Related Acute Lung Injury (TRALI)** (1:5000 or more common)
- Clinical presentation: Respiratory distress, hypoxia, fever, pulmonary edema without CHF/volume overload; onset within 2-6 hours after start of treatment
- Rapid rate of development: complete resolution generally seen within 96 hours
- Mediated by antibody activation of neutrophils along the pulmonary endothelium
  - Usually seen with recent surgery, infection, massive transfusion, or FFP administration
- Treatment is supportive; steroids are ineffective; Mortality ~ 10%

**Delayed TRALI** (up to 5-25% in transfused ICU patients; 40-57% with massive transfusion)
- Onset 6-72 hours; rate of development over several hours
- Mediated by ‘bioactive mediators’; Fever is uncommon
- Resolution is slow; may progress to fibroproliferative ARDS
- Mortality ~ 35-45%

**Bronchospasm/hypotension** (1:1000-2000)

**Bacterial Sepsis** (1:1,400,000) (more common with platelet transfusion 1:3,000)

**Transfusion Associated Cardiopulmonary Overload** = “TACO” (1:400 transfusions)
- Blood is THE most volume-expansive fluid (with a Hct~60) with VERY high risk for overload
- Consider empiric diuretic (i.e. furosemide 20 mg IV x 1 after first unit of PRBCs) in elderly, cardiac disease, chronic renal failure, diabetes, HTN, etc.)
- Rule out TRALI

**Fever** (1:100-200 transfusions)
- Differential diagnosis: Acute/ delayed hemolytic reaction, bacterial contamination, FNHTR (febrile non-hemolytic transfusion reaction), TRALI (transfusion related acute lung injury), pre-existing condition
- For every fever, the following process should be followed:
  - Stop transfusion
  - Draw STAT Coomb’s test from the opposite arm from the transfusion, along with serum free hemoglobin and UA with micro (looking for positive heme without RBCs)
  - Perform clerical check of transfused blood to rule out ABO incompatibility and hemolysis
  - Check vital signs
    - Hypotension with fever > 40º with no SOB or SOB with (-) CXR → consider bacterial contamination
    - Hypotension with dyspnea, fever 1-2º C up → consider TRALI
    - Normal/ high blood pressure with fever 1-2º up → consider FNHTR (benign, no long-term sequelae outside of patient discomfort and work-up and likely stoppage of transfusion; caused by cytokines (IL-1, IL-8, TNF) and directly correlated with length of storage and presence of WBC)
  - If Coomb’s test negative, may resume transfusion
  - Leukoreduction and acetaminophen pre-treatment are effective preventive therapies
• Urticaria (1:150-200)
  o Treat with IV Benadryl; consider steroids
  o Resume transfusion when urticaria wanes

• Viral transmission (<1:170,000) (HIV 1:1.5 million; Hepatitis C 1:1.14 million; Hepatitis B 1:282,000; West Nile Infection approaching zero; parasitic diseases: uncommon; bacterial infection from RBC transfusion very rare)

• Post-transfusion Purpura:
  o Rarely severe thrombocytopenia develops 5-10 days following transfusion with platelet containing products
  o Females 26 x more likely to develop than males
    ▪ 2% of population lacks PA-1a platelet Ag; get sensitized during pregnancy
    ▪ Unexplained destruction of PA-1a positive AND negative platelets
  o IVIg is treatment of choice
  o Avoid future problems with washed RBCs or PA-1a negative donor platelets

• Transfusion Related Immune Modulation (incidence unknown)
  o No data regarding severity/clinical significance
  o There are clear changes in RBCs as they approach 42 day shelf life, with increase in inflammation and immunosuppression (cytokines, phospholipids)

• Autoimmune hemolytic anemia
  o Tranfuse best matched units, though cannot completely rule out antibody

• Death from Transfusion (% of total deaths listed after cause) (TRALI – 55%; Acute hemolytic transfusion reaction – 23%, half of which are delayed; Transfusion-associated sepsis – 9%; Transfusion-associated Graft Versus Host Disease – 1%; Transfusion transmitted infection – 3%; Transfusion-Associated Cardiopulmonary Overload – 7%; Transfusion-Associated Anaphylaxis – 2%)

• Special Preparation of Blood Products:
  • Leukodepletion: All blood in Ventura County is routinely leukodepleted at collection
  • Irradiation:
    o Purpose: To inactivate donor T lymphocytes and prevent Graft vs. Host Disease
    o Indications:
      ▪ Severely immunocompromised patients:
        • Allogenic bone marrow transplants
        • Patients with lymphoma and leukemia on aggressive chemotherapy
        • Autologous stem cell transplant recipients
      ▪ Immunocompetent patients receiving directed donation from 1st degree relatives
    o Radiation dose: 2500 rads: no major effect on RBC, WBC or platelet function
  • CMV negative
    o Consider for bone marrow transplant recipients
    o If recipient is already CMV +, may transfuse CMV positive blood products

**Bleeding / Hemostatic Problems in the ICU**

The Formation of Clots (and their eventual removal) Involves:

- **Platelet Plug Formation**
- **Activation of the Coagulation Cascade**
- **Termination of Coagulation**
- **Eventual removal of the clot by Fibrinolysis**

### Bleeding:

#### Medical bleeding
(occurs from intrinsic or acquired deficiencies in the hemostatic pathway)

#### Surgical (Anatomic) bleeding
(e.g. from surgical incisions, disrupted blood vessels, trauma, etc.)

#### Coagulation-factor deficiency-type Bleeding
- bleeding from multiple sites (skin puncture sites, lines, etc.)
- ‘delayed and severe’ type associated with coagulation

#### Platelet-type bleeding
- Skin, mucus membranes (gingivae, nares, GI and GU tracts)
- Prolonged bleeding time (not usually measured)
- Bleeding after minor cuts
- Bleeding after surgery is ‘immediate, mild’
- Petechiae may be seen

#### Surgical bleeding is an important part of the differential of bleeding and should be ruled out in every case
- Examine the site of bleeding to see if it would be amenable to a figure-of-eight stitch or direct pressure

### Workup of Bleeding:

**History**

- History of bleeding with procedures, easy bruising, gums bleeding with brushing teeth, etc.
- Any anticoagulant or antiplatelet medication use, with timing of last dose

**Physical Exam**

- Examine the actual site of bleeding if possible, looking for bleeding that may be successfully stopped with a figure of 8 stitch or direct pressure
- Look for signs/symptoms of cirrhosis, uremia, sepsis, or other etiology of bleeding

**Labs**

<table>
<thead>
<tr>
<th>Test</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin/hematocrit</td>
<td></td>
</tr>
<tr>
<td>Platelet Count</td>
<td></td>
</tr>
<tr>
<td>PT/ INR</td>
<td>Prolonged with warfarin therapy, cirrhosis, argatroban therapy</td>
</tr>
<tr>
<td>aPTT</td>
<td>Prolonged with Heparin therapy, Hemophilia, inhibitors to specific coagulation factors (“mixing study” used for evaluation of this)</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>Decreased (&lt;100-150) with severe DIC, cirrhosis</td>
</tr>
<tr>
<td>D-Dimer</td>
<td>Higher in DIC (&gt;~2000-4000), lower with fibrinolysis</td>
</tr>
</tbody>
</table>
**Treatment of Bleeding:**

**Trauma Patient at risk for massive bleeding?**
- including but not limited to replacement of at least one blood volume (4-5 liters of blood, or approximately 10 units of PRBCs) in 24 hours

**No**

**Major Bleeding or Critical Bleeding, or Massive Bleeding in a Non-Trauma Patient?**
- Intracranial hemorrhage
- Bleeding resulting in substantial hemodynamic compromise requiring treatment (surgery or inotropic agents)
- ≥ 4-5 point drop in hemoglobin or bleeding leading to transfusion of ≥ 2-4 units of blood

**No**

**On Anticoagulant or Antiplatelet Agent?**

**No**

**Renal insufficiency?**
- Dialysis for severe uremia
- DDAVP 0.3 mcg/kg IV/subQ (IV preferred)

**No**

**Cirrhosis?**
- Blood products to achieve goals below
- Consider tranexamic acid

**No**

**DIC?**
- Treat the underlying cause

**Yes**

**Goals to achieve with Active Bleeding:**
- INR 1.5 or less
- Platelet count >50,000 to 75,000
- Fibrinogen > 100 to 150
- Hemoglobin > 10 g/dL (vs. >8 g/dL)
- pH normalized
- Temperature normalized

**For Trauma patients, initiate Massive Transfusion Protocol (page 122):**

<table>
<thead>
<tr>
<th>Agent</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>Transfuse 1 Unit Platelets x 1</td>
</tr>
<tr>
<td>Clopidogrel/Prasugrel/Ticagrelor</td>
<td>• Transfuse 2 units Platelets x 1&lt;br&gt;• Transfuse 1 Unit Platelets daily x 4 days</td>
</tr>
<tr>
<td>Warfarin (page 114)</td>
<td>• 4 Factor Prothrombin Complex Concentrate (PCC) (KCentra) OR&lt;br&gt;• 3 Factor PCC + 2 Units FFP&lt;br&gt;• Repeat x 1 to goal INR &lt;=1.4&lt;br&gt;• Also give Vit K 10 mg IV slowly</td>
</tr>
<tr>
<td>Dabigatran (page 118)</td>
<td>• NO ANTIDOTE&lt;br&gt;• Consider dialysis&lt;br&gt;• Consider charcoal within 2 hours of ingestion&lt;br&gt;• Consider activated PCC (Feiba) or activated Factor VII</td>
</tr>
<tr>
<td>Rivaroxaban/Apixaban</td>
<td>• NO ANTIDOTE&lt;br&gt;• Consider PCC or Factor VII</td>
</tr>
<tr>
<td>LMWH (i.e. enoxaparin) (page 117)</td>
<td>• Protamine 1 mg IV for each 1 mg of enoxaparin given in the last 4-12 hours slowly (&lt;= 50 mg/10 minutes)</td>
</tr>
<tr>
<td>Fondaparinux</td>
<td>• NO ANTIDOTE</td>
</tr>
<tr>
<td>Heparin (page 117)</td>
<td>• Protamine 1 mg IV for each 100 Units of heparin given in the last 4 hours (&lt;= 50 mg/10 minutes)</td>
</tr>
<tr>
<td>Argatroban/Bivalirudin</td>
<td>• NO ANTIDOTE&lt;br&gt;• 20% of argatroban is dialyzable</td>
</tr>
<tr>
<td>Thrombolytics</td>
<td>• Cryoprecipitate 10 Units&lt;br&gt;• Transfuse 1 Unit Platelets x 1</td>
</tr>
</tbody>
</table>
Hemorrhagic Shock

Compartments where Bleeding May Occur in the Unstable Trauma Patient

- Chest
  - Initial Chest Tube output of 1 Liter, or >200ml/hour, is an indication for surgical exploration; may also consider autotransfusion if no contamination of pleural blood
- Abdomen (including GI Tract)
- Retroperitoneum (with pelvic injuries)
- Long Bones → thigh
- Outside the Body (e.g. scalp lacerations)

Fluid Management of Hemorrhagic Shock

- Rapid fluid resuscitation may in fact be DETRIMENTAL to the patient in hemorrhagic shock, as, before definitive hemostasis, vigorous fluid administration leads to increased rate of bleeding from injured vessels
- This may lead to the vicious “bloody cycle” of improved cardiac output, increased blood pressure which counters local vasoconstrictive measures and exerts greater force on fragile clots; dilution and hypothermia from the fluids also contribute to coagulopathy and bleeding
- 2 trials support this concept
  - 600 penetrating chest or abdominal trauma patients randomized to standard care (2 large-bore IVs, IV fluids to keep SBP>100) vs. no IV fluids: no difference in blood pressure; survival was 60% in the no IV fluids group vs. 54% in the IV fluids group
  - Prospective trial in patients with hemorrhagic shock; liberal fluid strategy to keep SBP>100 vs. restrictive fluid strategy keeping SBP>80; no difference in mortality seen, but restrictive strategy had quicker control of bleeding
- Rapid transfuser (“Level One Transfuser”) may be associated with worsened mortality

<table>
<thead>
<tr>
<th>Goals for early resuscitation in trauma patients (prior to definitive control of hemorrhage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control of airway and ventilation</td>
</tr>
<tr>
<td>Expeditious control of hemorrhage</td>
</tr>
<tr>
<td>Systolic Blood Pressure 80–100 mmHg</td>
</tr>
<tr>
<td>Blood composition</td>
</tr>
<tr>
<td>▪ Limited use of crystalloid fluid</td>
</tr>
<tr>
<td>▪ Hematocrit 25%–30%, with early administration of red blood cells (RBCs) (including uncrossmatched Type O)</td>
</tr>
<tr>
<td>▪ Early use of plasma to maintain normal clotting studies</td>
</tr>
<tr>
<td>▪ Possible use of cryoprecipitate, Prothrombin Complex Concentrates (PCC) and/or Factor VIIa if patient is already coagulopathic</td>
</tr>
<tr>
<td>▪ Platelet count &gt;50,000</td>
</tr>
<tr>
<td>▪ Ionized calcium monitored and normalized</td>
</tr>
<tr>
<td>Maintained core temperature of &gt;35_C</td>
</tr>
<tr>
<td>Gradual conversion to deep general anesthesia</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Goals for late resuscitation in trauma patients (after definitive control of hemorrhage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete resuscitation is achieved by titrated administration of fluids until the following parameters are met</td>
</tr>
<tr>
<td>▪ Normal or hyperdynamic vital signs</td>
</tr>
<tr>
<td>▪ Hematocrit &gt;20% (transfusion threshold determined by patient’s age)</td>
</tr>
<tr>
<td>▪ Normal serum electrolytes</td>
</tr>
<tr>
<td>▪ Normal coagulation function, platelet count of at least 50,000</td>
</tr>
<tr>
<td>▪ Restoration of adequate microvascular perfusion, as indicated by</td>
</tr>
<tr>
<td>▪ pH = 7.40 with normal base deficit</td>
</tr>
<tr>
<td>▪ Normalized serum lactate</td>
</tr>
<tr>
<td>▪ Normal mixed venous oxygenation</td>
</tr>
<tr>
<td>▪ Normal or high cardiac output</td>
</tr>
<tr>
<td>▪ Normal urine output</td>
</tr>
</tbody>
</table>

Bleeding with Warfarin Therapy

Incidence and severity of bleeding is directly proportional to the degree of anticoagulation, and the time spent at a particular level of anticoagulation (higher the INR, the higher the risk of bleeding; exponential risk over an INR of 5.0).

### The HASBLED Score (risk of bleeding on warfarin therapy)

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Score/ Bleeds per 100 patient-years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension (SBP&gt;160)</td>
<td>0 / 1.13</td>
</tr>
<tr>
<td>Abnormal liver or renal function †</td>
<td>1 / 1.02</td>
</tr>
<tr>
<td>Stroke</td>
<td>2 / 1.88</td>
</tr>
<tr>
<td>History of bleeding</td>
<td>3 / 3.74</td>
</tr>
<tr>
<td>Labile INRs</td>
<td></td>
</tr>
<tr>
<td>Elderly (age &gt; 65)</td>
<td></td>
</tr>
<tr>
<td>Drugs or alcohol</td>
<td></td>
</tr>
<tr>
<td>(1 point each)</td>
<td></td>
</tr>
<tr>
<td>†= 1 point each; creatinine &gt; 2 or renal transplant; evidence of cirrhosis (bilirubin &gt; 2x ULN or LFTs &gt; 3x ULN)</td>
<td>4 / 8.7</td>
</tr>
</tbody>
</table>

**Correction of INR:** What’s your goal?
(Base your goal on the significance of bleeding and indications for anticoagulation in the first place)

a) correction of the INR down to NORMAL (<1.5); for serious bleeding (caution with prosthetic valves)
b) correction of the INR to the Therapeutic Range (for no bleeding or less-serious bleeding)

<table>
<thead>
<tr>
<th>INR</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5, no significant bleeding</td>
<td>omit a dose, resume therapy at a lower dose when the INR is therapeutic; may resume at same level if only slightly supratherapeutic</td>
</tr>
<tr>
<td>&gt;5 but &lt;9, no significant bleeding</td>
<td>Preferred: Omit next 1-2 doses, monitor INR more frequently, resume at a lower dose when the INR is therapeutic - OR - Alternatively: Omit 1 dose, administer Vitamin K 1-2.5 mg po (esp. if patient at increased risk of bleeding)</td>
</tr>
<tr>
<td>&gt;5 but &lt;9, no significant bleeding, high risk for thrombosis (i.e prosthetic valves)</td>
<td>Omit next 1-2 doses, use FFP 2 units IV †; do NOT use vitamin K</td>
</tr>
<tr>
<td>&gt;5 but &lt;9, no significant bleeding, urgent surgery needed</td>
<td>Give Vitamin K 2-4 mg po, with the expectation that the INR will fall within 24 hours; if INR still high, give additional Vitamin K 1-2mg po - OR - Give Vitamin K 2-4mg IV (should correct in 6-8 hours), with FFP † to cover if surgery needed more urgently.</td>
</tr>
<tr>
<td>INR&gt;9, no significant bleeding</td>
<td>Give Vitamin K 2.5-5mg po (1-1.5 mg po if mechanical heart valve) + FFP 2 Units IV †; hold warfarin Expect INR to be much lower in 24-48 hours; give more Vitamin K as needed, resume at lower warfarin dose when therapeutic</td>
</tr>
<tr>
<td>Life-threatening bleeding (e.g. intracranial hemorrhage; see page 112 for definition of &quot;critical bleeding&quot;)</td>
<td>Prothrombin Complex Concentrates (PCC)* (KCentra initial dose is 25 Units/kg at 0.12 Units/kg/minute) + Vitamin K 10mg slow IV (over 20 minutes acceptable, over 60 minutes preferred); see page 115 for Reversal of Warfarin Associated Critical Bleeding</td>
</tr>
</tbody>
</table>

Reference: American College of Chest Physicians (ACCP) guidelines (2012)

† Caution to be used in transfusion of FFP if patient fluid overloaded or at risk for becoming fluid overloaded

* Caution to be used with Prothrombin Complex Concentrates (PCC) as it can lead to clot formation and even DIC in some high risk patients. Prefer to avoid PCC for non-critical bleeding.
Heme: Bleeding

VCMC Protocol for the Reversal of Warfarin-Associated Traumatic Brain Injury, Spontaneous Intracranial Bleeding, and other Critical Bleeding in Adults

Intracranial hemorrhage or other critical bleeding (MUST BE CRITICAL BLEEDING)

Draw INR, PT, aPTT, fibrinogen, D-Dimer, CBCD, Type and Cross, along with other labs as dictated by presentation

Known Warfarin Use or INR 1.6 to 3.9

Give the following products (even before lab results known):
1. KCentra 25 Units/kg IV at 0.12 mL/kg/min† (MAX dose 2500 Units)
2. Vitamin K 10 mg IV over 20-60 minutes (must specify exact time)

INR 4 - 5.9:
Give an additional KCentra 10 Units/kg @ 0.12 mL/kg/min† (for a total dose 35 Units/kg) (MAX total dose 3500 Units)

INR ≥ 6:
Give an additional KCentra 25 Units/kg @ 0.12 mL/kg/min† (for a total dose 50 Units/kg) (MAX total dose 5000 Units)

Initial INR 4-5.9

Give the following products:
1. KCentra 35 Units/kg @ 0.12 mL/kg/min† (for a total dose 35 Units/kg) (MAX dose 3500 Units total)
2. Vitamin K 10 mg IV over 20-60 minutes (must specify exact time)

Initial INR ≥ 6

Give the following products:
1. Give KCentra 50 Units/kg @ 0.12 mL/kg/min† (for a total dose 50 Units/kg) (MAX dose 5000 Units)
2. Vitamin K 10 mg IV over 20-60 minutes (must specify exact time)

†: Rate of KCentra at maximum is 8.4 ml/minute (210 Units/minute)
NOTE: Redosing is NOT recommended

Products for Use in the Reversal of Warfarin

Fresh Frozen Plasma (FFP):
FFP is the plasma with the RBC removed; thus it has all of the plasma proteins including coagulation factors; it is an oncotic load and tends to stay in the intravascular space (use caution with patients with diastolic dysfunction of putting them into fluid overload/CHF); each Unit generally contains 200-250 ml

Indications:
- h/o coagulopathy with bleeding or prior to a surgical procedure, with INR > 1.5
- massive blood transfusion
- reversal of warfarin effect
- congenital or acquired coagulation factor deficiency for bleeding or before surgery
  - congenital factor II, V, VII, X, XI, or XIII deficiency
  - factor VIII or IX deficiency if concentrates not available
  - multiple factor deficiencies (liver disease, vitamin K deficiency, DIC)
- Hypogammaglobulinemic states (prefer IVIG)
- Antithrombin III deficiency, Heparin Co-Factor II or Protein C or Protein S deficiency
- Plasma exchange for TTP/HUS.

Dose:
- Begin with 2 Units (may begin with 1 Unit if PT is 18-22 sec or aPTT is 55-70 sec)
- Doses as high as 10-15 ml/kg may be needed
- Note: For every 5-6 Units of platelets given, the equivalent of 1 Unit FFP is also given
- Note: FFP is not efficacious for improving INR below 1.5 and should not be given for INR ≤ 1.5

Monitoring
- FFP has a somewhat short half-life (factor VII has a half-life of 5-6 hours, much shorter than the other factors), so high INRs should also be treated with Vitamin K, and with time, the patient may require more FFP
- If Coags are drawn >2 hours after FFP administration, aPTT is a more reliable indicator of efficacy (indeed, aPTT is always a better indicator of bleeding risk than the PT outside of warfarin therapy)

Vitamin K (Phytonadione):
- Oral is the best route (safe, cheap, effective and reliable), although it corrects the INR down to the normal range in ≥ 24-48 hours
- IV is the fastest/most reliable route, and is recommended as above, keeping the following in mind:
  - Major side effects: facial flushing, diaphoresis, fever, hypertension, cyanosis, chest tightness, anaphylaxis, cardiovascular collapse, or death; the American Heart Association/American College of Cardiology suggests avoidance of IV Vitamin K in patients with prosthetic valves, for the increased risk of thromboembolism
  - The “key” to avoiding adverse effects is “SLOW” IV infusion = over 20-60 minutes
- Sub Q administration is no more effective than placebo [Arch Intern Med 2006;166:391-397]

Prothrombin Complex Concentrates:
- New recommendation of 2012 American College of Chest Physician Antithrombotic Guidelines as first-line therapy for critical bleeding (see page 112 for definition of critical bleeding)
- NOT to be used for bleeding not considered to be critical (for cost and for risk of thrombosis)
- Three factor PCC: “Profilnine SD” Powdered form of factors II, IX and X with inadequate quantity of factor VII (usual dose 25 Units/kg IV slowly at 10 ml/minute; may repeat x 1 to total 50 Units/kg)
- Four factor PCC: “KCenta” Powdered form of factors II, VII, IX, X
- Reconstituted, can be administered in 20 ml of fluid; obtained from pharmacy and able to be prepared more rapidly than FFP (FFP needs to be thawed): $930 per 1000 Units (2013 pricing)
- Increased risk of thrombosis and DIC may be seen, as well as viral (e.g. Hep B) transmission

Return to Table of Contents
Products for Use in the Reversal of Heparin

Heparin Mechanism of Action: Binds to anti-thrombin (AT) [formerly known as Anti-thrombin III (AT III)], increasing its affinity for inactivating the active coagulants (factor Xa, thrombin).

Reversal of Heparin: Protamine: a low molecular weight protein from salmon sperm
The dose should correspond to the amount of Heparin given over the last 4 hours, with 1mg given for each 100 Units/ 1mg of UFH/LMWH, respectively.
- e.g. patient who begins bleeding with heparin running at 1200 units/hour, give protamine 50mg (4 x 12)
- e.g. patient who bleeds within 4 hours of getting enoxaparin 60mg, give protamine 60mg
- take into account the half-life of Heparin when giving protamine; if Heparin was turned off 1 hour ago, or LMWH given ~6 hours ago, cut the protamine dose in half
- Protamine has a shorter half-life than heparin (esp. when administered sc), so may need repeated protamine doses
- Always give protamine by SLOW IV Infusion (no more than 50 mg in a 10 minute period)

Reversal of Low Molecular Weight Heparin
- As above with Unfractionated Heparin
- Protamine only reverses approximately 60% of the effect of LMWH because the presence of low-sulfated molecules that are protamine resistant.
- LMWH is partially renally excreted and may have prolonged effects with decreased renal function

Protamine
- Allergic reactions are common (0.06-10.7%)
- Anaphylactic (Type I, IgE-mediated) reaction vs. Anaphylactoid (non-IgE mediated) reaction
- SEs: Hypotension, increased pulmonary artery pressure, brochospasm, skin flushing, severe angioedema, erythema, pruritis, chills, chest pain, nausea, decreased cardiac output, thrombocytopenia
- Risks for adverse protamine reaction: use of NPH insulin, h/o vasectomy, allergy to fish, previous exposure to protamine, rate of infusion too fast (quicker than over 5-15 minutes)
- Treatment of adverse reactions:
  o Stop infusion of Protamine immediately
  o Benadryl 50mg IV for any evidence of histamine release
  o Hypotension:
    ▪ large volume fluid resuscitation
    ▪ Epinephrine IV (1:10,000) 10mg IV over 10 minutes, titrated to SBP > 80
    ▪ May alternatively begin Epinephrine 1mg of 1:1000 diluted in D5W 250 ml = 4 mcg/ml
    ▪ Maximal infusion = 4mcg/minute (or 1 ml/minute)
    ▪ Dopamine and/or Isoproterenol may also be used
  o Bronchospasm:
    ▪ Oxygen
    ▪ Epinephrine 1:1000 0.3-0.5 ml subcutaneous q 10 minutes may help
    ▪ Albuterol may be used
    ▪ Steroids may also be used
    ▪ Consider intubation early if any threat of airway edema
  o If patient is Beta blockaded, consider IV Glucagon (1mg IV) (if effective, start Glucagon infusion 1-5mg/hour)
  o Monitor in ICU for at least 48 hours s/p severe reaction; reactions can have a bimodal component

References: Chest 2008; 133:71S-105S.
Bleeding in Liver and Kidney Disease

Bleeding in Uremia: Usually platelet-type bleeding

- Coagulation cascade usually not very contributory, but check PT and aPTT anyway (consider repletion of Vitamin K if PT elevated for possibility of malnutrition)
- Medications may have exaggerated effects with uremia:
  - ASA= causes more impairment in platelets in people with renal disease than in normals
  - Heparin boluses with Dialysis
  - Low Molecular Weight Heparin (LMWH): half life increased

Treatment:
- Desmopressin: 0.3mcg/kg IV: shortens bleeding times for the 4 hours after infusion by releasing vWF from Wally Bodies; may get tachyphylaxis with repeated dosing
- Cryoprecipitate: second-line; may not work for some patients
- Infusion of conjugated estrogen: 0.6mg/kg/d for 5 days; onset of action up to 1 day, but lasts for 2 weeks after infusion
- Raise Hematocrit above 30: Postulated to increase platelet-vessel wall interactions
- Erythropoietin: releases platelets too
- Aggressive Dialysis

Bleeding in Liver Disease:

Many facets of coagulation affected:

- Thrombocytopenia (hypersplenism); decreased production of thrombopoietin also
- Platelet dysfunction: increased fibrin degradation products, increased nitric oxide
- Increased consumption of clotting factors
- Increased fibrinolysis

Labs:

- PT increased secondary to decreased factor VII
- PTT increased secondary to other coagulation abnormalities and increased antiphospholipid Antibodies (especially in SLE)
- INR somewhat unreliable; it can be prolonged even though the patient can still clot (PTT becomes prolonged when Factor VII <30% of normal, but only 5-15% needed to form clot)
- Risk of DIC is increased (check D-Dimer)
- Initial screen in a bleeding patient: CBC, PT/PTT, fibrinogen, D-Dimer

Treatment:

- If Platelets <50-75,000 (goal>50**), give 6 platelet concentrates or 1 plasmapheresis product (As a bonus, platelet transfusions include some plasma, up to 2 Units per pheresis unit)
- If Fibrinogen<125 (goal>125**) give 10 Units cryoprecipitate
- If PTT abnormal: perform “Mixing Test”, give 2 Units FFP; goal=PTT 1.5 times or less than normal (FFP has 5% of all coag factors) (only 5-15% of factor VII needed to form clot)
- If Hematocrit <30, transfuse packed red blood cells
- Abnormal fibrinolysis: clinical diagnosis (oozing from minor trauma sites), shortened euglobulin clot lysis time, D-Dimer in 1500-2000 range (not >3000 of DIC)
  - Amino-epsilon caproic acid (4-5g over 1 hr. IV, then 1g/hr x 8 hours) (po=4g/4hr) OR
  - trexaminic acid: (10mg/kg IV bolus, then 10mg/kg q 6-8 hrs. IV, or 25mg/kg q6-8hrs. po) (contraindicated in Disseminated Intravascular Coagulation)

Coagulopathy Associated with Trauma and the ‘Coagulopathy of Trauma’

**Incidence:** 25-35% of trauma patients develop ‘biochemically evident coagulopathy’

**Causes:**
Causes of coagulopathy are generally multifactorial, including:

- **Acidosis**
  - related to tissue injury, shock, and hypoperfusion leading to lactic acidosis
  - pH 7.2 lower than leads to clotting factor dysfunction
  - correction of the acidosis does not always improve the clotting dysfunction, suggesting multi-factorial coagulopathy

- **Hypothermia**
  - from exposure (pre- and intra-hospital, particularly for trauma patients going to surgery) and lower-than-body-temperature fluid administration

- **Hemodilution**
  - from fluids and/or blood products given with insufficient quantity of clotting factors

- **DIC**
  - from consumption of clotting factors initially, or from sepsis later in the hospital stay
  - injury to tissues leads to exposure of Tissue Factor $\rightarrow$ activation of the extrinsic coagulation cascade $\rightarrow$ thrombin generation in proportion to the degree of trauma
  - Systemically embolized ‘thromboplastins’ from other site of injury (i.e. bone marrow fat, amniotic fluid, etc.) may also contribute to DIC

- **Transfusion of ‘old blood’**:
  - ‘storage lesion’ includes decreased pH, chelation of calcium, low 2,3 diphosphoglycerate levels, and decreased clotting factor concentration, particularly for blood older than 15 days, leading to impaired microvascular perfusion, increased inflammation and immune modulation.
  - There is controversy as to if there is a mortality impact (worsening) with older blood

- **Coagulopathy of Trauma**
  - Biochemical response to trauma and shock leads to hyperfibrinolysis and hypocoagulability—occurs early after injury and is biochemically evident prior to (and independent of) acidosis, hypothermia and hemodilution
  - Higher incidence with hypotension, higher injury severity score, worsening base deficit, and head injury; only occurs when there is tissue injury AND hypoperfusion.

**Pathophysiology:**

<table>
<thead>
<tr>
<th>Tissue Injury</th>
<th>Exposed Tissue Factor</th>
<th>Activation of the extrinsic clotting</th>
<th>Increased thrombin generation (local + systemic) and fibrin deposition, clot</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoperfusion</td>
<td>Release of circulating levels of thrombomodulin</td>
<td>Thrombin + Thrombomodulin complex activates Protein C</td>
<td></td>
</tr>
<tr>
<td>Activated Protein C breaks down Tissue Factor-mediated clot via inactivation of Factors Va and VIIIa</td>
<td>Wide spread Activated Protein C leads to increased breakdown of Plasminogen Activator Inhibitor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uninhibited Tissue Plasminogen Activator converts plasminogen to plasmin $\rightarrow$ break down fibrin</td>
<td>Reduction in thrombin-activated thrombolysis inhibitor leading to increased fibrinolysis and elevated D-dimer/ fibrin split products</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Secondary effects of Coagulopathy of Trauma:
- Extensive Protein C activation can lead to total body Protein C depletion after trauma
  - Protein C is anti-inflammatory and cytoprotective; its depletion can lead to potential infectious or other complications
    - Protein C depletion in a cohort of critically injured trauma patients was associated with increased risk of acute lung injury, pneumonia, multi-organ failure and death
    - Small prospective study in trauma patients with depleted Protein C levels had a 3-fold increase in death
  - Protein C depletion in trauma may also lead to a later hypercoagulable state
- Development of Coagulopathy of Trauma leads to:
  - Higher transfusion requirements, longer ICU and hospital stays, increased ventilator days, more multi-organ dysfunction
  - Compared with patients without coagulopathy, 3-4 times greater mortality, 8 times more likely to die within 24 hours of injury

Evaluation of Coagulopathy of Trauma:
- Standard tests:
  - Prothrombin time (PT): (prolonged PT incidence ~28%; odds ratio for mortality 1.35)
  - Activated Partial Thromboplastin Time (aPTT): (prolonged aPTT incidence 8%; odds ratio for mortality 4.26)
  - D-dimer, fibrinogen: high D-dimer, low fibrinogen consistent with hyper-fibrinolysis
  - Platelet Count: may decrease in trauma from consumption; platelet dysfunction also occurs in trauma patients
- Limitations of standard tests:
  - Coagulopathy of Trauma can occur even with normal PT and aPTT. High index of suspicion necessary in patients with Injury Severity Score > 15 and/ or acidosis
- Thromboelastography (TEG):
  - Assesses the viscoelastic properties of clot formation in fresh or citrated whole blood in real time, providing information regarding clot initiation, clot strength, and fibrinolysis simultaneously
  - Studies in support of the use of TEG in trauma:
    - TEG information regarding coagulopathy at 6 hours was correlated with mortality, but PT/ INR was not
    - TEG information regarding coagulopathy in 44 combat patients was more strongly associated with transfusion requirements than standard lab parameters
    - TEG information in a retrospective study of 832 trauma patients massive transfusion (21% of them trauma patients) whose transfusions were guided by TEG parameters received more plasma and platelets and had significantly better 30-day survival (32% vs. 20%) compared with retrospective controls transfused using standard lab parameters

Treatment of coagulopathy associated with trauma:
- Correction of acidosis (by restoring circulating volume)
- Achievement of early and sustained euthermia
- Correction of hypocalcemia caused by citrate preservative of blood products
- Use of ‘newer’ blood (<15 days old) for trauma patients
- For blood product treatment of Coagulopathy of Trauma, see Massive Transfusion Protocol (page 122)

References: Coagulopathy of Trauma, Up to Date Summary, December 2012.
VCMC Massive Transfusion Protocol

Introduction
The Massive Transfusion Protocol (MTP) is a multidisciplinary process whereby blood and blood products are obtained rapidly. At Ventura County Medical Center, massive transfusion is defined as transfusion of 4-6 pack Red Blood Cell units within an hour or 10 pack Red Blood Cells within 24 hours in an adult patient.

Procedure
Initiation of Massive Transfusion Protocol (MTP)
1. The attending physician will initiate the Massive Transfusion Protocol (MTP) when:
   a. the immediate transfusion of six (6) or more units of Red Blood Cells is anticipated.
   b. the patient uses, or is predictably going to use, the initial two (2) units of emergency release O negative Red Blood Cells within half an hour and there is a request for additional blood.
2. The Blood Transfusion Service will activate the Massive Transfusion Protocol after notification by phone by the attending physician or his/her designee (VCMC dedicated MTP line: 652-6020).
3. The Laboratory will ensure that the Blood Transfusion Service will have adequate staffing to provide for Massive Transfusion demands, determine the adequacy of in-house inventory, and establish adequate lines of supply for additional blood components.
4. The attending Physician will be notified by phone that six (6) units of crossmatched Red Blood Cells, two (2) units of thawed plasma, and one (1) plateletpheresis are ready for issue. The Blood Bank will continue to maintain four (4) units of crossmatched Red Blood Cells ready for issue during entire Massive Transfusion Protocol until termination of the protocol.
5. The Blood Bank is to issue blood products in sets; labs are to be drawn after every 2nd set issued
6. It is the attending physician’s responsibility to call the Blood Bank (652-6020) to terminate the MTP

RBC/FFP-Plasma/Platelet Ratio
The ratios of RBCs, plasma and platelets at each point in the protocol would be as follows (using “1” to represent our facilities’ platelet pack which contains at least 3.0 x 10^11 platelets per single donor pheresis unit and which approximates 4-6 single donor platelet concentrates):

<table>
<thead>
<tr>
<th></th>
<th>RBC/plasma/platelets Ready for Issue</th>
<th>RBC/plasma/platelets Given</th>
<th>Tranexamic Acid/ PCC/ Factor VII</th>
<th>Cryo-precipitate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial Resuscitation</td>
<td>2/0/0</td>
<td>2/0/0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Set 1</td>
<td>4/4/1</td>
<td>6/4/1</td>
<td>Consider TXA/ PCC/ Factor VII (see next page)</td>
<td></td>
</tr>
<tr>
<td>Set 2</td>
<td>4/4/0</td>
<td>10/8/1</td>
<td>**</td>
<td></td>
</tr>
<tr>
<td>Set 3</td>
<td>4/4/1</td>
<td>14/12/2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Set 4</td>
<td>4/4/0</td>
<td>18/16/2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Set 5</td>
<td>4/4/1</td>
<td>22/20/3</td>
<td>**</td>
<td></td>
</tr>
<tr>
<td>Set 6</td>
<td>4/4/0</td>
<td>26/24/3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Set 7</td>
<td>4/4/1</td>
<td>30/28/4</td>
<td>**</td>
<td></td>
</tr>
<tr>
<td>Set 8</td>
<td>4/4/0</td>
<td>34/32/4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

TXA = Tranexamic acid; PCC = Prothromin Complex Concentrates (KCentra at VCMC);
** Cryoprecipitate recommended for OB/GYN DIC patients if fibrinogen levels are low (<100, or <150 with active bleeding); must call blood bank to order cryoprecipitate; usually ordered as 1 pool (1 pool = 5 units), or 2 pools.

Note: After every 2nd set of products issued, a PT/INR, Hemoglobin, Hematocrit, Platelet Count, and Fibrinogen must be checked.
Tranexamic Acid (TXA):
- Potent inhibitor of thrombolysis (anti-fibrinolytic agent)
  - Lysine analog – attaches to the lysine site of plasminogen and prevents its conversion to plasmin (inhibiting proteolytic activity of plasmin), forming a reversible complex which inhibits fibrinolysis
- Greatest benefit (reduction in death due to bleeding) seen within 3 hours of injury; it is less effective and could be harmful if administered more than 3 hours after injury
  - CRASH-2 Trial: absolute mortality reduction of 1.5% in trauma patients with significant injury randomized to tranexamic acid vs. placebo within 8 hours of injury (greatest benefit seen within 3 hours)
  - MATTERs Trial: 896 military trauma patients, reduction in mortality with tranexamic acid from 24% to 17%; greatest mortality benefit seen in those patients requiring massive transfusion (24% mortality with placebo vs. 14% with tranexamic acid)
- Dose: 1 gram IV Piggyback over 10 minutes, followed by 1 gram additionally over 8 hours
- Adverse Reactions: hypotension (with fast infusion rates), nausea, vomiting, diarrhea
- Contraindications: hypersensitivity reaction, acquired defective color vision, active intravascular cloting, history of thrombosis or thromboembolism, thrombogenic cardiac rhythm disease, subarachnoid hemorrhage

Prothrombin Complex Concentrates (PCC):
- Pooled plasma products containing a mixture of vitamin K-dependent proteins
  - KCentra (“4-factor PCC”): non-activated factors II, VII, XI and X
  - Profilnine SD (“3-factor PCC”): non-activated factors II, XI and X; also has factor VII but a relative paucity of it; requires an additional 2 units of FFP
    ▪ Cost $930 for 1000 units (VCMC cost, 2013)
  - Feiba: Activated factors II, VII, IX and X; carries a much higher pro-thrombotic risk than inactivated PCC; administration requires hematology consult at VCMC
- Indications:
  - Reversal of the effects of oral anticoagulants (first line treatment for critical bleeding with known warfarin use; see page 115)
  - Congenital or acquired factor II or factor X deficiencies
  - May be used in situations where FFP is to be avoided (i.e. acute fluid overload), though must be critical bleeding
- Risks:
  - Thrombosis, including DIC (especially in patients with cirrhosis)
    ▪ ~1.4% with inactivated PCC, up to 10% of activated PCC

Recombinant Activated Factor VII (Factor 7) (r FVII a/ Novoseven)
- Vitamin K dependent glycoprotein structurally similar to human Factor VIIa
- Activates extrinsic coagulation cascade
- FDA Approved Indications: treatment of severe bleeding episodes in Hemophilia A and B patients with inhibitors to factor VIII or factor IX
- Off-label indications: ongoing coagulopathic bleeding despite surgical control following major trauma; all instances of use will be reviewed monthly at VCMC
- Consultation with a Pathologist or Hematologist is required
- The following criteria must be met:
  - The patient has been transfused with one complete volume of PRBC (8-10 units)
  - Surgical control of all bleeding has been performed, or in process
  - Documented coagulopathy
Attending Surgeon in presence determines that bleeding is not responsive to surgical treatment and coagulopathy will lead to death if not reversed immediately (less than 30 minutes).

- Note: every effort shall be made to diagnose the cause and quantify the severity of the coagulopathy with laboratory tests: PT, PTT, fibrinogen. These laboratory tests must be ordered and samples obtained prior to administration of Factor VII a.

- Efforts to keep patient normothermic in progress
- Efforts to correct acidosis in progress

- Factor VIIa is anecdotally more effective in an acidotic patient than other products

- Absolute contraindications: ongoing uncontrolled surgical bleeding
- Relative contraindications: known history of atherosclerotic coronary artery disease, ischemic cerebrovascular disease (CVA) or thromboembolic disease; patient with DIC, crush injury, or septicemia

- Dosing (again, consultation with a Pathologist or Hematologist is required)
  - Initial: 90 mcg/kg given as IV bolus
  - If hemostasis not achieved in 20 minutes, consider a second dose of 60-90 mcg/kg IV
  - If second dose not effective, consider additional PRBC, platelet, FFP, cryoprecipitate transfusion prior to a third dose
- Adverse effects (<1%): myocardial infarction, ischemic CVA, ischemic nephropathy, mesenteric ischemia, development of factor VII inhibitors
- Cost is prohibitive – $4500 or more for a 90 mcg/kg dose

### Cryoprecipitate

- Frozen blood product that contains primarily Factors VIII, fibrinogen and von Willebrand factor in addition to Factor V
- Orders for cryoprecipitate will not be anticipated by the Blood Bank unless specifically requested. Pooled cryoprecipitate will be available within 30 minutes of request.

### Calcium

- Consider calcium chloride administration for persistent hypotension after 4 units PRBCs

### Termination

The Blood Bank staff will notify the attending Physician or designee as blood and blood products are made available. Products will be issued upon request or held in the Blood Bank until needed. The Blood Bank staff will inquire at each notification if the Massive Transfusion Protocol (MTP) should continue. It is the responsibility of the attending physician to notify the Blood Bank staff to discontinue the Massive Transfusion Protocol (MTP).

### Massive Transfusion in Non-Trauma Patients

Massive blood loss can also occur during surgery or in a handful on non-surgical settings such as GI hemorrhage and abdominal aortic aneurysm rupture. Transfusion support of such patient can meet the VCMC definition of massive transfusion above. However, the likelihood of coagulopathy requiring aggressive and automatic transfusion of plasma and platelets is very much lower in the non-trauma setting for several reasons [Erber, Transfusion and Apheresis Science, 2002]. The MTP – which is designed on the assumption that the patient has significant complex coagulopathy contributing to uncontrolled hemorrhage – is usually not necessary for these patients. Instead, frequent measurement of platelet count, PT/INR, fibrinogen and hemoglobin should be obtained and transfusions given to maintain the various components of the coagulation system in the hemostatic ranges: Platelet count > 50,000/ microL, INR ≤ 1.5, and fibrinogen > 100 mg/dL.

Thrombocytopenia

Platelets play a critical role in normal hemostasis. They are activated when exposed to disrupted endothelium leading to platelet aggregation and formation of a hemostatic plug. In addition, the platelet membrane acts as a binding surface for the initiation and perpetuation of the coagulation cascade. Both quantitative and qualitative platelet disorders can lead to an increased risk of bleeding that can be potentially life threatening.

Quantitative Platelet Disorders

- Bone marrow failure – chemotherapy, infiltrative marrow disorders, aplastic anemia
  - Transfuse prophylactically for platelets < 10,000
  - Transfuse prophylactically for platelets < 20,000 if patient febrile or septic
  - Transfuse prophylactically if platelets < 50,000 for surgery or invasive procedures
  - Transfuse therapeutically if patient bleeding and platelet count < 50,000
- Immune thrombocytopenic purpura (including drug induced)
  - Transfuse prophylactically for platelets < 5,000 and wet purpura (mucosal membrane bleeding)
  - Transfuse therapeutically if poorly controlled bleeding (CNS, GI) and platelets < 50,000

Specifics of Platelet Transfusion

- One unit of single donor platelets is preferred (equivalent to 6 units random donor platelets). A one unit transfusion should raise platelet count by 50,000 (40,000-60,000) 1 hour after infusion
- Platelets should be leukodepleted to prevent febrile reaction and immunization
- Platelets should be irradiated if patients are severely immunosuppressed (lymphoma, leukemia, transplant) or the donor is a first or second degree relative to prevent graft vs. host disease
- In patients refractory to platelet transfusion because of immunization HLA matched donor platelets should be used
- Do not transfuse platelets from 1st or 2nd degree relative donors if patient a candidate for allogenic transplant
- Cytokine mediated febrile reactions occur in 15-20% of patients
- Bacterial contamination and subsequent sepsis in 1 in ~ 8,000 units, especially after prolonged storage

Qualitative Platelet Disorders

- Hereditary disorders such as Glanzman’s Thrombasthenia and Bernard Soullier Syndrome are treated with platelet transfusion for active bleeding
- Acquired disorders characterized by abnormalities in the vascular space (uremia, macroglobulinemia, essential thrombocytosis) do not respond to platelet transfusions and are best managed by treatment of the underlying disease (dialysis, plasmapheresis, plateletpheresis respectively)
- Bleeding related to drug induced platelet dysfunction (ASA, NSAIDS, clopidrogel) are appropriately treated with platelet transfusion

Contraindications to Platelet Transfusion

- Thrombotic thrombocytopenic purpura
- Heparin induced thrombocytopenia
- Antiphospholipid antibody syndrome

In these diseases the thrombocytopenia is due to platelet activation and consumption. Clotting catastrophes have been reported after platelet transfusion in these entities and should only be given for life threatening bleeding (CNS).
Disseminated Intravascular Coagulation

Pathophysiology:
Systemic Activation of Coagulation leading to:
- Intravascular deposition of Fibrin leading to multi-organ dysfunction, and
- Depletion of Platelets and clotting factors leading to bleeding

Clinical Manifestations:
- Bleeding is often of the ‘delayed and severe’ type associated with coagulation factor depletion
- Multi-organ failure alone or with bleeding may also be seen

Etiologies:
- Sepsis
- Trauma
  - Serious Tissue Injury
  - Head Injury
  - Fat Embolism
- Cancer
  - Myeloproliferative diseases
  - Solid Tumors (pancreas, ovary, lymphoma)
- Vascular disorders
  - Giant hemangioma
  - Aortic aneurysm
- Obstetrical complications
  - Amniotic fluid embolism
  - Placental abruption
- Reaction to Toxins
  - Snake venom, drugs, amphetamines
- Immunologic disorders
  - Anaphylaxis
  - Hemolytic transfusion reaction
  - Transplant rejection

Diagnosis:
Based on the DIC Scoring System; a score of 5 or more is consistent with overt DIC.

<table>
<thead>
<tr>
<th>DIC Score</th>
<th>Lab Test</th>
<th>Lab Value</th>
<th>Point Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Platelet Count</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;100</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>51-100</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;50</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Elevated Fibrin-Related Markers</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No increase</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Moderate Increase</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Strong Increase</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Prolongation of Prothrombin Time</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;3 seconds</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3-6 seconds</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;6 seconds</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fibrinogen</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;100g/dL</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;100g/dL</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

Treatment:
- TREAT THE UNDERLYING CAUSE
- If bleeding, support with blood products which may include:
  - FFP for INR > 1.5
  - Platelets for Platelet Count <10,000-30,000 (controversial, as adds ‘fuel to the fire’)
  - Cryoprecipitate for Fibrinogen < 100 to 150
  - Rule out fibrinolysis as a contributor to bleeding, particularly with liver disease

Thrombotic Thrombocytopenic Purpura

Pathophysiology
- Rapidly Fatal Severe Microvascular Occlusive (thrombotic microangiopathic) disease caused by immune-mediated depletion of the enzyme ADAMTS13 which normally cleaves von Willebrandt’s Factor multimers, leading to platelet-von Willebrandt’s Factor complexes in the arterioles and capillaries
- Levels of ADAMTS13 reduced to <5% of normal levels is the final common pathway to nearly all cases of TTP outside of bone-marrow transplant- or chemotherapy-related TTP (mechanism unknown)

Clinical Manifestations
- Classic Pentad
  - Fever
  - Altered Mental Status
  - Acute Renal Failure
  - Microangiopathic Hemolytic Anemia
  - Thrombocytopenia
- Other Symptoms
  - Abdominal Pain
  - Musculoskeletal Discomfort
  - Headaches
- Patients “look sick”

Etiologies:
- Familial
- Infection (HIV, E. coli O157:H7)
- Drugs (quinidine, cyclosporin, clopidogrel, ticlopidine)
- Malignancy (also causes DIC)
- Chemotherapy (mitomycin, cisplatin, gemcitabine)
- Bone Marrow Transplantation
- Pregnancy
- Autoimmune Diseases (SLE)

Diagnosis
- Based on peripheral blood smear and the right clinical scenario
  - Schistocytes in low percentage may be present in a subset of patients without TTP
  - Studies have demonstrated 1-18% of red cells to be schistocytes in TTP; therefore, >1% of red cells as schistocytes is strongly suggestive of TTP
- LDH is always significantly elevated at 3-10 times normal
- If this disease cannot be excluded at initial evaluation, the patient must be treated urgently for TTP
- Confirmatory test is the ADAMTS13 Activity, reported from ARUP Lab in 1-4 days, though the test is not 100% sensitive nor specific

Treatment
1. Contact the renal service for emergency plasma exchange (i.e. to start within a few hours)
2. In the interim give 3 units of fresh frozen plasma every 3-4 hours until exchange started – continue exchange daily until remission.
3. Begin solumedrol 1.5 mg/kg IV in divided doses.
4. Do not use cryoprecipitate or platelet transfusion except for a life-threatening CNS bleed
5. Transfuse leukodepleted packed red blood cells as indicated clinically.
6. Plasma exchange should be done daily until LDH and platelets are in the normal range, then tapered over 5-7 days.
7. Twice daily plasma exchange, Rituximab, IVIG and other modalities for refractory cases.

Prognosis: Untreated, mortality is quoted as 70-90%; treated, mortality still 20%.

Heparin-Induced Thrombocytopenia

Pathophysiology:
- An acquired, transient pro-thrombotic disorder caused by heparin
- Immune-mediated, caused by platelet-activating antibodies (IgG) that recognize complexes of platelet factor 4 (PF4) and heparin, binding and activating platelets

Clinical Manifestations:
Highly Characteristic Clinical Profile=4 T’s, with Scoring System:

<table>
<thead>
<tr>
<th>4 “T”s ↓ Points→</th>
<th>2</th>
<th>1</th>
<th>0</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombocytopenia (platelet count &lt; 150,000)</td>
<td>&gt;50% platelet fall to nadir ≥ 20</td>
<td>30-50% platelet fall, or nadir 10-19</td>
<td>&lt;30% platelet fall, or nadir &lt; 10</td>
<td>Usually a relatively mild fall in platelet count (30,000-90,000)</td>
</tr>
<tr>
<td>Timing of Platelet ↓</td>
<td>Days 5-10, or ≤ day 1 with recent heparin (past 30 days)</td>
<td>&gt;10 days or timing unclear; or &lt;day 1 with recent heparin (past 31-100 days)</td>
<td>&lt; day 4 (no recent heparin)</td>
<td>In 25% of patients with HIT, thrombosis precedes the fall in platelet count</td>
</tr>
<tr>
<td>Thrombosis or Skin Abnormalities</td>
<td>Proven new thrombosis; skin necrosis; or acute systemic reaction after IV UFH bolus</td>
<td>Progressive or recurrent thrombosis; erythematous skin lesions; suspected thrombosis (not proven)</td>
<td>None</td>
<td>Odds ratio of clotting in the face of HIT is 20-40 time baseline; 30-90% of patients with HIT develop thrombosis (arterial or venous)</td>
</tr>
<tr>
<td>Absence of Other Explanations</td>
<td>None</td>
<td>Possible</td>
<td>Definite</td>
<td></td>
</tr>
</tbody>
</table>

Pretest probability Score: 6-8 high probability (>80% likelihood); 4-5 intermediate; ≤3 low probability (<5% likelihood)

Patients May Also Develop:
- Coumadin-induced Thrombosis
  - Skin necrosis, venous limb gangrene (usually in a limb affected by clot)
  - Thought to be as a result of Coumadin-induced depletion of protein C
- Skin manifestations (10-20% of patients with HIT)
  - Necrotic lesions, erythematous plaques
- Acute systemic reaction
  - May occur 5-30 minutes after an IV bolus of heparin in patients with circulating HIT antibodies (or up to 2 hours after a subcutaneous injection)
  - FEVERS, CHILLS, FLUSHING
  - Cardiopulmonary effects (tachycardia, hypertension, tachypnea, dyspnea, cardiac or respiratory arrest)
  - Neurologic effects (headache, transient global amnesia)
  - GI effects (large volume diarrhea)
  - Accompanied with acute platelet count drop
- Adrenal Thrombosis +/- Hemorrhage (3-5% of patients with HIT)
  - Venous thrombosis of one or both adrenals
  - Can cause adrenal crisis if bilateral
  - Often manifests as abdominal pain or flank pain
- Intracerebral hemorrhage (very rare; <1% of patients with HIT)
  - Venous (dural) thrombosis with hemorrhagic transformation
Risk Factors:
- **Women** > **Men** 2.3:1
- **Surgical** > **Medical** 3.5:1 (particularly cardiac or orthopedic surgical patients)
- **Unfractionated heparin** > **Low Molecular Weight heparin** 5.2:1
- Patients with skin manifestations after heparin administration: at higher risk for HIT
- LESS likely in the critically ill: 30-50% incidence of thrombocytopenia in the ICU, with only a 0.3-0.5% incidence of ‘serologically-confirmed HIT’ in critically ill patients
- LESS likely with chronic renal failure

Diagnosis:
- Usually made clinically; must have a high index of suspicion
- Screening Test
  - Heparin-Induced Thrombocytopenia Antibodies = Platelet Factor 4 Antibodies
  - Returns in 1-2 days from ARUP Laboratory
- Confirmatory Test
  - Serotonin Release Assay = Platelet Activation test
  - Less false-positives for HIT than the HIT Antibody test
  - Returns in up to 10 days from ARUP Laboratory
- May be ordered as “HIT Antibody test with Reflex Serotonin Release Assay”

Treatment:
- Stop heparin
- Start alternative, non-heparin anticoagulant, in therapeutic doses even if there is no clot (>50% incidence of clot formation in the next 30 days with HIT)
- Do not begin Coumadin until platelet count >150
  - When platelet count is >150, may start Coumadin, and at a dose no greater than 5mg daily
  - Would overlap alternative anticoagulant with Coumadin for at least 5 days and until INR 2-3 x 24-48 hours, particularly in the face of active clot
  - If Coumadin was already given in the face of active HIT with thrombocytopenia, it is recommended to start a direct thrombin inhibitor, then give Vitamin K (10mg po or 5-10mg IV) to reverse the effects of Coumadin so as to not underdose the direct thrombin inhibitor
  - Coumadin is to be given for 3-6 months in the face of thrombosis, 6 weeks without thrombosis
- Avoid platelet transfusions
- Test for HIT antibodies as above
- Rule out lower extremity clot with Doppler ultrasound
- Do not rechallenge patient with heparin for at least 3 months – if heparin necessary (i.e. CABG) and no detectable antibody after 3 months, it is safe to use.

Prognosis:
- Platelet count usually recovers within 4 days after stopping all Heparin, although 10% of patients do not recover platelet count above 150 beyond 1 week
Alternative Anticoagulants for the Treatment of Heparin-Induced Thrombocytopenia

- Argatroban
  - Direct Thrombin Inhibitor
  - Hepatically cleared (no change with renal failure) (contraindicated in cirrhosis)
  - T $\frac{1}{2} = 40-50$ minutes
  - Goal PTT = 1.5 – 3 times baseline PTT
  - Monitoring = 2 hours after adjustment
  - Recommended IV Infusion Rate 1.2 mcg/kg/min (0.5mcg/kg/min with significant hepatic dysfunction or with otherwise critical illness, heart failure, anasarca, or after cardiac surgery [all situations with potential for hepatic congestion])
  - Also increases the INR significantly, and may lead to underdosing of Coumadin—leading to inappropriately early cessation and higher risk for thrombosis complications including amputation (13.7%, vs. 5.6% with Lepirudin) in many studies
    - When INR>4, discontinue the argatroban once daily for 4 to 6 hours and obtain a stat aPTT/INR. Restart the drip before the result has returned, at the current rate.
    - Adjust Coumadin dosing cautiously, based on the daily INRs off the argatroban drip.
    - Discontinue the argatroban drip when 2 consecutive daily INRs off of the argatroban drip are between 2 and 3 and the Coumadin has been given for at least 5 days.
  - There is NO ANTIDOTE for Argatroban; FFP may be used for bleeding. Recombinant Factor VII may be considered for refractory life-threatening bleeding

- Fondaparinux (Arixtra)
  - Still recommended for HIT in the latest guidelines (2008), though not FDA approved
  - Dosing should be for TREATMENT, not prophylaxis
  - Contraindicated with Creatinine Clearance < 30; adjustment for renal function is essential
  - There is NO ANTIDOTE for Arixtra

### Preventing DVT/PE in Hospitalized (Surgical & Medical) Patients

| CATEGORY | OPTIONS FOR DVT PROPHYLAXIS
| --- | --- |
| Low-risk patients | • Early ambulation  
• Leg exercises |
| Moderate-risk patients | • Heparin 5000 Units SQ q8h started 2h preop  
• Enoxaparin¥  
• Fondaparinux¶ 2.5 mg SQ daily  
• SCD’s |
| High-risk patients | • Heparin 5000 Units SQ q8h started 2h preop  
• Enoxaparin¥  
• Fondaparinux¶ 2.5 mg SQ daily  
• SCD’s only if pharmacological prophylaxis is contraindicated¥¶ |
| Highest-risk patients | • Heparin 5000 Units SQ q8h started 2h preop  
• Enoxaparin¥  
• Fondaparinux¶ 2.5 mg SQ daily  
• (Warfarin titrated to INR 2-3 option for THA or TKA)  
PLUS  
• SCD’s |
| Moderate-high risk patients at high risk for bleeding | • SCD’s until bleeding risk is low  
• Initiate thromboprophylaxis when bleeding risk low |

**Abbreviations:** SCD = Sequential Compression devices, THA = total hip arthroplasty, TKA = total knee arthroplasty, HFS = hip fracture surgery, CA = cancer, RF = risk factor

* - eye, ear, dermatologic, laparoscopic or arthroscopic operations  
‡ - severe burns, immobility, prior venous thromboembolism, active cancer, stroke with paresis, inherited thrombophilia, polycythemia, myeloproliferative disorder, marked obesity, CHF, nephrotic syndrome, inflammatory bowel disease, acute MI, acute respiratory failure, sickle cell disease, paroxysmal nocturnal hemoglobinuria, pregnancy, recent trauma, central venous catheter, mechanical ventilation, severe sepsis, shock, and use of the following medications: tamoxifen, raloxifene, thalidomide, lenalidomide, darbepoetin, epoetin alfa, bevacizumab, hormone replacement therapy or systemic chemotherapy  
# - thoracic, intraperitoneal, bariatric, open urologic and Gyn, cardiac, neurosurgical and cancer operations  
¥ - LMWH=Low molecular weight heparins: enoxaparin 40 mg SQ daily starting 1-2 hrs preop or 30 mg SQ q12h starting 12-24h postop; dosage adjustment required for CrCl 15-30 mL/min and may be needed if weight>155 kg; avoid if CrCl<15 mL/min or initial PLT < 50K or platelet count falls ≥ 50% or to a level < 100K  
¶ - Give 6-8h post-op; avoid if CrCl<30 mL/min, weight<50 kg, epidural infusions or endocarditis or initial PLT<50K; no antidote if active bleeding develops; T1/2 ~18h  
† - Thromboprophylaxis can generally be started within 36 hrs of major trauma or spinal cord injury unless intracranial bleeding, active internal bleeding, perispinal hematoma, or uncorrected coagulopathy present  
• Avoid unfractionated Heparin for initial PTL < 50K or PLT count falls ≥ 50% or to a level < 100K

Adapted from Chest, 2008; 133: 381-453. Borrowed with permission from Joseph Esherick, MD.

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**WARNING**  
Enoxaparin should not be used within 24 hours of epidural or intrathecal puncture AND should be withdrawn 24 hours before removal of epidural catheter.

**WARNING**  
Fondaparinux (Arixtra®) should not be used within 36 hours of epidural or intrathecal puncture AND avoid if epidural catheter is in place.

**SURGICAL GUIDELINES**  
In hip replacement, knee preplacement, hip fracture surgery and abdominal/pelvic cancer surgery continuation of anticoagulation for 30 days significantly reduces risk of venous thromboembolism.
Oncologic Emergencies

Acute Leukemia

Every effort should be made to get these patients transferred FROM THE ER. VCMC is not equipped to care for acute leukemic crises. Once these patients are admitted, it is nearly impossible to get them transferred to get the emergent care that they need. Call your attending if you have any questions about this, prior to writing admission orders.

Tumor Lysis Syndrome

Pathophysiology

- Most often seen after therapy for aggressive hematologic tumors (high grade lymphomas, acute leukemias). May also be seen after treatment of some solid tumors (e.g. testicular cancer, high-grade neuroendocrine tumors), and may also occur spontaneously.
- Caused by massive release of intracellular contents after tumor cell death

Clinical Manifestations

- Nucleic acid breakdown causes elevated uric acid
  - May crystallize in renal tubules and lead to renal failure
  - Dehydration can contribute to renal failure
  - Hyperkalemia from cell lysis
- Elevated phosphorus level can lead to severe symptomatic hypocalcemia
- LDH usually elevated
- Cairo-Bishop Grading of Tumor Lysis Syndrome:

<table>
<thead>
<tr>
<th>Cairo-Bishop Grading of Tumor Lysis</th>
<th>Grade 0</th>
<th>Grade I</th>
<th>Grade II</th>
<th>Grade III</th>
<th>Grade IV</th>
<th>Grade V</th>
</tr>
</thead>
<tbody>
<tr>
<td>LTLS</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Creatinine</td>
<td>≤1.5x ULN</td>
<td>1.5x ULN</td>
<td>1.5-3x ULN</td>
<td>3-6x ULN</td>
<td>&gt;6x ULN</td>
<td>Death</td>
</tr>
<tr>
<td>Cardiac Arrhythmias</td>
<td>None</td>
<td>Intervention not needed</td>
<td>Non-urgent intervention needed</td>
<td>Symptomatic and incompletely controlled medically or controlled with a device</td>
<td>Life-threatening (arrhythmia with CHF, hypotension or shock)</td>
<td>Death</td>
</tr>
<tr>
<td>Seizures</td>
<td>None</td>
<td>None</td>
<td>One brief, generalized seizure, seizure controlled with anticonvulsant, or infrequent motor seizures</td>
<td>Seizures with impaired consciousness, poorly controlled seizures, generalized seizures despite medical intervention</td>
<td>Status epilepticus</td>
<td>Death</td>
</tr>
</tbody>
</table>

Abbreviations: LTLS = Laboratory Tumor Lysis Syndrome; ULN= Upper Limit of Normal

Prevention

- Allopurinol 600 mg po daily for 2-3 days prior to therapy is helpful
- Adequate hydration status (up to 3 Liters IV Fluids/day if cardiac status allows for high risk patients during therapy)

Treatment

- Allopurinol (stops production of uric acid) or Rasburicase (= recombinant urate oxidase; reduces uric acid levels; indicated for Uric Acid in 15-range; get Oncology approval first)
- Treatment of the metabolic derangements aggressively

Return to Table of Contents
Brain Metastases

Clinical Manifestations
- Most commonly from lung, breast, and melanoma (also from renal, germ cell, and thyroid)
- Symptoms may be focal or generalized depending on the location(s) of tumor in the brain
  - Often subtle; only 50% of patients have headache at time of diagnosis
  - Other times, may present with signs of elevated Intracranial Pressure

Diagnosis
- MRI is the most sensitive; CT with contrast may miss metastases in the posterior fossa
- NOTE: CT without contrast is not sufficient to rule out metastases

Treatment
- Elevated ICP
  - Dexamethasone (the most lipid soluble steroid) at doses as high as 16-24mg IV bolus followed by 4mg IV q 6 hours
  - Mannitol 1gram/kg IV bolus, followed by 0.25-0.5mg/kg IV q3-6 hours; reserved for most urgent patients as a bridge to surgery
- Seizures
  - Treat as for Status Epilepticus
- Long-term therapy
  - Surgery vs. Radiation

Malignant Spinal Cord Compression

Clinical Manifestations
- Back pain + History of Cancer = cord compression until proven otherwise

Diagnosis
- Urgent MRI or CT Myelogram; Plain films may be helpful (abnormal in 80% of malignant cord compressions)

Treatment
- Steroids: Dexamethasone bolus of 10-16mg IV, then 4mg IV q 4 hours; may give steroids prior to imaging if the clinical suspicion is high
- Radiation vs. Surgery vs. Surgery followed by Radiation: choice depends on many factors, including extent of disease, performance status, stability of the spine, radiosensitivity of the underlying malignancy, etc.

SEPSIS

Definitions:

SIRS (Systemic Inflammatory Response Syndrome)
By definition, 2 or more of the following means SIRS:
- Fever >38º C or hypothermia <36º C
- Heart Rate >90 or > 2 standard deviations more than normal value for age
- Respiratory Rate >20 or PaCO₂<32
- Systolic Blood Pressure <90
- Abnormal WBC (>12,000 or <4,000) or >10% bands

Other criteria that may be signs of sepsis:
- Altered Mental Status
- C-reactive protein or procalcitonin > 2 standard deviations above normal value
- Significant edema or positive fluid balance (>20 mL/kg over 24 hours)
- Hypoxemia (PaO₂/FiO₂<300)
- Hypotension
- Creatinine increase >0.5 mg/dL over baseline
- Coagulation abnormalities (INR > 1.5 or aPTT>60 seconds)
- Ileus
- Thrombocytopenia (platelet count <100,000 / microL)
- Hyperbilirubinemia (total bilirubin > 4 mg/dL)
- Decreased capillary refill or mottling

SIRS + Infection (suspected or documented) = Sepsis

Sepsis + New Organ Dysfunction or Tissue Hypoperfusion = Severe sepsis

Hypotension, high lactate, or oliguria caused by infection=Septis-induced tissue hypoperfusion

Sepsis-induced hypotension persisting despite adequate fluid resuscitation = Septic Shock

Organ System Dysfunction Definitions for Severe Sepsis

- Sepsis-induced SBP<90 mmHg or MAP<65 mmHg
- SBP decrease>40mmHg from baseline
- Bilirubin>2mg/dl
- Platelet Count<100,000
- Lactate>2mmol/L
- Coagulopathy (INR>1.5 or aPTT>60 secs)
- Acute Lung Injury with PaO₂/FiO₂ < 250 in the absence of pneumonia as infection source
- Acute lung injury with PaO₂/FiO₂< 200 in the presence of pneumonia as infection source
- Creatinine>2.0mg/dl or urine output<0.5ml/kg/hour for 2 hours despite adequate fluid resuscitation

Return to Table of Contents
Pathophysiology:
- Pathogen evades body’s barriers of protection (skin, acidic pH of stomach, cough, etc.) leading to bacterial translocation across intestine, invasion into the lung, cellulitis, etc.
- Non-specific, or “innate” immune system responsible for initial recognition and defense against pathogenic microorganisms by recognition of “Pathogen Associated Molecular Patterns” (PAMPS) of microbes
  - PAMPSs may be surface molecules of microorganisms (such as endotoxin [lipopolysaccharide (LPS)], lipoprotein, flagellin, fimbriae, peptido-glycans, peptidoglycan-associated lipoprotein, and lipoteichoic acid) but also intracellular patterns that are released by lysis of bacteria (such as heat-shock proteins and DNA or RNA fragments)
  - Patterns are recognized by pattern recognition receptors (PRRs) present on macrophages, monocytes, and dendritic cells among others
    - Four families of PRRs have been described to date: toll-like receptors (TLRs), nucleotide oligomerization domain-like receptors (NLRs), C-type lectin receptors (CLRs), and RigI-helicases
  - Binding of a PAMP to a PRR results in activation of intracellular signaling cascades that subsequently leads to activation of the innate immune system
  - Innate immune system response is highly variable from individual to individual, and depends on a number of factors including bacterial load, pathogen virulence, host comorbidities and host genetics
  - Pro-inflammatory immune response = hyperinflammatory phase of sepsis
    - Release of pro-inflammatory cytokines (tumor necrosis factor (TNF-α), Interleukins 1-β and 6, and interferon-γ) and chemokines (neutrophil and macrophage chemotactic factors such as CCL2 (MCP-1), CCL3 (MIP-1α), CCL6 (C10), and CXCL8 (IL-8)
    - The proinflammatory cytokines stimulate the effector functions of neutrophils, macrophages, and Th1 cells, exacerbating cellular immune response
  - These responses are induced in a context in which the complement system and the coagulation cascade are also strongly activated and this can ultimately result in the typical septic shock clinical signs and symptoms – decrease in systemic vascular resistance (“bigger tank”=larger volume of distribution), leaky blood vessels with extravasation of fluid, inability of organs to utilize delivered oxygen (sometimes reflected in a high central or mixed venous O2 saturation > 82-85%), hemodynamic instability, coagulation abnormalities, and end-organ dysfunction
- Very importantly, an anti-inflammatory immune response (depending on the infection and the host) is also initiated early on in sepsis via a number of different mechanisms
  - Lymphocyte apoptosis and dysfunction, monocyte deactivation with decreased HLA-DR expression, neutrophil dysfunction, T-cell suppressing neutrophils
  - Subsets of lymphocytes (CD4, CD25, T regulatory (Treg) cells, natural killer T cells, and CD8 T cells) are known to actively suppress the adaptive immune response
  - Down to the cellular level, ‘epigenetic’ changes in gene expression leads to production of less inflammatory cytokines
  - Relatively more anti-inflammatory cytokines (IL-4, IL-10, IL-13, IL-1 receptor antagonist, transforming growth factor-β) than pro-inflammatory cytokines
  - Too-pronounced or sustained anti-inflammatory response can lead to generalized and long-term impairment of the host’s immune function, known as “immunoparalysis”
- Increased susceptibility to secondary infections
- Implicated in late mortality in sepsis
  - May be why anti-inflammatory agents have not improved mortality in septic patients
  - Immune stimulation (i.e. interferon-γ and granulocyte-macrophage colony stimulating factor (GM-CSF) are two examples) that have been studied in sepsis have shown early promise

**Workup**
- Detailed physical exam looking for any potential sites of infection (in patients who are immunosuppressed, localization of infection may not be present; be vigilant for peri-rectal abscesses, CNS infection, peripheral or central venous catheter infections, etc.)
- Labs to consider: ABG, Blood cultures x 2 (with at least one drawn percutaneously and 1 drawn through each vascular access device unless the device was recently (<48 hours) inserted), CBCD, Comprehensive Metabolic Panel, Cardiac Enzymes, Lactic Acid, Magnesium, phosphorus, DIC Panel, UA w/ gram stain + culture, Sputum gram stain + culture, +/- C-reactive protein, procalcitonin
- Imaging: Chest X-Ray, EKG; Consider Echocardiogram in hypotension, plain films for soft tissue infections, renal imaging in pyelonephritis, abdominal/pelvic CT for suspected abdominal/pelvic source
- Shock Index=Heart Rate / Systolic Blood Pressure
  - Normal range 0.5 to 0.7
  - Elevations above 0.7 may be indicative of hypovolemia and shock

**Evidence of Management Recommendations:**
- Since 2002, Surviving Sepsis Campaign has produced guidelines every 4 years (latest 2012) for the management of sepsis, severe sepsis and septic shock based on the best available evidence. 2015 interim recommendations have been released in the face of new evidence
- 2012 guidelines recommended the Early Goal Directed Therapy (EGTD) protocolized approach to management of sepsis, severe sepsis and septic shock.
  - Based on the landmark clinical trial “Early Goal Directed Therapy in the Treatment of Severe Sepsis and Septic Shock” (2001) in the New England Journal of Medicine by M. Rivers which randomized 263 patients to Early Goal Directed Therapy (EGDT) vs. Standard care (In-hospital mortality reduced from 46.5% (standard care) to 30.5% (EGDT) (p=0.009))
  - Protocolized approach of EGDT includes a 6 hour resuscitation bundle
    - First 3 hours: lactate drawn at time of sepsis diagnosis, blood cultures drawn prior to antibiotics (if no more than 45 minute delay), antibiotics administered within 1 hour of sepsis diagnosis, and 30 ml/kg fluid bolus if SBP < 90 mmHg or lactate > 4 mmol/dL
    - First 6 hours: lactate re-checked if initial elevation; pressors started if SBP<90 mmHg or MAP < 65 mmHg to maintain MAP ≥ 65 mmHg; central line with continuous CVP and central venous O2 sat (ScVO2) if lactate remained > 4 mmol/dL or hypotension after initial bolus, to maintain CVP 8-12 (or 12-15 if intubated or diastolic dysfunction) and central/mixed venous oxygen saturation ≥ 70%/65% respectively (optimized via protocolized blood transfusion to keep Hct>30, cardiac index > 2.5 with dobutamine, and oxygen)
Since 2012, 3 separate randomized clinical trials examining EGDT versus usual care have seriously challenged the protocolized approached, lending credence to usual care over EGDT.

- ProCESS Trial (“Protocolized Care for Early Septic Shock”) (2014)
  - Randomized 1341 patients in emergency departments in the US to one of three groups: protocol-based EGDT, protocol-based standard therapy, or usual care
  - Resuscitation strategies differed with respect to monitoring and oxygen and the use of IV fluids, vasopressors, inotropes, and blood transfusions
  - No difference in 90 day or 1 year mortality between the three groups

  - Randomized 1600 patients (mostly in Australia and New Zealand) to EGDT or usual care
  - Primary outcome (mortality rate at 90 days) NO different (18.6% vs. 18.8%)
  - Also no difference in survival time, in-hospital mortality, duration of organ support, or length of hospital stay
  - EGDT received more IV fluids, more vasopressors, more red cell transfusions, and more dobutamine

- ProMISe Trial (“Protocolized Management in Sepsis”) (2015)
  - Randomized 1260 patients in England to EGDT or usual care
  - Primary outcome (mortality at 90 days) NO different (29.5% vs. 29.2%)
  - EGDT group received more IV fluids, more vasopressors, and red cell transfusions, and had significantly worse organ failure scores, more days of advanced cardiovascular support, and longer ICU length of stay.

Management Recommendations for Sepsis, Severe Sepsis and Septic Shock:

Keys to Management and Resuscitation with the goal of rapid restoration of tissue perfusion:

- Early recognition is KEY – morbidity and mortality increase for each hour of delay in treatment; screening via protocolized approach (see sepsis protocol, page 141)
- Blood cultures should be drawn prior to administration of antibiotics if there will not be more than a 45 minute delay in administration of those antibiotics
- Early antibiotics effective against the causative agent(s) is key – administering antibiotics that are not effective is akin to not administering antibiotics at all
- Fluid administration
  - Start with a fluid bolus of 30 mL/kg in patients screening positive for sepsis
  - Estimate the amount of fluid the patient needs and administer over 12-48 hours
    - Septic patients may need anywhere from 4 to 10 liters of fluid
  - ‘Goldilocks’ approach to fluid management (not too much, not too little, just right)
  - Dynamic measures of resuscitation are most beneficial – look at blood pressure, pulse, IVC measurements or Central Venous Pressure (CVP), Stroke Volume Variability (SVV) and Cardiac Index (CI) (may also consider passive leg raise) after fluid boluses to see if the patient remains ‘fluid responsive’ (see page 89) (don’t give much more fluid to the patient who is not ‘fluid responsive’)
- Start vasopressors (norepinephrine (Levophed) as first line in patients with persistent hypotension
Goals of Resuscitation: to RESTORE TISSUE PERFUSION as reflected by:

- Urine output $\geq 0.5\text{ml/kg or } \geq 30\text{ml/kg}$
- Mean Arterial Pressure $\geq 65$
- Normalization of serum lactate for those with elevated lactate as sign of tissue hypoperfusion
  - Code sepsis will be called for lactate $> 4$ and/or SBP $< 90$
  - Lactic acid between 2-4
  - A negative lactic acid ($<2$) does NOT rule out sepsis or septic shock – must interpret all lab tests in the context of the patient
- Optional management goals to consider for patients not meeting the above goals:
  - Central Venous Pressure of 8-12 mm Hg (12-15 mm Hg if intubated or diastolic dysfunction)
  - Central Venous O2 Saturation (superior vena cava) (ScvO$_2$) $\geq 70\%$ or Mixed Venous O2 Saturation $> 65\%$
  - It is up to the discretion of the ICU Attending as to whether the monitors are to be used or not

Specific Therapies, Itemized:

Fluids:
- Initial bolus of 30ml/kg crystalloid over 30 minutes.
- Continue 500 ml boluses q 30 minutes thereafter to meet MAP and urine output goals while being mindful of preventing fluid overload
- If hypotension persists after initial fluid bolus, start norepinephrine (Levophed), and continue crystalloid infusion at 500-1000ml every 30 minutes until patient is no longer fluid responsive
  - Low dose norepinephrine ($\leq 5$ mcg/minute) may be administered via a very good peripheral IV with frequent IV checks to ensure there is no extravasation
  - Fluid responsiveness
- Adequate Resuscitative Access: 2 large bore ($\geq 18$ gauge) peripheral IVs, a Trauma Line, or a Cordis (a triple lumen alone is often not adequate)
- CRISTAL trial (2014) randomized 2857 patients to crystalloid vs. colloid
  - No difference in 28 day mortality; however, 90 day mortality 34.2% with crystalloid vs. 30.7% with colloid ($p=0.03$) (authors considered 90 day mortality reduction to be ‘exploratory’ requiring further study)
  - Statistically significantly less ventilator days and vasopressor days by days 7 and 28 (1 full day reduction in both by 28 days) with colloid vs. crystalloid
  - Recommendation: there is not yet enough evidence of benefit to recommend colloids such as albumin over crystalloid infusion, though albumin may be considered when patients require “substantial” amounts of crystalloids
- There is some evidence that excessive sodium chloride administration can lead to hyperchloremic metabolic acidosis and a higher incidence of acute kidney injury when compared to Lactated Ringers. Consider changing from sodium chloride to Lactated Ringers after an initial 1-2 liters of resuscitation in sepsis.

Antimicrobials and Source Control:
- Early (within 1 hour) appropriate antibiotic choice and administration is the most important intervention to improve survival from severe sepsis and septic shock
• Blood cultures should be drawn prior to antibiotics given if it will not delay administration of antibiotics by more than 45 minutes
• Initial empiric anti-infective therapy of one or more drugs that have activity against all likely pathogens (bacterial and/or fungal or viral) and that penetrate in adequate concentrations into tissues presumed to be the source of sepsis (see suggested antimicrobials of choice based on likely organ system infected and risk for multi-drug resistant organism – page 150)
• Antibiotics are ineffective without SOURCE CONTROL: Carefully consider potential infection sources including infected medical devices and catheters, superficial or deep abscesses, appendicitis, cholecystitis, necrotizing fasciitis, epidural abscess etc.

Vasopressors (Pressors):
• Vasopressors should be started if hypotension persists or recurs after 30ml/kg crystalloid bolus; should also continue fluid resuscitation if the patient remains fluid responsive
• Norepinephrine is first line therapy because of lower risk of arrhythmia related sudden death
  ◦ Dopamine may be considered as first line only for highly selected patients with severe bradycardia but should be stopped if heart rate increases above 120 bpm
• Epinephrine, low dose vasopressin (0.01 to 0.04 units per minute) and dopamine can be considered as second and third line agents to add to Norepinephrine infusions in refractory hypotension
• Dobutamine (a “perfuser”) should be considered in patients with an ScV02<70 with suspected myocardial dysfunction (cardiac index<2.5, EF<50% or clinical signs of heart failure) or ongoing signs of hypoperfusion despite achieving adequate intravascular volume and adequate MAP; caution with tachycardic effects

Steroids for Relative Adrenal Insufficiency of Sepsis:
• Hydrocortisone 50 mg IV bolus followed by 200 mg IV continuous infusion over 24 hours or 100mg IV every 8 hours should be administered to patients with vasopressor refractory septic shock (MAP<65 on high dose norepinephrine) or those with chronic steroid use (low level data suggests less hyperglycemia with 200 mg infusion over 24 hours compared to bolus dosing)
• Adrenal function testing currently plays no role in the use of steroids in septic shock

Selenium:
• No longer recommended for treatment of severe sepsis or septic shock

Bicarbonate:
• Bicarbonate IV (as 3 amps of Sodium Bicarbonate in 1 Liter D5W or 1.5 amps of Sodium Bicarbonate in a liter of ½ NS to make isotonic solutions) may be considered in the face of septic shock with a serum pH of ≤7.15 (and usually given with pH≤7.1)

Insulin Drip:
• Insulin therapy should be instituted after the initial resuscitation in all patients admitted to the ICU in septic shock when blood sugar goes above 180 x 2.
• Goal blood sugars is 120-180 mg/dl (insulin infusion with Glucommander targets 120-160 mg/dL)

Intravenous Immunoglobulin (IVIg):
Not currently recommended for septic shock
May consider in toxin-producing infections (C. dif, Necrotizing Soft Tissue Infection, Toxic Shock Syndrome)

Blood Transfusions:
- Restrictive transfusion goal of Hb ≥ 7 g/dL is recommended
  - Was initially recommended to have Hb >10 g/dL in the EGDT bundle for ScVO2 < 70% in first 6 hours; changed based on the following trial:
  - TRISS Trial (“Transfusion Requirements in Septic Shock”) (2014)
    - Randomized 998 patients to goal Hb of ≥ 7 g/dL (restrictive) vs. ≥ 9 g/dL (liberal)
    - Restrictive received on average 1 unit PRBCs; liberal received 4 units PRBCs
    - Mortality 43% in restrictive group vs. 45% in liberal group (no statistical difference)

Other Important Aspects of Care:
- VAP Prophylaxis (page 65)
- DVT Prophylaxis (page 131)
- Stress Ulcer Prophylaxis (page 86)
- Pressure Ulcer Prophylaxis (page 229)
- Enteral support when no longer severely hypotensive nor on very high doses of vasopressors (local convention is to withhold enteral feeds for Norepinephrine doses > 10 mcg/minute, and to give no more than trickle feeds (10 ml/ hour) for norepinephrine doses > 5 mcg/minute)
- Family updates, identifying decision-makers (see Code Discussions in the ICU, page 219)

Prognosis:

<table>
<thead>
<tr>
<th>Severity of Sepsis</th>
<th>Mortality Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Septic shock with both hypotension and lactate ≥ 4 mmol/L</td>
<td>46.1%</td>
</tr>
<tr>
<td>Severe sepsis with hypotension alone</td>
<td>36.7%</td>
</tr>
<tr>
<td>Severe sepsis with lactate ≥ 4 mmol/L with NO hypotension</td>
<td>30%</td>
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POLICY STATEMENT
Sepsis is the leading cause of death in noncardiac intensive care units in the United States. National mortality for hospitalized patients with severe sepsis approaches 20% and for hospitalized patients with septic shock mortality exceeds 40%. Recent studies have demonstrated a significant reduction in sepsis mortality through the use of Early Goal Directed Therapy and protocolized management of severe sepsis immediately after recognition. Nationwide, sepsis screening and protocolized care has resulted in an 18% reduction in mortality. This translates to a number needed to treat of 6 patients to save one life. To improve care and reduce sepsis mortality for patients at Ventura County Medical Center, a sepsis task force in 2012 was formed and the following policy developed. The policy was revised in 2015 to reflect more recent changes in evidence and guidelines related to sepsis management.

SEPSIS SCREENING
Emergency Department
Each patient who presents to the emergency department and Ventura County Medical Center is screened for sepsis. If a patient screens positive for sepsis, a Sepsis Triage Assessment Tool (STAT-ER) will be completed. Each patient with a positive screen will have a venous lactate drawn. The blood sample will be given to respiratory therapy and processed immediately. When the lactate is resulted, the result will be called to the nurse who screened the patient positive. If the lactate is less than 2 mmol/L there will be no change in management. If the lactate is between 2 and 4 mmol/L the attending emergency physician will be informed of the result and immediately evaluate the patient. If the lactate is greater than 4 mmol/L, a code sepsis will be initiated (see below).

Medical Surgical Floors (2W, 3W, 3N, DOU and ICU)
Every hospitalized patient will be screened for sepsis every 12 hours as part of the nursing shift assessment. Also if a nursing aid or nurse identifies that a patient has new abnormal vital signs between shift assessments, the bedside nurse will be notified immediately and the patient will be screened. If a patient has signs of sepsis at or between shift assessments a Sepsis Triage Assessment Tool will be completed by the bedside nurse. For a patient that screens positive, the bedside nurse will initiate lactate testing by calling respiratory therapy to bedside and either drawing the patient’s blood, asking a colleague, charge nurse or nursing supervisor to draw blood, calling phlebotomy to draw blood or calling the trauma support nurse to draw a venous sample for lactate testing. Blood will be drawn for lactate testing within 5 minutes of a positive screen. The bedside nurse will notify the treating physician of the positive screen and ask if additional orders are desired at the time of positive screen. The bedside nurse will also notify the ICU Trauma Support Nurse (TSN) to inform him/her of the positive screen. Respiratory therapy will run the lactate on the blood gas analyzer and inform the bedside nurse and TSN of the result. If the lactate is less than 2 mmol/L there will be no change in management. If the lactate is between 2 and 4 mmol/L the patient’s resident physician will be informed of the result and asked for any additional orders. If the lactate is greater than 4 mmol/L, a code sepsis will be initiated (see below).

CODE SEPSIS
Code Sepsis Emergency Department
If a patient presents to the emergency department with a positive sepsis screen and either a systolic blood pressure less than 90 mmHg or a lactate greater than 4 mmol/L a code sepsis will be called. The nurse who identifies code sepsis will initiate a silent page to the code sepsis team. The following information will be included in the page: CODE SEPSIS, Unit, Room #, Patient MR Number. The code sepsis team includes the following: Sepsis Task Force Director, Nurse manager of ICU, ICU attending physician, ICU resident physician, Trauma Support Nurse, respiratory therapist, pharmacist on duty, nursing supervisor and sepsis data team. The trauma support nurse and respiratory therapist will respond immediately to the bedside. The pharmacist will stay in the pharmacy but be on alert to give priority to the code sepsis patient in preparing and dispensing medication. The nursing supervisor and ICU staff will
determine if ICU bed needed, and if so, will work to expedite bed availability in the ICU. The bedside emergency room nurse will retrieve the sepsis tool box located in the medication room in the emergency department and bring this to the patient’s bedside. The attending emergency physician will run the code sepsis and order blood cultures, antibiotics and IV fluids. The bedside emergency room nurse, with the assistance of the trauma support nurse will carry out orders. Special efforts will be made to complete the following in an expedited fashion: 1) drawing blood cultures and a code sepsis panel 2) infusing broad spectrum antibiotics 3) administering 30 ml/kg crystalloid fluid bolus and starting a norepinephrine infusion if systolic blood pressure is < 90 mmHg after a single fluid bolus. If the initial lactate is greater than 4 mmol/L the emergency physician will order a repeat lactate will be drawn two hours after the first lactate. If the repeat lactate is > 4 mmol/L or if the systolic blood pressure is less than 90 mmHg after a single fluid bolus, the ICU physician will be consulted to evaluate the patient at the bedside. For persistent lactatemia or hypotension, the ICU team will continue management by applying vasopressors for persistent hypotension and continued assessment of volume status and tissue perfusion with at least two of the following methods: repeated focused examinations, measurement of CVP, measurement of Scv02, bedside cardiovascular ultrasound, and dynamic assessment of fluid responsiveness with passive leg raise or fluid challenges.

**Code Sepsis Outside of Emergency Department**

If a patient on 2W, 3W, 3N, DOU or ICU has a positive sepsis screen and either a systolic blood pressure less than 90 mmHg or a lactate greater than 4 mmol/L a rapid response will be called by the bedside nurse. That nurse who identifies code sepsis will also initiate a silent page to the code sepsis team and advise the treating provider that a code sepsis has been initiated for that patient. The following information will be included in the page: CODE SEPSIS, Unit, Room #, Patient MR Number. The code sepsis team includes the following: Sepsis Task Force Director, Director of Critical Care Nursing, ICU attending physician, ICU resident physician, Trauma Support Nurse, respiratory therapist, laboratory clerk, radiology technician, pharmacist on duty, nursing supervisor and sepsis data team. The ICU resident, ICU attending, trauma support nurse, respiratory therapist (rapid response therapist), phlebotomist (to be dispatched by lab clerk) and radiology technician will go urgently to the bedside of the patient. The pharmacist will stay in the pharmacy but be on alert to give priority to the code sepsis patient in preparing and dispensing medication. The nursing supervisor and ICU staff will determine if ICU bed needed, and if so, will work to expedite bed availability in the ICU. The TSN will retrieve the sepsis toolbox located in the ICU and bring this to the patient’s bedside. The resident and/or attending ICU physician will run the code sepsis and order blood cultures, antibiotics and IV fluids as indicated. The bedside nurse, with the assistance of the trauma support, nurse will carry out orders. Special efforts will be made to complete the following in an expedited fashion: 1) drawing blood cultures and a code sepsis panel 2) infusing broad spectrum antibiotics 3) administering 30 ml/kg crystalloid fluid bolus and starting a norepinephrine infusion if systolic blood pressure is < 90 mmHg after a single fluid bolus. If the initial lactate is greater than 4 mmol/L the ICU physician will order a repeat lactate that will be drawn two hours after the first lactate. If the repeat lactate is > 4 mmol/L, if the systolic blood pressure is less than 90 mmHg after a single fluid bolus, or if the ICU physician identifies another indication for intensive care, the patient will be transferred to the ICU. For persistent lactatemia or hypotension, the ICU team will continue management by applying vasopressors for persistent hypotension and continued assessment of volume status and tissue perfusion with at least two of the following methods: repeated focused examinations, measurement of CVP, measurement of Scv02, bedside cardiovascular ultrasound, and dynamic assessment of fluid responsiveness with passive leg raise or fluid challenges.

Reference: Draft of Policy from Sepsis Task Force, Richard Rutherford, MD
Abdominal Compartment Syndrome

Definition
- Sustained intra-abdominal pressure >20 mmHg that is associated with new organ dysfunction/failure (e.g. worsening respiratory failure or renal failure are the most common)
- Intra-abdominal hypertension is defined as pathologic intra-abdominal pressures ≥ 12mmHg
- Measured via the bladder, with maximal instillation volume of 25ml sterile saline; patient is to be supine, at end-expiration, without abdominal muscle contractions, transducer leveled at the mid-axillary line (if equivocal, check abdominal compartment pressure after paralysis with vecuronium)
- Abdominal perfusion pressure = Mean arterial pressure – intra-abdominal pressure (APP=MAP-IAP); a goal of APP>60mmHg has been associated with improved survival in Abdominal Compartment Syndrome
- Grading system:  Grade I: 10-15 cm H$_2$O; Grade 2: 16-25 cm H$_2$O; Grade III: 26-34 cm H$_2$O; Grade IV: >34 cm H$_2$O

Clinical Presentation
- Distension of the abdomen + elevated peak airway pressures/decreasing lung volumes with oliguria or hypotension; may be subtle, need to have a high index of suspicion

Risk Factors
- Acidosis (pH< 7.2)
- Hypothermia (core temperature < 33°C)
- Polytransfusion (>10U packed red blood/24 h)
- Coagulopathy (platelets < 55,000/mm$^3$ or PTT≥ 2x ULN or PT < 50% or international standardized ratio>1.5)
- Sepsis
- Bacteremia
- Intra-abdominal infection/abscess
- Peritonitis
- Liver dysfunction/cirrhosis with ascites
- Mechanical ventilation
- Use of positive end expiratory pressure (PEEP) or the presence of auto-PEEP
- Pneumonia
- Abdominal surgery, especially with tight fascial closures
- Massive fluid resuscitation (>5 L colloid or crystalloid/24 h)
- Gastroparesis/gastric distention/ileus
- Volvulus
- Hemoperitoneum/pneumoperitoneum
- Major burns
- Major trauma
- High body mass index (>30)
- Intra-abdominal or retroperitoneal tumors
- Prone positioning
- Massive incisional hernia repair
- Acute pancreatitis
- Distended abdomen
- Damage control laparotomy
- Laparoscopy with excessive inflation pressures
- Peritoneal dialysis

Treatment
- Medical management to reduce abdominal compartment pressures
  - Improve abdominal wall compliance (e.g. sedation, paralysis, improved body positioning—flattening the bed and putting it into reverse Trendelenberg to maintain head of bed > 30°)
  - Evacuate intra-luminal contents (e.g. nasogastric decompression, rectal decompression/enemas, gastro-/colo-prokinetic agents)
  - Evacuate abdominal fluid collections (e.g. Paracentesis)
  - Correct positive fluid balance/third spacing into the peritoneal cavity (e.g. fluid restriction, diuretics including Mannitol, colloids including albumin, hemodialysis)
- Surgical decompression with wound vacuum placement is the last resort for Abdominal Compartment Syndrome refractory to medical management

## APACHE II Score Form

<table>
<thead>
<tr>
<th>Physiologic Variable</th>
<th>High Abnormal Range</th>
<th>Low Abnormal Range</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+4</td>
<td>+3</td>
</tr>
<tr>
<td></td>
<td>+2</td>
<td>+1</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>+1</td>
</tr>
<tr>
<td></td>
<td>+2</td>
<td>+3</td>
</tr>
<tr>
<td></td>
<td>+4</td>
<td>+5</td>
</tr>
<tr>
<td>Temperature (°C)</td>
<td>≥41</td>
<td>35-40.9</td>
</tr>
<tr>
<td></td>
<td>38.5-36.9</td>
<td>36-36.4</td>
</tr>
<tr>
<td></td>
<td>34-35.9</td>
<td>32-35.5</td>
</tr>
<tr>
<td></td>
<td>30-31.9</td>
<td>&lt;29.9</td>
</tr>
<tr>
<td>Mean arterial pressure (mm Hg)</td>
<td>&gt;160</td>
<td>130-159</td>
</tr>
<tr>
<td></td>
<td>110-129</td>
<td>70-109</td>
</tr>
<tr>
<td></td>
<td>50-59</td>
<td>&lt;49</td>
</tr>
<tr>
<td>Heart rate (ventricular response)</td>
<td>&gt;180</td>
<td>140-179</td>
</tr>
<tr>
<td></td>
<td>110-139</td>
<td>70-109</td>
</tr>
<tr>
<td></td>
<td>55-69</td>
<td>&lt;38</td>
</tr>
<tr>
<td>Respiratory Rate (non-ventilated or ventilated)</td>
<td>≥50</td>
<td>35-49</td>
</tr>
<tr>
<td></td>
<td>25-34</td>
<td>12-24</td>
</tr>
<tr>
<td></td>
<td>10-11</td>
<td>6-9</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Oxygenation</td>
<td>≥500</td>
<td>350-499</td>
</tr>
<tr>
<td>PaO2</td>
<td>200-349</td>
<td>&lt;200</td>
</tr>
<tr>
<td>a) FIO2 &gt;0.5 record PaO2</td>
<td>≥70</td>
<td>61-70</td>
</tr>
<tr>
<td></td>
<td>55-60</td>
<td>&lt;55</td>
</tr>
<tr>
<td>Artidal pH</td>
<td>≥7.7</td>
<td>7.6-7.69</td>
</tr>
<tr>
<td></td>
<td>7.5-7.59</td>
<td>7.4-7.49</td>
</tr>
<tr>
<td></td>
<td>7.3-7.32</td>
<td>7.2-7.24</td>
</tr>
<tr>
<td></td>
<td>7.1-7.15</td>
<td>&lt;7.15</td>
</tr>
<tr>
<td>Serum Sodium (mM/L)</td>
<td>&gt;180</td>
<td>160-179</td>
</tr>
<tr>
<td></td>
<td>155-169</td>
<td>150-164</td>
</tr>
<tr>
<td></td>
<td>130-149</td>
<td>120-129</td>
</tr>
<tr>
<td></td>
<td>113-119</td>
<td>&lt;110</td>
</tr>
<tr>
<td>Serum Potassium (mM/L)</td>
<td>&gt;7</td>
<td>6-8</td>
</tr>
<tr>
<td></td>
<td>5.5-5.9</td>
<td>3-3.4</td>
</tr>
<tr>
<td></td>
<td>2.5-2.9</td>
<td>&lt;2.5</td>
</tr>
<tr>
<td>Serum Creatinine (mg/100mL)</td>
<td>≥3.5</td>
<td>2-3.4</td>
</tr>
<tr>
<td></td>
<td>1.5-1.8</td>
<td>0.5-1.4</td>
</tr>
<tr>
<td>Hemoacid (%):</td>
<td>260</td>
<td>50-55.9</td>
</tr>
<tr>
<td></td>
<td>45-49.9</td>
<td>30-45.9</td>
</tr>
<tr>
<td></td>
<td>20-25.9</td>
<td>&lt;15</td>
</tr>
<tr>
<td>Blood Count</td>
<td>≥40</td>
<td>20-39.9</td>
</tr>
<tr>
<td>White Cell Count (10/mm3 in 1000s)</td>
<td>15.19</td>
<td>3-14.9</td>
</tr>
<tr>
<td>Glasgow Coma Scale :</td>
<td>62</td>
<td>41-51.9</td>
</tr>
<tr>
<td>Total Acute Physiology Score (APS):</td>
<td>Sum of the 12 individual variable points =</td>
<td></td>
</tr>
</tbody>
</table>

### *Glasgow Coma Scale*

<table>
<thead>
<tr>
<th>Age Points</th>
<th>Chronic Health Points</th>
<th>APACHE II Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Points</td>
<td>A = APS points</td>
<td>B = Age points</td>
</tr>
<tr>
<td></td>
<td>C = Chronic Health Points</td>
<td></td>
</tr>
<tr>
<td></td>
<td>A =</td>
<td>B =</td>
</tr>
<tr>
<td></td>
<td>C =</td>
<td>APACHE II Score</td>
</tr>
<tr>
<td></td>
<td>(SUM OF A+B+C)</td>
<td></td>
</tr>
</tbody>
</table>

### References:
Website used to calculate APACHE II Score: [http://www.sfar.org/scores2/apache22.html](http://www.sfar.org/scores2/apache22.html)
INFECTIOUS DISEASE

Workup of Fever in the ICU

Definition of Fever
- >38.3°C Celsius or 101°F Fahrenheit considered a fever in all ICU patients
- >38°C Celsius or 100.4°F Fahrenheit considered a fever in immunocompromised patients
- Immunocompromised patients may not mount a fever at all in the face of infection
- Patients may have fever from non-infectious causes

Common Etiologies of Fever in the ICU (not an exhaustive list)
- Ventilator-Associated Pneumonia/Community-Acquired Pneumonia
- Bacteremia / endocarditis
- Fungemia
- Urinary Tract Infections, usually catheter-related
- Indwelling catheters / central venous catheters / arterial catheters / foreign bodies (e.g. pacemaker wires, orthopedic hardware, etc.)
- Skin and Soft Tissue Infections
- Sinusitis (in the face of an NG-tube)
- C. diff colitis
- Acalculous cholecystitis
- Viruses (e.g. CMV)
- Less common ‘silent’ sources of infection: otitis media, decubitus ulcers at the sacrum or the back of the head, perineal or perianal abscesses, undetected retained tampons, others
- Non-infectious causes include drug fever, intracranial hemorrhage, venous thromboembolism, pancreatitis

“Infection” versus “Colonization”
- “Colonization” is microbial presence without causing infection

Blood cultures
- Amount of blood drawn is a very key component to adequacy of blood cultured 20-30ml of blood from a single site into 2 bottles is considered 1 blood culture
- Drawing 3-4 blood cultures in the first 24 hours of onset of fever (all cultures with adequate amount of blood) has the highest yield for detection of bacteremia
- All attempts should be made to draw the first set of blood cultures prior to initiation of antimicrobial therapy
- Suggest AGAINST obtaining blood culture from a peripheral IV at the time of insertion, as this leads to high rate of contamination
- Additional blood cultures should be drawn thereafter only when there is clinical suspicion of continuing or recurrent bacteremia or fungemia, 48-96 hours after initiation of appropriate therapy
- If a patient has a vascular catheter, one blood culture may be drawn from that catheter while the other is to be drawn via venipuncture; the catheter site should be the newest catheter site (<3 days duration is ideal)
Concern for Indwelling Line Infections
(see “Prevention of Catheter-Related Blood Stream Infections” section, page 158)

- Gold standard of workup is to remove the line and send the tip (5-7cm intracutaneous segment if possible) for “semi-quantitative culture” (>10^5 organisms highly suspicious for catheter infection) (“semi-quantitative culture” must be ordered specifically for it to happen)
- High suspicion for catheter-related blood stream infection if the blood culture from the catheter becomes positive ≥ 120 minutes sooner than a venipuncture culture, with the same organism being recovered from both
- Recommend AGAINST routinely culturing lines if no clinical suspicion for infection
- Daily examination of the catheter insertion site is recommended, though most cases of catheter-related blood stream infections do not have purulence at the insertion site
- Tunneled catheters should be removed if evidence of embolic phenomenon, vascular compromise, or septic shock (if no other source found)
- For central venous catheters, if catheter-related bloodstream infection is considered likely, the catheter(s) should be removed and, if needed, replaced at a new site

Concern for Pneumonia

- See VAP/HAP/HCAP in the Pulmonary section
- Organisms that, if identified, nearly always represent pathogens: *Legionella, Chlamydia, M. tuberculosis, Rhodococcus equi*, influenza virus, respiratory syncytial virus, parainfluenza virus, *Strongyloides, Toxoplasma gondii, P. jiroveci, Histoplasma capsulatum, Coccidioides immitis, Blastomyces dermatitidis, and Cryptococcus neoformans*.
- Organisms that, if recovered, rarely if ever represent pathogens: enterococci, viridans streptococci, coagulase-negative staphylococci, and *Candida*
- Organisms that may be pathogenic or may only colonize the respiratory tract: *Pseudomonas aeruginosa, Enterobacteriaceae, S. pneumoniae, S. aureus, and Haemophilus influenzae*
- Recommend AGAINST routinely culturing sputum if no clinical suspicion of infection
- Thoracentesis for Pleural Effusions
  - Not indicated in every patient with a pleural effusion, particularly if there is not enough fluid to safely aspirate using ultrasound guidance
  - Indications:
    - Effusion with adjacent pulmonary infiltrate
    - Effusion with suspicion for tuberculosis
    - Possible contamination of the pleural space by surgery, trauma, fistula

Concern for Stool Pathogen

- By far the most common enteric cause of fever in the ICU is *Clostridium difficile*
  - Suspected in any patient with fever or leukocytosis and diarrhea who received an antibacterial agent or chemotherapy within 60 days before the onset of the diarrhea
  - *C. difficile* accounts for 10–25% of all cases of antibiotic-associated diarrhea
  - Stool for *C. dif* toxins A and B are to be sent in 3 separate samples on 3 separate days
- Other organisms that can cause fever and diarrhea include *Salmonella, Shigella, Campylobacter jejuni, Aeromonas, Yersinia, Escherichia coli, Entamoeba histolytica*, and multiple viruses
  - Stool for routine culture can usually be sent x 1
  - Stool for Ova and Parasites should not routinely be checked unless the patient is HIV positive, was admitted with diarrhea, or is part of an outbreak investigation
Concern for Urinary Tract Infection
- Usually is catheter-related, usually represents colonization and is rarely symptomatic
- Urine sample from the catheter port (NOT from the bag) should be obtained, with concomitant Urinalysis with Microscopy
- Refrigerate specimens that will not be processed for >1 hour
- Cultures from catheterized patients showing >10^3 colony forming units (cfu)/mL represent true bacteriuria or candiduria; however, true bacteriuria or candiduria, even in present, are not often the cause of a patient’s fever. Even if they are present, continue to rule out other causes of infection

Concern for Sinusitis
- Highest risk in those that are nasotracheally intubated (33% incidence after 7 days)
- Difficult to diagnose; even if present, is rarely the cause of sepsis
  - Purulent nasal discharge present only in 25% of cases
  - Outpatient criteria often unreliable in the ICU:
    - ≥ 7 days of Either two major criteria (cough, purulent nasal discharge) or one major and two minor criteria (headache or earache, facial or tooth pain, fever, malodorous breath, sore throat, wheezing)
  - CT Scan of the nasal sinuses is often the first step towards diagnosis
- Gram negative rods (particularly Pseudomonas aeruginosa) account for 60% of cases
- Gram positive cocci (particularly S. aureus and Coag negative Staph account for 33%)
- Fungi account for 5-10%
- Infections are often polymicrobial
- If empiric antibiotic therapy + removal of foreign body / obstruction + saline or neosynephrine spray is not effective, sinuses should be aspirated under aseptic conditions

Post-Operative Fever
- Surgical wounds should be examined daily (with or without fever)
- High level of suspicion is to be maintained for DVT, PE, superficial thrombophlebitis
- Workup in the first 72 hours post-op may include
  - Chest X-ray (not mandatory)
  - Blood cultures (not mandatory)
  - Urine culture (not mandatory, but suggested for febrile patients with indwelling catheters for >72 hours)

Surgical Site Infections (SSIs) (rare until > 4 days post-operative)
- If there is suspicion for infection, the incision should be opened and cultured
- There is generally no benefit to antibiotics, as long as the infected site is adequately drained
- Early (<2 days) SSI with signs of systemic infection raises suspicion for Strep or Clostridium
  - Check wound gram stain; if positive, drain wound and start penicillin or clindamycin
- For fever > 4 days after surgery with SSI with systemic signs of infection (T>38.5°C or pulse > 100 or erythema diameter > 5cm from incision with induration or any necrosis):
  - Clean wound, head, neck or extremity: start cefazolin, oxacillin, or clindamycin
  - For all other categories of procedures, the indigenous polymicrobial aerobic-anaerobic flora of the organ or tissue being operated on are the most common pathogens of surgical site infection (e.g. GI or female GU tract: start ampicillin/sulbactam or fluoroquinolone AND clindamycin)
  - For concern for hospital-acquired organism (e.g. MRSA), consider empiric vancomycin
CNS Infections
- Head CT followed by lumbar puncture in patients with new fever and new neurological findings, recent neurosurgery or indwelling neurosurgical devices, head trauma with CSF leak, or possible parameningeal focus

Non-Infectious Causes of Fever (generally diagnoses of exclusion)
- Drug fever
  - Most often attributed to antimicrobials (especially Beta-lactam drugs), anti-epileptic drugs (especially phenytoin), antiarrhythmics (especially quinidine and procainamide), and antihypertensives (methyldopa), HMG-CoA Reductase Inhibitors
  - May take >7 days to resolve after stopping the offending agent
- Malignant hyperthermia
  - Caused by succinylcholine or inhalational anesthetics (halothane most commonly)
  - Leads to dysregulation of cytoplasmic calcium regulation, leading to intense muscle spasms, fever, elevated Creatinine Kinase (CPK)
  - Usually immediate after exposure; may be delayed up to 24 hours in presence of steroids
- Substance withdrawal: alcohol, benzodiazepine, opiate, barbiturate

Medical conditions associated with fever:
- Acute myocardial infarction
- Adrenal insufficiency
- Blood product transfusion
- Cytokine-related fever
- Dressler syndrome (pericardial injury syndrome)
- Fat emboli
- Fibroproliferative phase of Acute Respiratory Distress Syndrome (ARDS)
- Gout
- Heterotopic ossification
- Immune reconstitution inflammatory syndrome
- Intracranial bleed
- Jarisch-Herxheimer reaction
- Pancreatitis
- Pulmonary infarction
- Pneumonitis without infection
- Stroke
- Thyroid storm
- Transplant rejection
- Tumor lysis syndrome
- Venous thrombosis

Empiric Treatment of Fever
- “When clinical evaluation suggests that infection is the cause of fever, consideration should be given to administering empirical antimicrobial therapy as soon as possible after cultures are obtained, especially if the patient is seriously ill or deteriorating.”
- “Initial empirical antibiotic therapy should be directed against likely pathogens, as suggested by the suspected source of infection, the patient risk for infection by multidrug-resistant pathogens, and local knowledge of antimicrobial susceptibility patterns.”

Antibiotic Use in the ICU

General Overview

Often competing goals of Antimicrobial Therapy in the ICU:
- Initiating effective antimicrobial therapy early to minimize infection-related morbidity and mortality…
- …while minimizing antimicrobial use to reduce the incidence of bacterial resistance (“Antibiotic Stewardship”)   

Improper Use of Antibiotics in the ICU
- Using antimicrobials for indications that do not require antibiotics
- Excessive duration of use for treatment or prophylaxis
- Selection of inadequate empiric treatment for patients with sepsis
  o Treatment with antibiotics that do not cover the infecting organism is akin to not starting antibiotics at all
  o Inappropriately chosen empiric antibiotics for blood stream infections or ventilator associated pneumonia increases absolute mortality rates by anywhere from 14% to over 54% (relative odds of death from inappropriately chosen antibiotics is 1.5 to 4.25) versus appropriately chosen empiric antibiotics
  o The most common mistake is the underestimation of the degree of resistance of the infecting organism (risk factors for multi-drug resistant pathogens are as follows: increasing length of hospital stay, recent antibiotic use, incidence of certain resistant pathogens within the hospital or ICU, current nosocomial epidemics, and patient history of multi-drug resistant organism).
- Inappropriate dosing
  o Not dosing for degree of renal or hepatic insufficiency
  o Not giving high-dose for sites that need high dose (e.g. Quinolones, Penicillins, Vancomycin, etc.) (for CNS, Osteomyelitis, Lung, Heart Valves)

Empiric Therapy Guidelines
- Initiated based on suspicion that there is infection present.
  o Labs: elevated WBC Count, neutrophilia, bandemia (“Left Shift”), neutropenia, low WBC, positive cultures, elevated C-reactive Protein (CRP), elevated pro-calcitonin
  o Radiology: Chest X-Ray, Symptom-specific radiographic studies/CTs/MRIs
- High index of suspicion is needed for those patients with cirrhosis, cancer, patients on chemotherapy or on steroids or other immunosuppressive agents, where the usual markers of infection listed above may not be abnormal/out of range. Serial lactic acid levels may be beneficial in cirrhotics and others.
- Appropriate empiric therapy should be administered within 1 hour of the diagnosis of sepsis, and as soon as possible to a hemodynamically unstable patient.
- Antibiotics are to be chosen with appropriate spectrum and penetration of the suspected site of infection
- Consider pathogens that the patient may be colonized with (look at prior culture results)
- Local susceptibility patterns are key to guiding therapies (see “VCMC Antibiogram”)
- “Source control” up front is paramount to successful treatment of many infections (e.g. draining abscesses, removing a source of necrotizing soft tissue infection, etc.)
## Pathogens Implicated in Selected Infections, with EMPIRIC Treatment Options for SEVERE ICU ONLY

<table>
<thead>
<tr>
<th>Site</th>
<th>Community-Acquired Pathogens</th>
<th>Suggested Regimen</th>
<th>At Risk for MDR Pathogen</th>
<th>Suggested Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genitourinary</td>
<td>GNR, Enterococcus</td>
<td>Quinolone or 3rd gen cephalosporins +/- Enterococcus</td>
<td>Pseudomonas, MDR GNR, Enterococcus</td>
<td>Anti-pseudomonal +/- Enterococcus Rx</td>
</tr>
<tr>
<td>Cellulitis</td>
<td>MSSA, MRSA, strep Diabetics: polymicrobial</td>
<td>Vancomycin</td>
<td>MSSA, MRSA, MDR GNR, candida, Aspergillus</td>
<td>Vanco +/- anti-pseudomonal +/- anti-fungal (p129)</td>
</tr>
<tr>
<td>Meningitis</td>
<td>Neisseria, Strep pneumonia, H. flu.</td>
<td>Ceftriaxone or Cefotaxime +/- Amoxicillin for Listeria</td>
<td>Venticulostomy-related: Staph aureus, Staph epi, Group A strep, P. aeruginosa, MRSA, Enterococcus</td>
<td>Vanco +/- anti-pseudomonal +/- anti-fungal (see page 160)</td>
</tr>
<tr>
<td>Intra-abdominal/hepato-biliary</td>
<td>Polymicrobial including anaerobes</td>
<td>Amp/gent/metro, or levaquin/metro plus pip/taz</td>
<td>Polymicrobial, MDR GNR, fungus</td>
<td>Anti-pseudomonal +/- anti-fungal</td>
</tr>
<tr>
<td>Native Valve Endocarditis</td>
<td>No illicit drugs</td>
<td>Viridans strep, Staph, Enterococcus, Staph</td>
<td>(PCN or Ampicillin) + (Nafcin or Oxacillin) + Gentamicin</td>
<td>All therapies listed for endocarditis are empiric therapies; antimicrobials are to be tailored when the infecting agent is identified and MICs are known.</td>
</tr>
<tr>
<td>Prosthetic Valve Endocarditis</td>
<td>Staph epi, viridans strep, Staph aureus, Enterococcus</td>
<td>Vanco 15mg/kg q 12 + Gent 1 mg/kg q 8 + Rifampin 600q 24</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

‡ pregnancy (3rd trimester), cancer, HIV, organ transplant recipients, steroids, other debilitating disease, age >50, newborns

≡ Do not double-cover anaerobes;

Abbreviations: PCN, penicillin; Gent, gentamicin; Vanco, vancomycin; Metro, metronidazole; pip/taz, piperacillin/tazobactam

### Selected Organisms, and Antimicrobials Generally Active Against Them

<table>
<thead>
<tr>
<th>Organism</th>
<th>Active Antimicrobial Agents</th>
<th>Alternative Antimicrobial Agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staph, MSSA</td>
<td>Nafcillin, Cefazolin, Ampicillin/Subtactam</td>
<td>PO: Cephalexin, Amp/Subtactam, Dicloxacillin</td>
</tr>
<tr>
<td>Staph, MRSA</td>
<td>Vancomycin, Linezolid (NOTE: do NOT use linezolid for catheter-related blood stream infections)</td>
<td>Daptomycin (does NOT treat lung) Quinupristin/Dalfopristin.; PO: Doxycycline, Trimethoprim/Sulfamethoxazole, Clindamycin</td>
</tr>
<tr>
<td>Enterococcus</td>
<td>Sensitive: Ampicillin, Quinolones (maybe)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Resistant to Ampicillin: Vancomycin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Resistant to Vancomycin (VRE): Linezolid</td>
<td>Quinupristin/Dalfopristin, Daptomycin, Tigecycline</td>
</tr>
<tr>
<td>Atypical and Legionella</td>
<td>Macrolides (erythro misses H. flu; Azithro/ Clarithro don’t), Quinolones</td>
<td>Doxycycline (gets Q fever)</td>
</tr>
<tr>
<td>Anaerobes</td>
<td>Metronidazole, Clindamycin, Ampicillin/Subtactam, Piperacillin/Tazobactam</td>
<td>Tigecycline, Penicillins, Carbapenems (should be reserved for refractory infections)</td>
</tr>
<tr>
<td>Pseudomonas †</td>
<td>Beta-Lactams Piperacillin/Tazobactam, Cefazidime, Cefepime</td>
<td>Non-Beta Lactams Aminoglycosides, OR Quinolones</td>
</tr>
<tr>
<td></td>
<td>Carbapenems (NOT ertapenem), alternative for the Beta-Lactams (should be reserved for refractory infections)</td>
<td></td>
</tr>
</tbody>
</table>

† when double-covering *Pseudomonas*, choose one beta-lactam and one non-beta lactam

### Difficult-to-Reach Anatomical Sites

<table>
<thead>
<tr>
<th>Site</th>
<th>Effective Antimicrobials</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNS</td>
<td>All penicillins, cefuroxime, 3rd and 4th generation cephalosporins, doxycycline, trimethoprim/ sulfamethoxazole, metronidazole, meropenem, imipenem, amphotericin, fluconazole, voriconazole. NOTE: Vancomycin only penetrates inflamed meninges (goal trough 15-20, see page 156).</td>
</tr>
</tbody>
</table>

† Ceftazidime is preferred over piperacillin/tazobactam for CNS *Pseudomonas* infections if sensitive to Ceftazidime

‡ Imipenem is not preferred for CNS infections due to increased risk of seizures

Modification of Empiric Coverage After 48 to 72 hours (“De-escalation”)
- Narrowing the spectrum of antibiotics used should occur in stepwise fashion over the first 24 to 72 hours of therapy, based on:  
  o Clinical condition of the patient  
  o Culture Results and source of infection  
    ▪ Beware of False Negatives if the patient had already been started on antibiotics  
    ▪ Beware of False Positive Gram Stains, particularly for sputum specimens

Duration of Antimicrobial Therapy
- Depends on many factors, including the integrity of the host’s immune system, nutritional status, bacterial type, and location of infection, and decided on a case-by-case basis

<table>
<thead>
<tr>
<th>Infection</th>
<th>Usual Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventilator Associated Pneumonia</td>
<td>8 days</td>
</tr>
<tr>
<td>Ventilator Associated Pneumonia caused by Non-fermenting Gram (-) rod</td>
<td>15 days</td>
</tr>
<tr>
<td>(Acinetobacter spcc., Flavobacterium spcc., Pseudomonas aeruginosa,</td>
<td></td>
</tr>
<tr>
<td>Burkholderia cepacia, Burkholderia pseudomallei, Stenotrophomonas maltophilia)</td>
<td></td>
</tr>
<tr>
<td>Bacteremia (see specific recommendations for organism)</td>
<td>7 days</td>
</tr>
<tr>
<td>Meningitis (see specific recommendations for organism)</td>
<td></td>
</tr>
<tr>
<td>Osteomyelitis, Endocarditis (see specific recommendations for organism)</td>
<td></td>
</tr>
<tr>
<td>Septic Shock</td>
<td>7-10 days</td>
</tr>
</tbody>
</table>

Procalcitonin and Duration of Antimicrobial Therapy
- Procalcitonin is released in response to a body’s exposure to bacterial antigens or toxins  
  o Level of elevation directly correlated with severity of bacterial infection  
  o Rises 6-12 hours after symptom onset in bacterial infections  
  o Decreases 50% per day once a bacterial infection is under control  
- Procalcitonin is suppressed by exposure to cytokines activated during vital infections (Ifn-γ)  
- 2011 systematic review of >4,400 adult patients found no difference in mortality or morbidity between the procalcitonin guided treatment groups and control treatment groups despite a reduction in antibiotic use of roughly 35% across the spectrum of clinical settings  
- Recommendations vary based on clinical scenario:

<table>
<thead>
<tr>
<th>High Acuity Infection in the ICU (Sepsis or Pneumonia)</th>
<th>Procalcitonin Level (mcg/L)</th>
<th>Recommendation for Antibiotics</th>
<th>Overruling the Algorithm</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial Level</td>
<td>&lt;0.25</td>
<td>Strongly discouraged</td>
<td>Consider antibiotics if patient is clinically unstable</td>
<td>5 randomized clinical trials, showed 32% reduction in antibiotic duration with no change in clinical outcome</td>
</tr>
<tr>
<td></td>
<td>0.25-0.49</td>
<td>Discouraged</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.5-1</td>
<td>Encouraged</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;1</td>
<td>Strongly encouraged</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow-up Levels q 1-2 d</td>
<td>&lt;0.25 or drop by &gt;90%</td>
<td>Stopping strongly encouraged</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.25-0.49 or drop by &gt;80%</td>
<td>Stopping encouraged</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.5-1</td>
<td>Stopping discouraged</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;1</td>
<td>Stopping strongly discouraged</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Return to Table of Contents
### Moderate Acuity Respiratory Infection in the ED or Hospital

<table>
<thead>
<tr>
<th>Procalcitonin Level (mcg/L)</th>
<th>Recommendation for Antibiotics</th>
<th>Overruling the Algorithm</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.1</td>
<td>Strongly discouraged</td>
<td>Consider antibiotics if patient is clinically unstable, immunosuppressed, has a high Pneumonia Severity Index, or strong evidence of bacterial infection</td>
<td>6 randomized clinical trials, showed 18% reduction in antibiotic initiation and 34% reduction in duration of antibiotic use with no change in clinical outcome</td>
</tr>
<tr>
<td>0.1-0.24</td>
<td>Discouraged</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.25-0.5</td>
<td>Encouraged</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;0.5</td>
<td>Strongly encouraged</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Follow-up Levels q 2-3 d</th>
<th>Recommendation for Antibiotics</th>
<th>Overruling the Algorithm</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.1</td>
<td>Stopping strongly encouraged</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.1-0.24</td>
<td>Stopping encouraged</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.25-0.5</td>
<td>Stopping discouraged</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;0.5</td>
<td>Stopping strongly discouraged</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Respiratory Infection Primary Care Setting

<table>
<thead>
<tr>
<th>Procalcitonin Level (mcg/L)</th>
<th>Recommendation for Antibiotics</th>
<th>Overruling the Algorithm</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.1</td>
<td>Strongly discouraged</td>
<td>Recommend antibiotics if patient is clinically unstable, has strong evidence of pneumonia, advanced COPD, or needs hospitalization</td>
<td>2 randomized clinical trials, showed 57% reduction in the initiation of antibiotics with no change in clinical outcome</td>
</tr>
<tr>
<td>0.1-0.24</td>
<td>Discouraged</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.25-0.5</td>
<td>Encouraged</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;0.5</td>
<td>Strongly encouraged</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Blood cultures positive: Empiric Antibiotics vs. Watch and Wait?**
- Gram negative rods: Start treatment (almost never a contaminant)
- Gram positive rods, Gram positive cocci: *may* be a contaminant
  - If unstable, start antibiotics
  - If cirrhotic, cancer patient, chronic dialysis, on chronic prednisone, indwelling catheter, etc., repeat blood cultures and start empiric antibiotics.
  - If clinically stable and none of the above risk factors, it is ok to observe for signs and symptoms of infection and repeat the blood cultures

**Issues to Consider in Patients Who Are Failing Seemingly Adequate Antimicrobial Therapy**
- Undrained infected material (abscess, devitalized tissue)
  - (lack of “source control”)
- Recurrent aspiration (pneumonia)
- Neutropenia
- Infected Prosthetic Material
  - Removable: Intravascular catheters, bladder catheter
  - Permanent: Orthopedic hardware, vascular grafts
- High in vivo innoculum (endocarditis, abscess)
- Poor tissue penetration caused by inadequate microcirculation
- Superinfection with new pathogens (fungus, multi-drug resistant bacteria caused by lines/catheters, TPN and antibiotic selection pressure)
- Evolved resistance of original pathogen to original antimicrobial(s)
- Inadequate antimicrobial dosing
- Antagonistic antimicrobial combination
Time-Dependent vs. Concentration-Dependent Antibiotics

- Concentration-Dependent Pharmacodynamics (e.g. Aminoglycosides, Quinolones)
  - Killing of bacteria depends on maximal concentration achieved
  - Quantified by AUC:MIC ratio or Cmax: MIC ratio (MIC=minimum inhibitory concentration, AUC=area under the curve, Cmax=maximal drug concentration)
  - Optimal dosing is at higher doses over longer intervals
- Time-Dependent Pharmacodynamics (e.g. Beta-lactam, glycopeptide antibiotics)
  - Killing of bacteria depends on maintaining the serum concentration above the MIC for most (>50%) of the dosing interval
  - Optimal dosing is for smaller doses at more frequent intervals or by prolonged or continuous infusions
  - It is VCMC Policy to infuse the following antibiotics over three hours: Zosyn, Imipenem, Meropenem, Cefepime, and Ceftazidime

Specific Antibiotics for Specific Cases/Organisms

- MSSA (Methicillin-Sensitive *Staph aureus*) should be treated with a specific Staphylococcal medication (nafcillin, cefazolin or ampicillin/subactam), not vancomycin, as clinical cure rates and clearance of bacteria are both worse with vancomycin compared to these agents.
- See Multi-Drug Resistant Pathogens (page 167)

### Cidal or Static?

<table>
<thead>
<tr>
<th>Cidal</th>
<th>Static</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillins*</td>
<td>TMP/SMX</td>
</tr>
<tr>
<td>Cephalosporins</td>
<td>Clindamycin</td>
</tr>
<tr>
<td>Carbapenems</td>
<td>Linezolid</td>
</tr>
<tr>
<td>Monobactams</td>
<td>Macrolides</td>
</tr>
<tr>
<td>Vancomycin*, **</td>
<td>Chloramphenicol</td>
</tr>
<tr>
<td>Quinolones</td>
<td>Tetracyclines</td>
</tr>
<tr>
<td>Aminoglycosides</td>
<td>Tigecycline</td>
</tr>
<tr>
<td>Quinpristin/dalfopristin*, **</td>
<td></td>
</tr>
<tr>
<td>Daptomycin</td>
<td>* = bacteriostatic vs. enterococcus</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>**= bacteriostatic or slow bactericidal effect vs. S. aureus</td>
</tr>
</tbody>
</table>

What’s better, Static or Cidal? Cidal is theoretically better for meningitis, endocarditis, and gram negative bacteremia in neutropenia. A potential DOWN-side of Cidal antibiotics is greater endotoxin release and proinflammatory cytokine response. Clindamycin and, to a lesser degree, Linezolid, turn off toxin production and are theoretically helpful in Necrotizing Soft Tissue Infections and Severe Necrotizing Pneumonias.

### Strategies to Minimize Antibiotic Resistance

- Minimize use of Ceftazidime and, to a lesser extent, other 3rd generation Cephalosporins.
- Minimize use of broad spectrum antibiotics.
- Appropriate and expeditious “de-escalation” tailoring antibiotic regimen to culture results.
- Double-coverage of organisms known to develop resistance to mono-agent therapies (e.g. *Serratia, Pseudomonas, Acinetobacter, Citrobacter, Enterobacter*) may lead to organism eradication and less resistance problems for endemic flora of the institution (controversial)

References: Borrowed from the Society of Critical Care Medicine Board Review, 2007, Philip Barie, MD. Adapted from Antibiotic Stewardship with Aid of Procalcitonin Measurements, blog by Joseph Esherick, MD. Reviewed by Gail Simpson, MD.
**Ventura County Medical Center**

Inpatient and Emergency Room  
January 2012 - December 2012

<table>
<thead>
<tr>
<th>Gram negative organisms</th>
<th># Isolates Tested</th>
<th>Ampicillin</th>
<th>Ampicillin/Sulbactam</th>
<th>Piperacillin/Tazobactam</th>
<th>Ticarcillin/Clavulenate (NF)</th>
<th>Cefazolin</th>
<th>Cephalothin</th>
<th>Cefuroxime</th>
<th>Cefotaxime</th>
<th>Ceftriaxone</th>
<th>Cefepime</th>
<th>Aztreonam (ID)</th>
<th>Ertapenem (ID)</th>
<th>Imipenem (ID)</th>
<th>Meropenem (ID)</th>
<th>Amikacin (ID)</th>
<th>Gentamicin</th>
<th>Tobramycin</th>
<th>Ciprofloxacin</th>
<th>Levofloxacin</th>
<th>Trimeth/ Sulfa</th>
<th>Nitrofurantoin</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Escherichia coli</em></td>
<td>655</td>
<td>46</td>
<td>50</td>
<td>96</td>
<td>88</td>
<td>87</td>
<td>31</td>
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<td>91</td>
<td>86</td>
<td>86</td>
<td>66</td>
<td>98*</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em></td>
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<td>85</td>
<td>97</td>
<td>94</td>
<td>97</td>
<td>85</td>
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<td>95</td>
<td>95</td>
<td>97</td>
<td>95*</td>
<td>63*</td>
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<tr>
<td><em>Proteus mirabilis</em></td>
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<td>83</td>
<td>90</td>
<td>100</td>
<td>98</td>
<td>90</td>
<td>87</td>
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<td>92</td>
<td>81</td>
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<td>83</td>
<td>0</td>
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<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>81</td>
<td>0</td>
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<td>91</td>
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<td>90</td>
<td>96</td>
<td>85</td>
<td>81</td>
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</table>

*= urine isolates
### VCMC Antibiogram 2012: Gram Positive Organisms

<table>
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<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>MS Staph aureus</strong></td>
<td>255</td>
<td>27</td>
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<td>100</td>
<td>100</td>
<td>--</td>
<td>--</td>
<td>--</td>
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<td>98</td>
<td>87</td>
<td>100</td>
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<tr>
<td><strong>MR Staph aureus</strong></td>
<td>244</td>
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<td>0</td>
<td>0</td>
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<td>0</td>
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<tr>
<td><strong>Staph ( coag. neg.)</strong></td>
<td>47</td>
<td>11</td>
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<td>43</td>
<td>--</td>
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<td>42</td>
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<tr>
<td><strong>Strep. Pneumoniae</strong></td>
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<td>59</td>
<td>--</td>
<td>--</td>
<td>89</td>
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<td>85</td>
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<tr>
<td><strong>E. faecalis</strong></td>
<td>68</td>
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<td>100</td>
<td>100</td>
<td>100</td>
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<td>100</td>
</tr>
</tbody>
</table>

(--) Indicates organisms that may be susceptible but are not first or second line agents and therefore should be avoided

Susceptibility data does not discriminate between various routes of administration

[0%] Not all isolates were tested against every antibiotic listed due to intrinsic resistance

*Urine isolates** Not to be used alone (NF) = non-formulary (ID) = ID approval

Note: Susceptibility patterns cannot accurately be determined based on <20 isolates

Cystic fibrosis isolates are not included in this antibiogram (e.g. *P. aeru*, *H. influenzae*)

*Strep. pneumoniae* susceptibility is not broken down by site of infection e.g. pneumonia vs meningitis. In addition, comparison of penicillin susceptibility to intermediate penicillin susceptibility is not carried out due to the small number of isolates

Updates to the Antiobiograms are generally made on an annual basis, and are available on the Ventura County Medical Center Medical Staff Office website, Pharmacy Resources page, at http://www.vchca.org/hospitals/pharmacy-resources.
Vancomycin Protocol

Vancomycin Order Form (Adult)

Allergies (Reactions) ____________________________ Age _______ Sex _______ Ht _______ Wt _______ kg
Diagnosis ________________________ SCR _______ Clcr _______
Ideal body weight _______ kg

☐ Initiation of Vancomycin: Loading Dose (Use Actual Body Weight. Round dose to nearest 250 mg, not to exceed 2.5 grams per dose)

Step 1: ☐ Vancomycin loading dose 25 mg/kg = _________ mg IV x 1, to be given: DATE/TIME

Step 2:
☐ Mandatory Pharmacy Consultation required for patients with:
--- Changing volume of distribution (patients in septic shock, resolving septic shock or diuretic use).
--- Abnormal volume of distribution (pregnancy, morbidly obese, amputee or burn patients).
--- Poor renal function (hemodialysis, peritoneal dialysis or unstable renal function).
--- Concurrent nephrotoxic medication administration (ACE-inhibitors, acyclovir, aminoglycosides, amphotericin, diuretics, IV contrast, NSAIDs or vasopressors).
--- Patients with a normal calculated clearance but serum creatinine does not reflect estimated renal function (anuric patient with initial normal creatinine, patient with high creatinine but improving urine output with hydration or patients with muscle disease).

If Step 2 is checked, do NOT advance to Maintenance Dosing in Step 3.

Maintenance Dose: (Goal trough 15-20 mcg/mL) Round dose to nearest 250 mg, not to exceed 2 grams per dose

Step 3:
☐ Clcr > 70 mL/min Q 8 hours
Vancomycin 15 mg/kg = _________ mg IV q 8 h, Starting on: DATE/TIME
To be drawn: DATE/TIME

☐ Clcr 40-69 mL/min Q 12 hours
Vancomycin 15 mg/kg = _________ mg IV q 12 h, Starting on: DATE/TIME
To be drawn: DATE/TIME

☐ Clcr 20-39 mL/min Q 24 hours
Vancomycin 10 mg/kg = _________ mg IV q 24 h, Starting on: DATE/TIME
To be drawn: DATE/TIME

☐ Clcr 10-19 mL/min Q 48 hours
Vancomycin 10 mg/kg = _________ mg IV q 48 h, Starting on: DATE/TIME
To be drawn: DATE/TIME

☐ Clcr <10 mL/min Consult Pharmacy for maintenance dose.

USE ACTUAL BODY WEIGHT UNLESS OBSESE (Refer to reverse, reference page 2)

Labs:

Step 4:
☐ SCR daily with AM Labs for ________ consecutive days (for pts with unstable renal function or changing volume of distribution as in sepsis or resolving sepsis)
☐ SCR Q Monday, Wednesday, Saturday with AM Labs (for patients with stable renal function)

Vancomycin Dose Modification: (Goal trough 15-20 mcg/mL)

Modified Dose (Use Actual Body Weight. Round dose to nearest 250 mg, not to exceed 2 grams per dose)

Step 1: Vancomycin _________ mg IV Q _________ hrs, starting on: DATE/TIME
Trough level 30 min prior to _________ dose, to be drawn: DATE/TIME

Labs:

Step 2:
☐ SCR daily with AM Labs for ________ consecutive days (for pts with unstable renal function or changing volume of distribution as in sepsis or resolving sepsis)
☐ SCR Q Monday, Wednesday, Saturday with AM Labs (for patients with stable renal function)

Physician Signature ____________________________ ID# _______ Date _______ Time _______
RN Noted ____________________________ Date _______ Time _______

Return to Table of Contents
Vancomycin Order Form (Adult), Page 2

USE THIS PAGE FOR REFERENCE ONLY

In Obesity, use Adjusted Body Weight (ABW) for maintenance dosing when Actual Body Weight (Actual BW) > 120% of Ideal Body Weight (IBW).

\[
\text{IBW (male)} = 50 \text{ kg} + 2.3 \text{ kg/in for each in > 5ft} \\
\text{IBW (female)} = 45 \text{ kg} + 2.3 \text{ kg/in for each in > 5ft} \\
\text{Adjusted BW} = \text{IBW} + 0.4 \times (\text{Actual BW} - \text{IBW})
\]

How to calculate Creatinine Clearance

\[
Clr = \frac{(140 - \text{age}) \times \text{IBW weight (kg)}}{72 \times \text{Scr}} \times (0.85 \text{ if female})
\]

When to normalize Scr:
- If patient is ≤ 65 yrs and Scr < 0.8 mg/dL, use 0.8 mg/dL to calculate Clr.
- If patient is over 65 yrs and Scr < 1 mg/dL, use 1 mg/dL to calculate Clr.

Pharmacy Consultation for Subsequent Maintenance Dosing Indicated for the Following:
Most patients will follow the outlined maintenance dosing intervals (step 3). The patients that fall out of this maintenance dosing are the following type of patients:
- Situations with changing volume of distribution: Initial septic shock, resolving septic shock, or diuretic use.
- Situations with abnormal volume of distribution: Pregnancy, morbidly obese, amputee and burn patients.
- Renal failure patient’s on hemodialysis or peritoneal dialysis.
- Unstable renal function to include the use of other renally toxic medications such as: Aminoglycosides, NSAIDS, chemotherapy (platinum), amphotericin, diuretics, IV contrast or vaspressors.
- Serum creatinine does not reflect estimated renal function, for example: Anuric patient initially with low creatinine, or patient with high creatinine with improving urine output with hydration.
- Septic Shock and Meningitis, serious conditions requiring rapid achievement of desired trough of 15-20 mcg/mL.
- Patients where creatinine clearance may be overestimated: Amputee, muscle diseases, or morbidly obese where use of adjusted body weight is recommended.

Monitoring of Patients Receiving Vancomycin:

| Serum creatinine         | • In patients with serious infections or are high risk for the reasons indicated above (i.e. renal failure, obesity, septic shock, etc.), obtain serum creatinine daily.  
|                         | • In patients with stable renal function, recommend obtain serum creatinine 2-3 times per week. |
| Vancomycin Levels        | • Once therapeutic level is obtained, troughs should be ordered 2.3 times weekly.  
|                         | • Pharmacy consult is mandatory for patients with serious infection, changing clinical condition or changing renal function. |
|                         | • In patients at goal with stable renal function and stable clinical conditions, recommend repeat trough levels weekly. |
| Serum Albumin            | • Serum Albumin weekly Q Monday with AM Labs |

Vancomycin Dosage Modification: (Goal trough 15-20 mcg/mL)
All dosage adjustments will be cleared through the pharmacy. A dose modification is needed when patient is not within goal trough range of 15-20 or changes in the patient’s clinical status.

Infectious Disease Consultation: Indicated for patients with: endocarditis, meningitis, patients on long term outpatient vancomycin therapy.
Prevention and Treatment of Catheter-related Blood Stream Infections (CRBSI)

Definitions

- **Central venous catheter**: defined by the Centers for Disease Control as any catheter percutaneously inserted into a central vein (subclavian vein, internal jugular vein or femoral vein) and the tip lies close to the heart or one of the great vessels (aorta, superior vena cava, inferior vena cava, brachiocephalic vein, internal jugular or subclavian vein.

- **Primary catheter-related blood stream infection if:**
  - Bacteremia, fungemia or clinical sepsis with no other source of infection.
    - Recovery of certain microorganisms in multiple blood cultures, such as staphylococci, *Corynebacterium jeikeium*, *Bacillus* species, atypical mycobacteria, *Candida*, or *Malassezia* species, strongly suggest infection of an intravascular device.
  - Signs and symptoms of localized infection at the vascular insertion site.
  - The CVC has been used in the 48 hours preceding a blood stream infection.

Institute for Healthcare Improvement (IHI) Central Line Bundle

- **Hand hygiene**
  - Before and after palpating catheter insertion sites
  - Before and after manipulating, accessing or dressing a CVC
  - Before donning and after removing gloves

- **Maximal barrier precautions**
  - Includes wearing a cap covering all hair, mask covering the nose and mouth, sterile gown and sterile gloves
  - Relative risk reduction between 2.2-6.3 compared with controls

- **Chlorhexidine skin antisepsis**
  - Pinch wings on the chlorhexidine swab and hold the applicator down to allow the solution to saturate the pad. Prep area for at least 30 seconds.
  - Allow at least 2 minutes for the antiseptic solution to dry completely before the skin is punctured.

- **Optimal catheter site selection**
  - Subclavian vein may be the preferred site for non-tunneled catheters to minimize infection
    - Lower risk of vein thrombosis (0.5% vs. 1.9%) or arterial puncture (3.1-4.9% vs. 6.3-9.4%) with subclavian vein compared with internal jugular location
    - Higher risk of pneumothorax (1.5-3.1 vs <0.1-0.2), hemothorax (0.4-0.6 vs. negligible) and catheter malposition (9.3% vs 5.3%) with subclavian vein compared with internal jugular location
  - Femoral catheters have higher rates of infection, thrombosis and arterial puncture.
    - Both subclavian vein and internal jugular vein preferred over femoral vein insertions.

- **Daily review of line necessity**

Additional Interventions that are of proven benefit

- **Use of antimicrobial-impregnated catheters**
  - Chlorhexidine and sulfur sulfadiazine: relative risk reduction 0.21 and decreases direct medical costs by about $200 per catheter inserted if the rate of CRBSI is >2%
  - Minocycline and rifampin: may be more effective than chlorhexidine and sulfur sulfadiazine-impregnated catheters, but no head-to-head studies to date.

- **Avoid antibiotic ointments to catheter entry sites**

- **Cover all catheters with a wide transparent sterile dressing, assuring that the dressing is 100% adherent around the catheter to avoid bacterial migration to the catheter insertion site**

- **Sterile dressings should be dated legibly either on the dressing or electronically in the computerized medical record**

- **Avoid excessive use of stopcocks outside of pressure tubing**
Anyone utilizing a catheter port should thoroughly wash hands and don clean gloves prior to accessing or manipulating catheter port(s).

- Chlorhexidine patches
- Avoid insertion of new central venous catheters while the patient is actively bacteremic or fungemic if at all possible

**Interventions that are NOT beneficial**

- Catheter replacement at scheduled time intervals makes NO difference in terms of CRBSIs.
  - Routine scheduled line changes may be more harmful by increasing the likelihood of a procedure-related complication.
- In the setting of a suspected CRBSI or a tunnel infection, avoid replacement of a non-tunneled catheter over a guidewire.
  - The skin tract from the insertion site to the vein is usually the source of infection and remains colonized even after removal of the first CVC.
  - Exchange of a catheter over a guidewire is an acceptable solution for a malfunctional catheter or replacement of a cordis catheter with a triple lumen catheter

### Treatment of Catheter-Related Blood Stream Infections

<table>
<thead>
<tr>
<th>Complicated †</th>
<th>Uncomplicated ‡</th>
<th>Gram (-) bacilli</th>
<th>Candida</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Non-Tunneled catheter</strong></td>
<td><strong>Coag (-) Staph</strong></td>
<td><strong>Staph aureus</strong></td>
<td><strong>Enterococcus</strong></td>
</tr>
<tr>
<td>Remove catheter. Treat with antibiotics x 4-6 weeks; 6-8 weeks for osteomyelitis</td>
<td>Remove catheter. Treat with systemic antibiotics x 5-7 d; or if catheter retained, systemic antibiotics + antibiotic lock* x 10-14 days</td>
<td>Remove catheter. Treat with systemic antibiotics x ≥ 14 d</td>
<td>Remove catheter. Treat with systemic antibiotics x 7-14 d</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tunneled catheter</th>
<th><strong>Systemic antibiotics + antibiotic lock</strong> x 10-14 days, or remove catheter ¥</th>
<th>Remove catheter. Treat with antibiotics x 4-6 weeks €</th>
<th>May retain catheter and use systemic antibiotics x 7-14 d + antibiotic lock therapy* x 7-14 d ¥</th>
<th>Remove catheter. Treat with systemic antibiotics x 7-14 d</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Remove catheter. Treat with antibiotics x 4-6 weeks; 6-8 weeks for osteomyelitis ≡</td>
<td></td>
<td></td>
<td>Remove catheter. Treat with systemic antibiotics x 7-14 d</td>
</tr>
</tbody>
</table>

† Suppurative thrombo-phlebitis, endocarditis or osteomyelitis
‡ Uncomplicated means that bloodstream infection and fever resolve within 72 hours in a patient with no intravascular hardware and no evidence of endocarditis or suppurative thrombophlebitis and for S. aureus is also without active malignancy or immunosuppression
≡ For tunneled catheters, tunnel infection or port abscess may be treated with catheter removal and antibiotics x 7-10 days.
¥ Must remove catheters for clinical deterioration or persisting or relapsing bacteremia; work-up for complicated infection (i.e. endocarditis) and treat accordingly.
€ May consider for a shorter duration of antimicrobial therapy (i.e., a minimum of 14 days of therapy) if fever and bacteremia resolve within 72 h after initiation of appropriate antimicrobial therapy, patient not immunosuppressed, and no evidence of any metastatic infection (including negative TEE and other testing).
‡ For catheter salvage, systemic + antibiotic lock x 10-14d; if no response, remove catheter and rule out endocarditis/suppurative thrombophlebitis; if not present, treat with antibiotic x 10-14d.
* Antibiotic lock therapy is infusion of high concentration antibiotic directly into the catheter; specifics will not be discussed here.

Invasive Candidal Infections

“Candida Score” Assessment

The “Candida Score” helps to predict which patients are at risk for invasive fungal infections, infections that are often indolent and difficult to diagnose but may lead to significant morbidity and mortality. Patients with a high “Candida Score” are considered to be higher risk for fungemia.

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe sepsis</td>
<td>2 points</td>
</tr>
<tr>
<td>Multifocal Candida colonization</td>
<td>1 point</td>
</tr>
<tr>
<td>Surgery on ICU admission</td>
<td>1 point</td>
</tr>
<tr>
<td>Total Parenteral Nutrition</td>
<td>1 point</td>
</tr>
</tbody>
</table>

- Score > 2.5: consider antifungal treatment for invasive candidal infection. (Sensitivity 81%, Specificity 74%)
- Drawbacks: Relies on weekly multifocal cultures (tracheal, pharyngeal, gastric and urine) which is not routinely done in our ICU and may not be cost effective
- No other scoring system has been prospectively proven to accurately predict invasive fungal infections (Crit Care Med 2009; 37: 1587.)

*albicans vs. Non-albicans* Candidemia Risk Factors

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Odds Ratio for developing Non-albicans Candidemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluconazole Exposure</td>
<td>11.6 Odds Ratio [2.2-58 95% confidence interval]</td>
</tr>
<tr>
<td>Central Venous Catheter</td>
<td>1.95 Odds Ratio [1.1-3.4 95% confidence interval]</td>
</tr>
<tr>
<td>Mean number of antibiotics per day</td>
<td>2.31 Odds Ratio [0.71-7.5 95% confidence interval]</td>
</tr>
<tr>
<td>TPN/CPN (Parenteral Nutrition)</td>
<td>DECREASE in Odds Ratio (0.16 Odds Ratio, 0.05-0.47 Confidence Interval) (in other words, these patients are more likely to get Candida albicans species)</td>
</tr>
</tbody>
</table>

General Susceptibility Patterns of Candida Species

<table>
<thead>
<tr>
<th>Species</th>
<th>Fluconazole</th>
<th>Itraconazole</th>
<th>Voriconazole</th>
<th>Posaconazole</th>
<th>Flucytosine</th>
<th>Amphotericin B</th>
<th>Echinocandins</th>
</tr>
</thead>
<tbody>
<tr>
<td>Candida albicans</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
</tr>
<tr>
<td>Candida tropicalis</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
</tr>
<tr>
<td>Candida parapsilosis</td>
<td>S-DD to R</td>
<td>S-DD to R</td>
<td>S-DD to R</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S to R*</td>
</tr>
<tr>
<td>Candida glabrata</td>
<td>S-DD to R</td>
<td>S-DD to R</td>
<td>S-DD to R</td>
<td>S</td>
<td>S</td>
<td>S to I</td>
<td>S</td>
</tr>
<tr>
<td>Candida kruzei</td>
<td>R</td>
<td>S-DD to R</td>
<td>S</td>
<td>I to R</td>
<td>S</td>
<td>S to I</td>
<td>S</td>
</tr>
<tr>
<td>Candida lusitaniae</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S to R</td>
<td>S</td>
</tr>
</tbody>
</table>

S= susceptible; I= intermediately susceptible; R= resistant; S-DD= susceptible dose-dependent

*Echinocandin resistance among C. parapsilosis isolates is uncommon
### Treatment of Invasive Fungal Infections in the ICU

<table>
<thead>
<tr>
<th>Clinical Situation</th>
<th>Primary therapy</th>
<th>Alternative therapy</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proven Candidemia *, non-neutropenic adult</td>
<td>Fluconazole †</td>
<td>Echinocandin ‡ or</td>
<td>Favor echinocandin for moderately-severe to severe disease or recent azole exposure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>AmB-d ¥ or LFAmB ≡</td>
<td></td>
</tr>
<tr>
<td>Proven Candidemia *, neutropenic adult</td>
<td>Echinocandin ‡ or</td>
<td>Fluconazole † or</td>
<td>Less critically ill and no recent azole exposure, consider fluconazole</td>
</tr>
<tr>
<td></td>
<td>LFAmB ≡</td>
<td>voriconazole ζ</td>
<td></td>
</tr>
<tr>
<td>Suspected candidemia *, non-neutropenic adult</td>
<td>LFAmB ≡, Caspofungin †</td>
<td>Fluconazole † or</td>
<td>• Consider empiric treatment for critically ill patients with risk factors for invasive candidiasis and no other cause for fever</td>
</tr>
<tr>
<td></td>
<td></td>
<td>voriconazole 200mg bid</td>
<td>• Base decision on clinical risk factors, serologic markers and/or culture data</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• In most neutropenic patients, it is reasonable to initiate empiric antifungal therapy after 4 days of persistent fever despite antibiotics.</td>
</tr>
<tr>
<td>Candida isolated from respiratory secretions</td>
<td>Therapy is not indicated (lower respiratory tract infection is rare and requires histopathologic evidence to confirm a diagnosis)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Candiduria</td>
<td>Asymptomatic: observe / remove indwelling catheter if possible</td>
<td>Symptomatic cystitis: fluconazole 200mg daily (3 mg/kg/day) x 2 weeks</td>
<td>Pyelonephritis: fluconazole 200-400mg daily (3-6mg/kg/day) x 2 weeks</td>
</tr>
<tr>
<td>CNS Candidiasis</td>
<td>LFAmB ≡ +/- 5-FC^ x several weeks, then fluconazole 400-800 mg daily</td>
<td>Fluconazole 400-800 mg daily if unable to tolerate LFAmB</td>
<td>Removal of intraventricular devices (if present/possible) is also recommended</td>
</tr>
<tr>
<td>Candida Endocarditis</td>
<td>LFAmB ≡ +/- 5-FC^, or AmB-d 0.6-1mg/kg +/- 5-FC^, or Echinocandin ‡</td>
<td>Step down to fluconazole 400-800mg daily if culture negative stable patient</td>
<td>• Valve replacement strongly recommended</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• If unable to remove valve, lifelong fluconazole 400-800 mg daily</td>
</tr>
</tbody>
</table>

* Duration of therapy: 2 weeks past documented clearance of Candida from the bloodstream and resolution of symptoms attributable to candidemia  
# IV catheter removal should be considered  
† Fluconazole dose: 800mg (12 mg/kg) x 1, then 400mg daily  
‡ Echinocandin doses: Caspofungin 70mg load, then 50mg/d or micafungin 100mg/d or anidulafungin 200mg load, then 100mg/d. Echinocandins are preferred for *Candida glabrata* isolates. 
¥ AmB-d: Amphotericin B deoxycholate (AmB-d) 0.5-1 mg/kg daily  
≡ LFAmB: lipid formulation of Amphotericin B (LFAmB) at 3-5mg/kg/d  
ζ Voriconazole dose: 400 mg po bid x 2 doses load, then 200 mg po bid; reduced dose for mild to moderate hepatic impairment; avoid IV voriconazole for creatinine clearance < 50 ml/min  
∫ Caspofungin 70mg load, then 50mg daily  
^ 5-FC: flucytosine 25mg/kg qid  

### Prophylactic Anti-Fungal Therapy

<table>
<thead>
<tr>
<th>Clinical Situation</th>
<th>Primary therapy</th>
<th>Alternative therapy</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prophylaxis, ICU patient</td>
<td>Fluconazole 400 mg po bid</td>
<td></td>
<td>Recommended for high-risk patients in adult ICUs that have a high incidence of invasive candidiasis; however, no mortality benefit is seen.</td>
</tr>
<tr>
<td>Prophylaxis, chemotherapy-induced neutropenia</td>
<td>Fluconazole 400mg po bid, posaconazole 300 mg po tid, or caspofungin 50 mg/d</td>
<td>Itraconazole 200 mg po bid (less well-tolerated than other agents)</td>
<td>Continue for the duration of neutropenia.</td>
</tr>
</tbody>
</table>

HIV Infected Patients in the ICU

HIV Testing
- Each state has specific laws regarding the obtaining of informed consent for HIV testing. †
- California law mandates that medical providers are required to inform patients that an HIV test will be performed, provide information about the test and HIV treatment options, and advise the patient of their right to refuse the test
- There are no specific provisions if the patient is critically ill/comatose/otherwise unable to give informed consent
- The CDC states that ‘general informed consent for medical care should be considered sufficient to encompass informed consent for HIV testing’.
- Surrogate decision-makers or hospital ethics committees may also be consulted.

Adverse Reactions Caused by HIV Medications

<table>
<thead>
<tr>
<th>Adverse Effect</th>
<th>Principal Antiretroviral Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systemic hypersensitivity reaction</td>
<td>Abacavir</td>
</tr>
<tr>
<td>Stevens-Johnson or Toxic Epidermal Necrolysis</td>
<td>Nevirapine</td>
</tr>
<tr>
<td>Hepatotoxicity</td>
<td>All antiretrovirals, especially nevirapine</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>Didanosine, stavudine</td>
</tr>
<tr>
<td>Lactic acidosis syndrome, hepatotoxicity and hepatic steatosis</td>
<td>Nucleoside reverse transcriptase inhibitors (NRTIs), especially stavudine, didanosine, zidovudine</td>
</tr>
<tr>
<td>Nephrotoxicity, acute renal failure</td>
<td>Indinavir, tenofovir</td>
</tr>
</tbody>
</table>

HIV Medications in the ICU

| Drugs requiring dose adjustment in patients with renal insufficiency | All NRTIs except for abacavir                                      |
| Drugs requiring dose adjustments in patients with hepatic impairment | Atazanavir, fosamprenavir, indinavir                                |
| Drugs contraindicated with NNRTIs                          | Midazolam, triazolam                                               |
| Common ICU drugs contraindicated with protease inhibitors   | Midazolam, triazolam, amiodarone (w/ IND, RIT, TIP), bepridil (w/ATA, FOS, RIT, TIP), proton pump inhibitors (w/ATA), histamine-2 blockers (if bid, w/ATA), propafenone (w/lopinavir/RIT combo, RIT monotherapy, or TIP), and quinidine (w/ RIT or TIP) |

Abbreviations: IND, indinavir; RIT, ritonavir; ATA, atazanavir; FOS, fosamprina; TIP, tipranavir

HIV Medications in the ICU: To Give or Not To Give?
- Should be decided on a case-by-case basis, in consultation with Infectious Disease specialist
- Continue anti-retroviral therapy if patient already on therapy and viral load undetectable, unless compelling indication to stop therapy
- Consider starting anti-retroviral therapy if the patient is in the ICU with an AIDS associated condition, or if they have a prolonged ICU course from a non-AIDS condition with a CD4 count ≤ 200 cells
- Consider drug resistance testing if viral load detectable and already on anti-retroviral therapy
- Defer anti-retroviral therapy if significant concern for Immune Reconstitution Syndrome or concern for toxic effects of anti-retroviral drugs, or if CD4 > 200 cells

† State guidelines at: National HIV/AIDS Clinician Consultation Center (http://www.nccc.ucsf.edu/StateLaws/Index.html)
Anaphylaxis

**Definition:**
- Acute, life-threatening reaction that results from sudden release of allergic and inflammatory mediators from mast cells and basophils
- Signs/symptoms: include urticaria and angioedema (85-90%), swelling of lips/tongue/throat, dyspnea/wheeze (45-50%), dizziness, syncope, confusion, loss of consciousness, headache, anxiety, hypotension (30-35%), nausea, vomiting, diarrhea, cramping pain (25-30%), fast or slow heart rate, low blood pressure, dysphagia, hoarseness
- Occurs within seconds to minutes of an offending stimulus
  - May be delayed for even > 30 minutes
  - May be monophasic, biphasic (up to 72 hours), or prolonged in course
- Etiologies include foods, medications, bites/stings, latex, exercise, or idiopathic

**Management of Angioedema:**
- H1 Blocker (e.g. diphenhydramine 50 mg IV q6)
- Epinephrine subcutaneous: 0.2-0.5 ml of 1:1000 solution (0.01mg/kg in children, maximum 0.3 mg dosage; max 0.5 mg in adults); may repeat q 3-5 minutes as needed
- Consider Ranitidine 50 mg IV over 5 minutes

**Management of Bronchospasm:**
- Albuterol 2.5-5mg nebulized
- +/- IV Aminophylline: 5-6 mg/kg load, then 0.2-0.9 mg/kg/hr
- +/- Subcutaneous Epinephrine as above

**Management of Laryngeal Stridor:**
- Aerosolized Epinephrine (racemic): 0.25mg of 1% Solution (10mg/ml) in 2 ml NS

**Management of Hypotension:**
- Volume expansion with Isotonic IV Fluids
- Consider Trendelenberg positioning/elevation of the legs
- H1 Blocker (e.g. diphenhydramine 50mg IV q6)
- IV Epinephrine: 3-5ml of 1:10,000 solution (0.1mg/ml)

**Management of Persistent Hypotension:**
- Pressors:
  - Epinephrine: 2-8 mcg/minute or
  - Dopamine: 5-15 mcg/min or
  - Norepinephrine 2-8 mcg/min
- IV Steroids:
  - Equivalent to methylprednisolone 1-2mg/kg/daily divided q 6 hours may be beneficial
- If patient has been on a Beta blocker, consider Glucagon 1-5mg IV over 5 minutes, then 5-15mcg/minute titrated to clinical response

**Management of Cardiopulmonary Arrest During Anaphylaxis:**
- CPR and Advanced Life Support Measures
- High-dose (escalating dose) Epinephrine IV:
  - Epinephrine 1-3mg of 1:10,000 dilution IV slowly over 3 minutes, then
  - Epinephrine 3-5mg of 1:10,000 dilution IV slowly over 3 minutes, then
  - Epinephrine 4-10mcg/min IV Infusion

Necrotizing Soft Tissue Infections (NSTIs)

Etiology
- Often polymicrobial, particularly in diabetics
- Clostridium or Group A Strep are classically implicated. MRSA is more recently implicated.

Diagnosis
- You must have a high index of suspicion to diagnose it. Think about it early!

Risk Factors
- Injection Drug Use
- Chronic Debilitating Conditions (diabetes, immunosuppression, obesity)

Clinical Characteristics
- Locally: Initial: swelling, erythema, pain, and tachycardia
- Progressive signs and symptoms: tense edema outside the area of compromised skin, pain disproportionate to appearance, skin discoloration (ecchymosis), anesthesia of affected area, blisters/bullae and necrosis, and crepitus +/- subcutaneous gas.
- Systemically: fever, tachycardia, hypotension, and shock.
- The above signs are specific but not sensitive for diagnosing NSTIs (present in only 10%-40% of patients with NSTI)
- The progression of these signs and symptoms is usually relatively fast (particularly if group A Streptococcus or Clostridium species are involved), but not always fast, making the diagnosis even more difficult
- Bedside skin incision with finger exploration revealing fascial plane disruption may prove diagnosis in unclear cases

Labs/Radiology
- Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC)
  - LRINEC score ≤ 5 = “Low Risk” = Risk of NSTI < 50%
  - LRINEC score 6-7 = “Intermediate Risk” = Risk of NSTI 50-75%
  - LRINEC score ≥ 8 = “High Risk” = Risk of NSTI >75%
  - For a score >6, Positive Predictive Value = 92% and Negative Predictive Value 96%
- Plain films looking for subcutaneous gas may be helpful
- CT, MRI, and ultrasound may also be helpful
- Hyperbaric oxygen therapy (3 dives daily) may be beneficial, particularly with Clostridial etiology
- Think about IVIg if they are getting sicker despite maximal therapy (especially with Group A Streptococcal infection)

Prognosis
Mortality approaches 100% without source control; Mortality Rate is 34% despite best medical practice

**Clostridium difficile-Associated Disease (CDAD)**

**Etiology/ Pathophysiology**
- Spore-forming anaerobic Gram negative rod
- Toxin A and Toxin B production along with Cytolethal Distending Toxin (CDT)

**Risk Factors**
- Antibiotic use (even 1 dose peri-operatively) in the last 60 days
- Use of Cephalosporin, Quinolone, or Clindamycin (LESS incidence with Piperacillin/Tazobactam); or administration of 3 or more antibiotics
- Serum albumin <3g/dL, <1 year since admission to a long-term care facility, use of Proton Pump Inhibitors or H2 blockers, Female Sex, Prior renal failure, Hospital admission within 90 days

**Clinical Manifestations**
- Diarrhea, Abdominal cramping, Leukocytosis (often as high as WBC~30,000 range), low grade fever
- Causes a severe colitis worst in the distal colon and rectum which may progress to “pseudomembranous colitis”, toxic megacolon, and/or bowel perforation
- Worse clinical manifestations with increased heart rate, ≥30% bands, respiratory failure, immunosuppression, prior bowel surgery unrelated to CDAD, oliguria, hypotension.

**Diagnosis**
- C. dif PCR on unformed stool is rapid, sensitive and specific; it is the test used at VCMC
- Stool EIA (enzyme immunoassay) for C. dif Toxins A and B are highly specific (95-100%) but not very sensitive (65-85% only); Tissue culture is slower (turnaround 24-48 hours) but more sensitive and just as specific; Stool culture is not recommended (may be positive without pathogenic C. dif)

**Treatment**
- D/C all antibiotics if possible
- C. dif-targeted antibiotic therapy

<table>
<thead>
<tr>
<th>Clinical definition</th>
<th>Supportive Clinical Data</th>
<th>Recommended Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial episode, mild or moderate</td>
<td>Leukocytosis with a WBC 15,000 cells/mcL or lower and serum creatinine &lt; 1.5 times the premorbid level</td>
<td>Metronidazole 500 mg po tid x 10-14 days (there may be higher complication rate vs. vancomycin)</td>
</tr>
<tr>
<td>Initial episode, severe</td>
<td>Serum albumin &lt; 3 g/dL and one of the following:</td>
<td>Vancomycin 125 mg PO QID x 10-14 days</td>
</tr>
<tr>
<td></td>
<td>• Leukocytosis with a WBC 15,000 cells/mcL or higher</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Serum creatinine &gt; 1.5 times the premorbid level</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Abdominal tenderness</td>
<td></td>
</tr>
<tr>
<td>Initial episode, severe, complicated</td>
<td>Any of the following attributed to CDAD:</td>
<td>Vancomycin 500 mg po qid AND Metronidazole 500 mg IV q 8 hours +/- vancomycin 500mg in 100 ml NS retention enema qid for ileus</td>
</tr>
<tr>
<td></td>
<td>Hypotension or shock; ileus or significant abdominal distension; megacolon; admission to ICU; hypotension with or without pressor use; fever ≥ 38.5; WBC ≥ 35,000 cells/mm3; serum lactate &gt; 2.2 mmol/L; end organ failure (respiratory or renal failure, etc.)</td>
<td>Advanced treatment for severe disease may include IVIG (150-400mg/kg IV x1, though efficacy is seriously in question), probiotics, bile-acid sequestrants (e.g. cholestyramine, colestipol), “stool transplant” (duodenal or colonoscopic infusion of screened donor stool), and/or surgical intervention (total colectomy vs. loop ileostomy + colon lavage)</td>
</tr>
</tbody>
</table>
• General Medical Support:
  o Electrolyte normalization
  o Fluid replacement
  o Avoidance of Antimotility Agents (risk of increased toxin exposure with decreased transit time)
• Relapse of CDAD occurs in 10-25% of patients; patients with ≥ 1 recurrence have a 65% likelihood of re-recurring
• Treatment of recurrent CDAD:

<table>
<thead>
<tr>
<th>First recurrence</th>
<th>Second recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Same as for initial episode</td>
<td></td>
</tr>
<tr>
<td>Vancomycin PO in a tapered and/or pulsed regimen (many regimens exist, such as this one: vancomycin 125 mg PO QID x 10-14 days, the 125 mg PO BID x 7 days, then 125 mg PO daily x 7 days, then 125 mg q 2-3 d x 2-8 weeks)</td>
<td></td>
</tr>
</tbody>
</table>

Prevention
• Wash your hands with soap and water when you are concerned about *C. dif*, as the alcohol-based cleanser from the wall dispensers is ineffective at killing this bacteria.
• Limit unnecessary gastric acid suppression and unnecessary antibiotic use

Multi-Drug Resistant (MDR) Pathogens

Methicillin-Resistant Staph aureus (MRSA)

Definition
- *Staphylococcus aureus* with a Mean Inhibitory Concentration to Methicillin >= 4mcg/ml
- All *Staph aureus* sppc. resistant to methicillin are resistant to all beta-lactam antibiotics, including penicillins and cephalosporins
- Healthcare-acquired MRSA and Community-Acquired MRSA behave very differently and will be discussed separately
- Implicated in Soft Tissue Infections, Pneumonia, Necrotizing Pneumonia, Bacteremia

Epidemiology
- Of *Staph aureus* species isolated at VCMC, >50% are resistant to methicillin
- VISA (Vancomycin Intermediate *Staph aureus*), with MIC ≤16 mcg/ml, is also increasing
- VRSA (Vancomycin Resistant *Staph aureus*) has an MIC > 64 mcg/ml; still rare
- “MIC Creep”: MIC is slowly rising, from a mean of 0.62mcg/ml to a mean of 0.94mcg/ml from 2001 to 2006
  - Infection with a MRSA species with a higher MIC is associated with poorer outcomes

Healthcare-Acquired MRSA
- Common in the ICU; often highly resistant to conventional antibiotics
- Does prolong hospital stay and costs, but does not have the increased virulence seen with Community-Acquired MRSA
- Pneumonia is not often toxin-producing/severe

Community-Acquired MRSA
- USA300 strain of MRSA is implicated in many severe CA-MRSA cases (not the only strain)
- The Panton-Valentine Leukocidin (PVL) enzyme, a leukocidal and dermatonecrotic enzyme, is responsible for at least some of the increase in virulence
- PVL Toxin produced by an increasing proportion of MRSA and MSSA strains
- In necrotizing pneumonia, the PVL released breaks down cell membranes of inflammatory cells, leading to overwhelming inflammatory response

Sites of MRSA Infection
Skin and Soft Tissue Infections
  - Linezolid may have better tissue penetration with better clinical cure rates than vancomycin
MRSA bacteremia
  - If catheter-related, linezolid should be AVOIDED (higher mortality rate seen)
  - If NOT catheter-related, vancomycin may have worse clinical cure rate vs. linezolid

MRSA Pneumonia
- For Health-Care Associated Pneumonia and Ventilator-associated pneumonia, the Infectious Disease Society of America and American Thoracic Society recommend vancomycin trough levels of 15-20

MRSA Necrotizing Pneumonia
- Estimated nearly 70-75% mortality from necrotizing pneumonia from *Staphylococcus aureus*
- ~50% of PVL-producing strains are Methicillin resistant; MSSA is becoming more of a problem as well (and may even possess more severe disease than some MRSA species)
- Clindamycin and Linezolid do turn off toxin production and should be considered in severe necrotizing pneumonia (Clindamycin > Linezolid in *in vitro* studies)
- IVIG Therapy may be considered at a dose of 2g / kg (only case reports are available)

Preferred ICU Treatment Options for MRSA
Drug-Resistant Pathogens

### Vancomycin Resistant Enterococcus (VRE)

<table>
<thead>
<tr>
<th>Organism</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vancomycin Resistant <em>Enterococcus faecalis</em></td>
<td>Usually remains susceptible to penicillin G or ampicillin</td>
</tr>
<tr>
<td>Vancomycin Resistant <em>Enterococcus faecalis</em>, with penicillin/ampicillin MIC &gt; 8 but ≤ 64</td>
<td>Ampicillin 300 mg/kg may be effective</td>
</tr>
<tr>
<td>Vancomycin Resistant <em>Enterococcus faecium</em>, resistant also to penicillin/ampicillin/ streptomycin/gentamicin</td>
<td>Linezolid 600 mg po or IV q 12 hours, OR Quinupristin/dalfopristin 7.5 mg/kg IV q 8 hours</td>
</tr>
</tbody>
</table>

**Multi-Drug Resistant (MDR) Gram Negative Rods**

<table>
<thead>
<tr>
<th>Organism</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Acinetobacter baumannii</em>, resistant to imipenem, anti-pseudomonal penicillins and cephalosporins, aminoglycosides, fluoroquinolones</td>
<td>Ampicillin/sulbactam</td>
</tr>
<tr>
<td>Extended Spectrum Beta Lactamases (ESBL) † (Klebsiella pneumonia, E. coli primarily; less commonly seen in other gram negative rods)</td>
<td>Carbapenems are most effective therapy, even if laboratory evidence of sensitivity to beta lactams</td>
</tr>
<tr>
<td>Klebsiella Pneumonia Carbapenemases (KPC) ≡ (starting to be seen in other gram negative rods)</td>
<td>Some KPC organisms resistant to all antimicrobials except colistin Tigecycline active <em>in vitro</em></td>
</tr>
</tbody>
</table>

† suspect with resistance to multiple 3rd generation cephalosporins; ≡ suspect with resistance to ertapenem

Diabetic Ketoacidosis

**ENDOCRINE**

*Diabetic Ketoacidosis*

### Initial Evaluation:

History and Physical, focused on any potential sites of infection

**Labs:** ABG PLUS, CMP, CBCD, UA, Magnesium, Phosphorus, EKG, Chest X-ray, Head CT, Cultures as needed

**IV Fluids**

- Isotonic Normal Saline
  - Initially 1-1.5 Liters in first hour, then 500ml-1000ml per hour until euvolemic
  - Once euvolemic, change to ½ NS at 200-250ml/hour
  - Once glucose<250mg/dl, change to D5 ½ NS at 200-250ml/hour until DKA resolves

**Potassium/Phosphorus**

- If serum potassium level < 3.3mEq/L, DO NOT GIVE INSULIN as it will lower potassium levels further. Give Potassium 40mEq IV first.
  - If serum potassium level > 5.5mEq/L, do not give potassium; recheck serum potassium in 2 hours
  - If serum potassium 3.3-5.5mEq/L, give 20 to 30mEq of potassium in each liter of IV fluid to keep serum potassium level 4 to 5 mEq/L; Check Chem 7, Phos q 2 to 4 hrs.

**Insulin**

- If potassium level is adequate (≥3.3), give 0.1 Units/kg IV x 1, then start insulin drip at 0.1 Units/kg/hour
  - Desired fall in glucose at rate of 50-100mg/dl/hour until glucose < 250; q 1 hour glucose checks
  - Adjust drip to maintain glucose 150-200mg/dL until DKA resolves (Glucommander insulin infusion range 120-160)
  - For low blood sugars, add IV dextrose and don’t stop insulin within the first 48 hours of DKA diagnosis
  - Transition to SubQ insulin when Anion Gap normal, bicarbonate>18mEq/L and tolerating diet

**Factors Contributing to Morbidity and Mortality in DKA:**

1. The underlying cause of the DKA – rule out infection, abscesses, bacteremia, substance abuse, myocardial infarction, etc.
2. Electrolyte Disturbances
   a. Hypokalemia (all patients in DKA are total body potassium depleted)
   b. Hyperkalemia (due to severe acidosis and K+H+ antepartment)
   c. Hypophosphatemia
3. Severe Acidemia
   a. Consider IV Bicarbonate for pH<7 or for symptomatic hyperkalemia
4. Cerebral Edema
   a. More common with hypotonic fluids, more common in children
   b. Beware of obtundation; give Mannitol while waiting for your head CT
5. Hypoglycemia (check glucose q 1 hour while on the drip)
6. Return to ketoacidosis: Patients in DKA are ketogenic and remain so for 24-48 hours after their DKA resolves. Should the patient go hypoglycemic, give them more sugar. DON’T stop their insulin completely if possible.

**DKA Typical Deficits**

- Water: 6 Liters, or 100ml per kg of body weight
- Sodium: 7 to 10mEq/kg of body weight
- Potassium: 3-5mEq per kg of body weight
- Phosphate: 1 mmol/kg body weight

**DKA Diagnostic Criteria**

- Glucose>250mg/dL
- pH<7.3
- Bicarbonate <18 mEq/L
- Anion gap >10 and ketonemia

**Diabetic Ketoacidosis Typical Deficits**

- Water: 6 Liters, or 100ml per kg of body weight
- Sodium: 7 to 10mEq/kg of body weight
- Potassium: 3-5mEq per kg of body weight
- Phosphate: 1 mmol/kg body weight

Intensive Insulin Therapy in the ICU

Mildly conflicting Data Regarding Tight Glucose Control in Critically Ill patients is presented below. In the VCMC ICU, the target glucose level for critically ill patients is 120-160.

Findings of a meta-analysis of 29 randomized-controlled trials totaling 8432 critically ill patients
No change in hospital mortality in tight glucose control vs. usual care (definition of “usual care” varied between the studies)
No significant difference in mortality when stratified by glucose goal:
Very tight control (glucose < 110): 23% (tight) vs. 25.2% (usual)
Moderately tight control (glucose < 150): 17.3% (tight) vs. 18% (usual)
Significantly increased risk of hypoglycemia (glucose < 40mg/dL) 13.7% (tight) vs. 2.5% (usual)
Significantly decreased risk of septicemia: 10.9% (tight) vs. 13.4% (usual)

Summary of Large Trials of Intensive Glycemic Control in Critically Ill Patients

<table>
<thead>
<tr>
<th>Trial</th>
<th># of patients</th>
<th>Type of ICU</th>
<th>Intensive vs. conventional glucose goals</th>
<th>Intensive vs. conventional mean glucose</th>
<th>Primary outcome</th>
<th>Rate of outcome (intensive vs. conventional)</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leuven I (van den Berghe)</td>
<td>1548</td>
<td>Surgical ICU</td>
<td>80-110 vs. 180-200</td>
<td>103 vs. 153</td>
<td>Death in ICU</td>
<td>4.6% vs. 8%</td>
<td>0.58 (0.38-0.78)</td>
</tr>
<tr>
<td>Leuven II</td>
<td>1200</td>
<td>Medical ICU</td>
<td>80-110 vs. 180-200</td>
<td>111 vs. 153</td>
<td>Death in hospital</td>
<td>37.3% vs. 40%</td>
<td>0.94 (0.84-1.06)</td>
</tr>
<tr>
<td>Glucontrol</td>
<td>1101</td>
<td>General</td>
<td>80-110 vs. 140-180</td>
<td>118 vs. 144</td>
<td>Death in ICU</td>
<td>16.7% vs. 15.2%</td>
<td>1.10 (0.84-1.44)</td>
</tr>
<tr>
<td>VISEP</td>
<td>537</td>
<td>General</td>
<td>80-110 vs. 180-200</td>
<td>112 vs. 151</td>
<td>Death at 28 days</td>
<td>24.7% vs. 26%</td>
<td>Not reported</td>
</tr>
<tr>
<td>NICE-SUGAR (2009)</td>
<td>6104</td>
<td>General</td>
<td>81-108 vs. 144-180</td>
<td>118 vs. 145</td>
<td>Death at 90 days</td>
<td>27.5% vs. 24.9%</td>
<td>1.14 (1.02-1.28)</td>
</tr>
</tbody>
</table>

Random Glucose Factoids:
- Patients without diabetes with new hyperglycemia in 1 study had a 31% ICU mortality (vs. 11% ICU mortality in known diabetics)
- In cardiac surgery, a single blood glucose level ≥ 200 in the first 48 hours post-thoracic surgery doubles the risk of infection, including deep sternal infection (2.8% risk pre-insulin drips vs. 0.7% risk w/ drip)
- In a small study of 97 patients, a single blood sugar ≥ 220 conveyed an odds ratio of 2.7 times higher (risk of infection 5.7%) than patients with blood sugar <220

Insulin Infusions

- Insulin infusion may be used in the ED, ICU, DOU, or OR. 3 North Telemetry is also an option if there are no DOU beds.
- Target blood sugar: 120-160 at VCMC / Santa Paula Hospital

Indications:
- Life or limb threatening infection with blood sugar > 180 mg/dL
- Diabetic ketoacidosis
- Acute myocardial infarction, for very tight control
- Critically ill patients in ICU / occasionally DOU; trigger for starting in ICU blood glucose ≥ 180 x 2

Insulin Infusion Software details:
- ‘Glucommander’ is the software used for insulin infusions at VCMC: ventura.glytecenterprise.com
  - Most nurses have logins, with desktop icon
  - Physician login is usually Meditech login (D.”initials”), password Welcome01
- Order via phase “PHA Adult IV Insulin Orders Using Glucommander (VCMC 516-084, 516-085)”
- Glucommander uses a mathematical methodology to change the “multiplier” based on the glucose response to the insulin drip dose.
  - Choose default “Multiplier” of 0.02; choose 0.01 for thin Type 1 patients with renal failure who are prone to hypoglycemia
  - Software has improved with management of very high blood sugars—in the past, the goal was to get the patient down to goal (120-160) as fast as possible; goal now is to bring blood glucose down by 50-100 mg/dL, with safer rates of blood glucose change seen
- For Type 1 diabetics, dextrose IV infusions are used to avoid hypoglycemia when the patient’s blood glucose is < 250 mg/dL
  - For Type 2 patients, particularly those who are fluid overloaded, recommend not using dextrose even when blood glucose < 250 mg/dL (Glucommander does not require dextrose)
- Meal boluses DO need to be ordered through the subphase (“PHA Adult IV Insulin Orders Using Glucommander”) when the patient starts eating.
  - Meal boluses through Glucommander sometimes yield very high rates of insulin for short times (i.e. 36 units/hour, recheck in 30 minutes), leading to some angst among providers.
  - It is not currently recommended to do any subQ insulin for meals when the patient is on a drip.
- Glucommander specifics on transition to subQ insulin
  - Suggests a long-acting insulin dose when the patient is ready for transition to subQ insulin.
  - Requires patient to be ‘in-range’ (120-160). Ideally the patient has been in-range for 4 consecutive hours.
  - Discontinue the insulin drip 2 hours after subQ glargine insulin dose

Transition to Subcutaneous Insulin:
- Eligibility for transition to subcutaneous insulin (must meet all of the following criteria):
  1. Hemodynamically stable (i.e. not on pressors) (if on pressors, unreliable insulin absorption)
  2. Infection improving and not uncontrolled
  3. Not too many changing variables (change in steroid dose, change in carbohydrate intake, etc.)
  4. Transition needs to happen in morning-time or at bedtime (22:00)
     a. If the transition is done in the morning but patient uses bedtime glargine at home, NPH may be used as a bridge, understanding that NPH does have a peak; it is very important that the patient is eating if they are to receive NPH
     b. If transition is desired in the middle of the day (i.e. between the hours of noon and 6 pm), mandatory consultation with Dr. Cho is required

Return to Table of Contents
2 options for transition to subcutaneous insulin:
  o Choice #1: Using Glucommander
    1. In Glucommander, click on “Transition to SubQ” box above glucose graph
    2. For basal % of TDD, use 80%; for basal time, round UP to the NEXT hour, then “Save”
    3. Glucommander will give a suggested dose of glargine insulin
      i. If you accept that dose, click “Save” again
      ii. If you feel that the dose is very different than what you calculate the patient
          needs, you may override that suggested glargine insulin dose by clicking
          “Modify dose” on the Glucommander; note that if the calculated dose is very
          different from the home dose, consider that the patient has recently been in DKA
          and potentially also on 5 grams of dextrose per hour IV, both potentially
          contributing to higher needs
    4. Use “PHA Transition IV to SubQ insulin” when ready to transition from IV to subQ
       insulin; this is a multi-phase powerplan containing an “Initiate” now portion and a “Sign”
       portion titled “Post-transition to subQ insulin” which is to be initiated by the nurse 2
       hours after the insulin infusion has been discontinued
  o Choice #2: Calculate transition dose on your own
    1. To calculate dose of glargine insulin to be given:
      a. Determine mean insulin infusion rate for last 6-8 hours
      b. Multiply hourly rate by 24, then multiply by 0.8 (safety factor when converting drip to
         subcutaneous insulin). This is the Total Daily Dose (TDD)
      c. Determine if this TDD covers basal needs only or basal and mealtime needs based on
         current nutrition:
         i. If patient is eating > 50% of their meals, on goal tube feeds, or on TPN, use ½ of
            TDD as basal insulin dose and the other half for mealtime insulin coverage
            (divided by 3) (alternatively, may use Insulin-to-Carb ratio (450 ÷ TDD) and
            order ratio-based lispro dose with meals
         ii. If patient is NPO, taking <50% of their meals, or is on a clear liquid diet, use
            entire TDD as basal dose
    2. Use “PHA Transition IV to SubQ insulin” when ready to transition from IV to subQ insulin;
       this is a multi-phase powerplan containing an “Initiate” now portion and a “Sign” portion
       titled “Post-transition to subQ insulin” which is to be initiated by the nurse 2 hours after the
       insulin infusion has been discontinued

Adapted with permission from Dr. Theresa Cho
Glucommander Downtime Protocol (adapted from update from 3-24-13)

Physician Reference when Glucommander unavailable:
1. Continue q 1 hour blood glucose checks
2. Determine the most recent insulin drip rate and blood glucose level.
3. Refer to the table and find the algorithm that most closely correlates to the current insulin drip dose and blood glucose. Clinical judgment will be needed when numbers do not correlate exactly. For example, if the most recent insulin dose is 2.7 units/hr and blood glucose is 154 mg/dL, use Algorithm C.
4. If blood glucose is greater than 160 mg/dL x 2, move to the next algorithm column to the right (one algorithm up).
5. If blood glucose is less than 120 mg/dL, stop insulin drip. Continue hourly BG checks. Once blood glucose is greater than 120 mg/dL, resume insulin drip using algorithm column to left of the previous one (one algorithm down).
6. If blood glucose is less than 70 mg/dL, stop insulin drip. Treat hypoglycemia per protocol. Once blood glucose is greater than 70 mg/dL, resume hourly blood glucose checks. When blood glucose is greater than 120 mg/dL, resume insulin drip using algorithm column to left of the previous one (one algorithm down).
7. Contact Dr. Cho with any questions or concerns.

<table>
<thead>
<tr>
<th>Algorithm A</th>
<th>Algorithm B</th>
<th>Algorithm C</th>
<th>Algorithm D</th>
</tr>
</thead>
<tbody>
<tr>
<td>BG</td>
<td>Units/hr</td>
<td>BG</td>
<td>Units/hr</td>
</tr>
<tr>
<td>70-79</td>
<td>Off</td>
<td>70-79</td>
<td>Off</td>
</tr>
<tr>
<td>80-119</td>
<td>0.2</td>
<td>80-119</td>
<td>0.5</td>
</tr>
<tr>
<td>120-129</td>
<td>1</td>
<td>150-169</td>
<td>1.5</td>
</tr>
<tr>
<td>170-189</td>
<td>2</td>
<td>170-189</td>
<td>4</td>
</tr>
<tr>
<td>190-209</td>
<td>3</td>
<td>190-209</td>
<td>5</td>
</tr>
<tr>
<td>210-239</td>
<td>4</td>
<td>210-239</td>
<td>6</td>
</tr>
<tr>
<td>240-269</td>
<td>5</td>
<td>240-269</td>
<td>8</td>
</tr>
<tr>
<td>270-299</td>
<td>6</td>
<td>270-299</td>
<td>10</td>
</tr>
<tr>
<td>300-329</td>
<td>7</td>
<td>300-329</td>
<td>13</td>
</tr>
<tr>
<td>330-359</td>
<td>8</td>
<td>330-359</td>
<td>16</td>
</tr>
<tr>
<td>≥360</td>
<td>9</td>
<td>≥360</td>
<td>10</td>
</tr>
</tbody>
</table>

Glucommander Downtime Procedure for Diabetic Ketoacidosis/ Hyperglycemia

Hyperosmolar State (HHS):
1. Recommend initial bolus of regular insulin at 0.1 Units/kg IV, up to 10-15 units x 1
2. Start insulin infusion at 0.1 Units/kg/hour
3. Check blood glucose hourly
4. While blood glucose ≥ 350 mg/dL, adjust IV insulin infusion in the following manner:
   - If blood glucose has decreased by < 50 mg/dL in the 1 hour period, increase the insulin drip rate by 50%
   - If blood glucose has decreased by > 200 mg/dL in the 1 hour period, decrease the insulin drip rate by 50%
5. When blood glucose is < 350, or after 6 hours, convert to algorithmic approach to insulin management above.
Relative Adrenal Insufficiency of Sepsis

The latest Surviving Sepsis Campaign recommendations (2012) suggest against the routine check of the Cosyntropin Stimulation Test for patients with refractory hypotension in the face of sepsis, while recommending empiric steroid therapy for those with refractory septic shock (refractory = hemodynamically unstable despite adequate fluid and pressor administration). The rationale is that, for patients without relative adrenal insufficiency who are given steroids, the duration of their refractory hypotension goes down with steroid administration. For patients with relative adrenal insufficiency, mortality improves with the administration of steroids.

For most cases of refractory septic shock, the 2012 Surviving Sepsis guidelines now recommend a continuous infusion of 200 mg hydrocortisone over 24 hours, to be weaned when pressor requirement has resolved. Hydrocortisone at a dose of 100mg IV q 8 hours is also acceptable treatment but may be associated with higher incidence of hyperglycemia.

Diagnosis of Adrenal Insufficiency

Cosyntropin Stimulation Test: Cosyntropin 250 mcg IV at time 0, with check of Serum Cortisol level at times 0, 30, and 60 minutes. Customarily performed at 06:00.

<table>
<thead>
<tr>
<th>Critical Illness</th>
<th>Mild Illness</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline level low</strong></td>
<td><strong>Baseline level high</strong></td>
</tr>
<tr>
<td>Cortisol Level</td>
<td>Interpretation</td>
</tr>
<tr>
<td>&lt; 15 mcg/dL</td>
<td>Relative adrenal insufficiency (RAI) likely</td>
</tr>
<tr>
<td>&gt; 34 mcg/dL</td>
<td>RAI unlikely</td>
</tr>
</tbody>
</table>

Baseline level in equivocal range: Perform Cosyntropin Stim Test

<table>
<thead>
<tr>
<th>Response to Cosyntropin Stim Test Inadequate</th>
<th>Response to Cosyntropin Stim Test Adequate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in baseline &lt; 9 mcg/dL</td>
<td>Change in baseline ≥ 9 mcg/dL</td>
</tr>
<tr>
<td>RAI likely</td>
<td>RAI unlikely</td>
</tr>
<tr>
<td>Level &lt; 18 mcg/dL</td>
<td>Level ≥ 18 mcg/dL</td>
</tr>
<tr>
<td>Diagnoses primary or secondary adrenal insufficiency</td>
<td>Rules out primary adrenal insufficiency (and most secondary)</td>
</tr>
</tbody>
</table>

Steroid Relative Potencies

<table>
<thead>
<tr>
<th>Steroid Compound</th>
<th>Relative Potency</th>
<th>Half life (hrs)</th>
<th>Mineralocorticoid Activity?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocortisone</td>
<td>20 (least potent)</td>
<td>8-12</td>
<td>Yes</td>
</tr>
<tr>
<td>Prednisone</td>
<td>5</td>
<td>18-36</td>
<td>No</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>5</td>
<td>18-36</td>
<td>No</td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>4</td>
<td>18-36</td>
<td>No</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>0.75 (most potent)</td>
<td>36-54</td>
<td>No</td>
</tr>
</tbody>
</table>

Adapted from: N Engl J Med 2003; 348: 731. Tarascon Internal Medicine, p. 80, Joseph Esherick MD.
Thyroid Storm

**Definition**
- Severe symptoms related to the release of large amounts of thyroid hormone
- Usually precipitated by surgery, sepsis, burns injury, DKA, cardiovascular accident, parturition, status epilepticus, I\textsuperscript{131} treatment or iodinated contrast dyes

**Diagnosis**
- Based on the Burch-Wartofsky Criteria for Thyroid Storm:

<table>
<thead>
<tr>
<th>Thermoregulatory Dysfunction</th>
<th>Central Nervous System Effects</th>
<th>Tachycardia</th>
<th>Congestive Heart Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temperature</td>
<td>Mild</td>
<td>99-109</td>
<td>Mild</td>
</tr>
<tr>
<td></td>
<td>Agitation</td>
<td>10</td>
<td>Pedal Edema</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>110-119</td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td>Delirium</td>
<td>120-129</td>
<td>Bibasilar Rales</td>
</tr>
<tr>
<td></td>
<td>Psychosis</td>
<td>130-139</td>
<td>Severe</td>
</tr>
<tr>
<td></td>
<td>Extreme Lethargy</td>
<td>≥140</td>
<td>Pulmonary Edema</td>
</tr>
<tr>
<td></td>
<td>Severe</td>
<td></td>
<td>Atrial Fibrillation</td>
</tr>
<tr>
<td></td>
<td>Seizure</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Coma</td>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>

- Score ≥45: Highly suggestive of Thyroid Storm
- Score 25-44: Supports the diagnosis of Thyroid Storm
- Score <25: Thyroid Storm is unlikely

**Treatment**
- Decrease the production and release of thyroid hormones
  - Block thyroid hormone synthesis
    - Methimazole 20 mg IV every 4–6 h (until able to take oral carbimazole 30 mg twice daily) (preferred)
    - Propylthiouracil 200 mg every 4 h (orally or via nasogastric tube) (will also block T4 to T3 conversion)
    - Both drugs can also be given per rectum.
  - Block conversion of T4 to T3
    - Lugol’s iodine (0.3 ml diluted to 50 ml every 8 h given orally or via nasogastric tube for 5 days) or SSKI 5 drops every 6 hours, > 1 hour after anti-thyroid drugs are administered
    - If iodine allergy, lithium carbonate 300 mg q 6 h, with twice daily lithium levels checked until a therapeutic level of 1 mmol/L
    - Steroids also do this: dexamethasone 4 mg IV qid or hydrocortisone 100 mg IV qid
- Block the effects of circulating T4 and T3
  - Propranolol 80 mg po tid or 1 mg/min intravenously until the pulse rate is <100
  - If Beta-blocker is contraindicated, consider calcium channel blockers or digoxin.
- Treat the underlying precipitants
- Supportive Care
  - Aggressive IV fluid resuscitation, Multivitamin, Thiamine
  - Acetaminophen for fever (AVOID salicylates)

**References:** Up to Date 2009, Postgraduate Medicine 2007; 83: 79-86.
Neurology: Delirium

Delirium in the ICU

Definition
- DSM IV: Disturbance of consciousness with inattention accompanied by a change in cognition or perceptual disturbance that develops over a short period (hours to days) and fluctuates over time.
- May also be described as an acute confusional state defined by fluctuating mental status, inattention, and either disorganized thinking or an altered level of consciousness.
- In the past, this has been labeled ‘ICU Psychosis’, ‘ICU Syndrome’, ‘Acute Confusional State’, ‘Septic Encephalopathy’, and ‘Acute Brain Failure’
- Should now be classified as ‘delirium’ and subclassified according to psychomotor symptoms (hyperactive, hypoactive, or mixed)
  - Hyperactive: characterized by agitation, restlessness, attempting to remove catheters, emotional lability; associated with better prognosis; estimated ~2% incidence
  - Hypoactive: withdrawal, flat affect, apathy, lethargy, decreased responsiveness; remains unrecognized in up to 66-84% of cases; carries a worse prognosis; estimated 43% incidence; “if you don’t look, you won’t find it”
    - Mixed: estimated 54% incidence
- Thought to be related to imbalances in neurotransmitters that modulate cognition, behavior, and mood.

Epidemiology
- Develops in 20-50% of lower-severity ICU patients not receiving mechanical ventilation
- Develops in 60-80% of ICU patients who are mechanically ventilated
- Occurrence of delirium causes a three-fold re-intubation rate and >10 day increase in hospital stay duration; also associated with a higher ICU and in-hospital mortality (3-fold increased risk of mortality at 6 months vs. those not delirious; unclear if there is causation or marker of unidentified covariate)
- Each additional day of delirium increases mortality (by 10%) and hospital stay (by 20%)
- 10-24% of patients experience persistent delirium that may be related to long-term cognitive impairment

<table>
<thead>
<tr>
<th>Predisposing</th>
<th>Precipitating (hospital-related or iatrogenic)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior dementia (delirium may also CAUSE dementia; up to 1/3 of mechanically ventilated patients will have some form of cognitive impairment that may be present for years)</td>
<td>Hypoxia</td>
</tr>
<tr>
<td>Advanced Age</td>
<td>Metabolic disturbances, Electrolyte imbalances</td>
</tr>
<tr>
<td>Chronic Illness (including hypertension)</td>
<td>Sleep deficits†</td>
</tr>
<tr>
<td>Depression</td>
<td>Congestive heart failure</td>
</tr>
<tr>
<td>Tobacco Abuse, Alcohol Abuse</td>
<td>Sepsis</td>
</tr>
<tr>
<td>Severity of Illness on Hospital Admission</td>
<td>Prolonged restraint use and immobility</td>
</tr>
<tr>
<td>Predictive model of delirium in hospitalized elders: 1 point each for visual impairment, cognitive impairment, severe illness (APACHE II &gt; 16 or nursing rating of severe), Blood Urea Nitrogen (BUN) &gt; 16: 3-4 points = 80% risk of delirium; 1-2 points = 25% risk of delirium</td>
<td>Withdrawal syndromes (alcohol, benzos, etc.)</td>
</tr>
<tr>
<td></td>
<td>Acute infections (systemic and intracranial)</td>
</tr>
<tr>
<td></td>
<td>Seizures</td>
</tr>
<tr>
<td></td>
<td>Dehydration or Hyperthermia</td>
</tr>
<tr>
<td></td>
<td>Head trauma</td>
</tr>
<tr>
<td></td>
<td>Vascular disorders</td>
</tr>
<tr>
<td></td>
<td>Intracranial space-occupying lesions</td>
</tr>
<tr>
<td></td>
<td>Medications (Benzodiazepines, Narcotics, Propofol, anticholinergics, anticonvulsants, antihistamines, psychiatric medications)</td>
</tr>
</tbody>
</table>

† ICU patients sleep on average 2 hours per day due to excessive noise/ lighting, patient care activities, sedatives and analgesics, ventilation, critical illness.
Assessment Tools for Delirium

ICU Delirium Screening Checklist
- Altered level of consciousness (if A or B, do not complete patient evaluation for the period)
  A: No response, score: none
  B: Response to intense and repeated stimulation (loud voice and pain), score: none
  C: Response to mild or moderate stimulation, score: 1
  D: Normal wakefulness, score: 0
  E: Exaggerated response to normal stimulation, score: 1
- Inattention (score: 0 to 1)
- Disorientation (score: 0 to 1)
- Hallucination-delusion-psychosis (score: 0 to 1)
- Psychomotor agitation or retardation (score: 0 to 1)
- Inappropriate speech or mood (score: 0 to 1)
- Sleep/wake cycle disturbance (score: 0 to 1)
- Symptom fluctuation (score: 0 to 1)
Total (score: 0 to 8): ≥ 4 points indicates delirium

Confusion Assessment Method (CAM-ICU)

Acute onset of mental status changes or a fluctuating course
AND
Inattention
AND
Disorganized thinking
OR
Altered Level of Consciousness
= Delirium

Treatment
- Non-pharmacologic risk factor modification in a non-ICU setting may reduce the incidence of delirium by 40%, and may be beneficial in ICU patients as well:
  o Repeated reorientation of patients
  o Repetitive provision of cognitively stimulating activities
  o Non-pharmacologic sleep protocol
  o Early mobilization
  o Range of motion exercises
  o Timely removal of catheters and physical restraints
  o Use of eyeglasses and magnifying lenses
  o Hearing aids, earwax removal
  o Adequate hydration
  o Use of a scheduled pain protocol
  o Minimizing excessive noise/stimuli
- Pharmacologic Prevention
  o Avoiding benzodiazepines
    ▪ GABA-mimetic medications result in decreased level of consciousness while impairing slow-wave sleep, which may predispose to delirium
    ▪ Daily interruption of sedatives and protocolizing their delivery improve outcomes
  o Consider use of dexmedetomidine for sedation (CABG patients who received post-operative sedation with dexmedetomidine had an 8% incidence of delirium vs. 50% with propofol or midazolam in an unblinded randomized trial) (more trials needed)
- Pharmacologic Treatment
  o Haloperidol
    ▪ Be vigilant for prolonged QT, extrapyramidal side effects, torsades de pointes, neuroleptic malignant syndrome, akathisia
    ▪ May reduce duration and severity of delirium but not its incidence
  o Atypical antipsychotics
  o Consider benzodiazepines ONLY if alcohol or benzodiazepine withdrawal, Parkinson’s disease, or neuroleptic malignant syndrome.

Anxiety / Agitation in the ICU

Agitation and Delirium

- The relationship is best described as such (some patients are agitated and not delirious, some patients are delirious but not agitated, and some are both)

Etiologies

- There is an imperative to rule out a “Medical Cause” of Anxiety / Agitation in the ICU.
- The most deadly potential medical causes of Anxiety / Agitation are hypercarbia and/or hypoxemia.
  - Obtain an ABG to rule out hypercarbia in any patient with increased work of breathing
    - Estimate your expected PCO₂ (should usually be 30 or below with very increased work of breathing except in CO₂ retainers, in whom the pH should be alkalotic); if the PCO₂ level is much higher than expected (even a “normal” PCO₂ of 40 or pH of 7.40 may be very abnormal in a patient with increased work of breathing), you need to treat their hypercarbia—treat the underlying cause, consider non-invasive ventilation if a candidate, observe the patient closely for response to therapy.
    - Giving benzodiazepines to an agitated patient who is actually in respiratory failure will worsen their respiratory failure and could be fatal.
    - Occasionally, very low-dose benzodiazepines (e.g. lorazepam 0.5mg or lower) may be given to aid an agitated patient in tolerating their non-invasive ventilation.
  - Other dangerous medical causes include, but are not limited to: hypotension, hypoglycemia, hyperglycemia, patient-ventilator dyssynchrony, alcohol or benzodiazepine withdrawal, severe hypertensive encephalopathy (which came first, the agitation or the hypertension?), sepsis, elevated intracranial pressure, intracranial or subarachnoid hemorrhage
  - Dangerous medical causes more likely to manifest as somnolence and lethargy but may still present as agitation include, but are not limited to: infections (systemic), meningitis, meningoencephalitis, acute renal failure, acute hepatic failure
  - Medications associated with agitation include:
    - Antibiotics (especially quinolones, also cephalosporins, amphotericin, imipenem, ketoconazole, penicillins, rifampin, trimethoprim-sulfamethoxazole, ketoconazole)
    - Anticholinergics (particularly in the elderly)
    - Anticonvulsants (phenobarbital, phenytoin)
    - Steroids
    - Narcotics
    - Benzodiazepines
    - Cardiac Drugs (digoxin, clonidine, dopamine, lidocaine, quinidine, procainamide)
    - Miscellaneous Drugs (ketamine, metoclopramide (Reglan), theophylline, NSAIDs)
  - Other medical conditions associated with agitation include: pain, B-12 deficiency, niacin deficiency, thiamine deficiency, heavy metal intoxications (lead, mercury, manganese), bladder distension, severe constipation, nausea, narcotic or other substance withdrawal
  - Isolated psychiatric Anxiety / Agitation, while very common in the ICU, needs to be a diagnosis of exclusion.

Treatment

- Always treat the underlying cause
- Anxiolytic medications are to be given only when serious causes of agitation have been ruled out; consider antipsychotics over benzodiazepines, particularly in the elderly, as they do not depress the respiratory drive
- Complications of agitation include patient removal of arterial/venous/urinary catheters, increased systemic and cardiac oxygen consumption, self extubation, falls, patient-ventilator dyssynchrony leading to worsening hypercarbia/hypoxia and leading to increasing agitation, etc.

References: Crit Care Med 2002; 30 [Suppl.]: S97-S123
## Altered Mental Status

### MOVE STUPID

<table>
<thead>
<tr>
<th>Metabolic</th>
<th>Seizure (postictal), Sugar</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxygen (hypoxemia), Overdose</td>
<td>Tumor/Trauma/Temperature/Toxins</td>
</tr>
<tr>
<td>Vascular (CVA, Vasculitis)</td>
<td>Uremia/liver</td>
</tr>
<tr>
<td>Endocrine (Addison's, Cushing's, thyroid, DM), Encephalopathy (hepatic)</td>
<td>Psychiatric, pain, porphyria</td>
</tr>
<tr>
<td></td>
<td>Infection, Intussusception, Inborn Errors of Metabolism</td>
</tr>
<tr>
<td></td>
<td>Drugs</td>
</tr>
</tbody>
</table>

### AEIOU TIPS

<table>
<thead>
<tr>
<th>Alcohols</th>
<th>Trauma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Encephalopathy, Electrolytes, Endo</td>
<td>Infection, Inborn Errors, Insulin</td>
</tr>
<tr>
<td>Intussusception, Infarct</td>
<td>Post-Ictal, Psychogenic</td>
</tr>
<tr>
<td>Overdoses</td>
<td>Sugar, Shock, Seizure, Stroke</td>
</tr>
<tr>
<td>Uremia</td>
<td></td>
</tr>
</tbody>
</table>

### Suggested Workup for Altered Mental Status

*(judgment should be applied on a case-by-case basis)*

- Perform a complete physical and neurologic exam, including assessing Glasgow Coma Scale
- Review the Medication List (if it’s new in the hospital, it could be a medication adverse effect)
- Comprehensive Metabolic Panel, Magnesium, Phosphorus
- Urine Toxicology Screen, Urinalysis
- CBCD
- Urine Culture, Blood Culture x 2, Sputum Culture if Indicated
- Chest X-Ray
- Non-contrast Head CT Scan

**Should Consider:**
- Lumbar Puncture
- ABG
- Head CT with Contrast or MRI
Coma

Glasgow Coma Scale

<table>
<thead>
<tr>
<th>Score</th>
<th>Eye opening</th>
<th>Verbal response</th>
<th>Motor response</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>-</td>
<td>-</td>
<td>Follows commands</td>
</tr>
<tr>
<td>5</td>
<td>-</td>
<td>Normal conversation</td>
<td>Localizes pain</td>
</tr>
<tr>
<td>4</td>
<td>Spontaneous</td>
<td>Disoriented/inappropriate</td>
<td>Withdraws to pain</td>
</tr>
<tr>
<td>3</td>
<td>To voice</td>
<td>Incoherent</td>
<td>Decorticate posturing</td>
</tr>
<tr>
<td>2</td>
<td>To pain</td>
<td>Moans</td>
<td>Decerebrate posturing</td>
</tr>
<tr>
<td>1</td>
<td>None</td>
<td>None</td>
<td>No movement</td>
</tr>
</tbody>
</table>

Approach to the Comatose Patient

- Bag-valve mask ventilation with 100% FiO₂
- Establish vascular access; check chemstick
- Give “coma cocktail”
  - Thiamine 100 mg IV
  - Dextrose 50% (D50) 50 mL (25 gm glucose) IV (if glucose < 60 mg/dL)
  - Naloxone 0.4-2 mg IV (can repeat q3 min if effective)
  - Flumazenil 0.2 mg IV q1-2 min (max 1 mg) only if benzodiazepine OD
    - **AVOID Flumazenil if concern for chronic benzodiazepine or alcohol abuse as it will precipitate acute withdrawal and potentially seizures**
- Perform a quick neurological exam prior to paralyzing patient

- Intubate if GCS≤8 or if severe agitation prohibits necessary testing
- Ventilate to normal pH; keep SaO₂≥92%
- Maintain a MAP≥70 mmHg
- If ↑ ICP, keep PaCO₂~35 mmHg; give mannitol 0.5-1 gm/kg IV; place ICP monitor

- **Labs:** CBCD, chemistry panel, ABG, TSH, ECG, CXR, cardiac enzymes, urine drug screen, acetaminophen, salicylate and blood alcohol levels, serum osmolality to calculate osmolar gap (>10 abnormal), urinalysis, and blood cultures x 2 (if infection possible)
- For overdoses: gastric lavage for ingestions ≤1 hour; then activated charcoal 0.5-1 g/kg po/ng (ineffective for alcohols, acids, alkali, carbamates, cyanide, DDT, hydrocarbons, iron, lead, lithium, mercury, organophosphates, potassium and solvents; consider whole bowel irrigation for enteric-coated/extended-release medications or “body packers”
- Noncontrast head CT

- Consider an EEG and lumbar puncture if etiology remains unclear
- Brain MRI unlikely to alter management but could be considered in equivocal cases

Adapted from Crit Care Med 2006; 34: 31
### Neurology: Coma

#### Disorders of Consciousness

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Arousal ‡ (state of wakefulness)</th>
<th>Awareness</th>
<th>Sleep/wake cyclic patterns</th>
<th>Motor function</th>
<th>Respiratory function</th>
<th>EEG Activity</th>
<th>Cerebral metabolism (% activity)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Brain death</strong></td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
<td>None</td>
<td>Absent</td>
<td>Electrographic silence</td>
<td>0%</td>
</tr>
<tr>
<td><strong>Coma (GCS≤8)</strong></td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
<td>Non-purposeful</td>
<td>Variable*</td>
<td>Polymorphic delta or theta</td>
<td>&lt;50%</td>
</tr>
<tr>
<td><strong>Vegetative state</strong></td>
<td>Present</td>
<td>Absent</td>
<td>Present</td>
<td>Non-purposeful</td>
<td>Present</td>
<td>Polymorphic delta or theta; sometimes slow alpha</td>
<td>40-60%</td>
</tr>
<tr>
<td><strong>Minimally conscious state</strong></td>
<td>Present</td>
<td>Partial</td>
<td>Present</td>
<td>Intermittently purposeful</td>
<td>Present</td>
<td>Mixed theta and alpha</td>
<td>50-60%</td>
</tr>
<tr>
<td><strong>Akinetic mutism</strong></td>
<td>Present</td>
<td>Partial</td>
<td>Present</td>
<td>Paucity of movement</td>
<td>Present</td>
<td>Diffuse nonspecific slowing</td>
<td>40-80%</td>
</tr>
</tbody>
</table>

‡ - comatose patients have no eye opening. * - disordered breathing patterns common in coma: Cheyne-Stokes respiration; central hyperventilation syndrome; apneustic breathing; or ataxic breathing. Adapted from Crit Care Med 2006; 34: 31.

### Differential Diagnosis List of Coma

**Primary Cerebral Disorders:**
- Traumatic brain injury (contusions, diffuse axonal injury); ischemia (thrombotic/embolic); intracranial hemorrhage; hypoxic-ischemic encephalopathy; brain tumor (metastasis or primary brain); cerebral vein thrombosis; meningoencephalitis; brain abscess; generalized or complex partial seizures, status epilepticus; hypertensive encephalopathy; hydrocephalus, brainstem disorder; osmotic demyelination syndrome
- Systemic Derangements Causing Coma:
  - Toxic ingestion (opiates, alcohol, methanol, ethylene glycol, amphetamines, cocaine) or medication (opioids, benzodiazepines, barbiturates, tricyclic, neuroleptics, aspirin, SSRIs, acetaminophen, anticonvulsants); carbon monoxide poisoning; heavy metal poisoning; severe hypoglycemia; diabetic ketoacidosis; hyperglycemic hyperosmolar coma; severe hyponatremia/hypernatremia or hypercalcemia; Systemic Inflammatory Response Syndrome; Hepatic Failure; Renal Failure; Wemicke’s encephalopathy; adrenal crisis; myxedema coma; thyroid storm, panhypopituitarism.

**Reference:** Crit Care Med 2006; 34: 34.
Weakness in the ICU

Differential Diagnosis of Weakness in the ICU

- Primary Brain or Spinal Cord or Nerve Root Disorder: infarct, tumor, encephalitis, multiple sclerosis, transverse myelitis, extrinsic compression from abscess or tumor, spinal stenosis, etc.
- Anterior Horn Cell Abnormalities: poliomyelitis, West Nile virus
- Myopathy: polymyositis, dermatomyositis, rhabdomyolysis, Critical Illness Myopathy, steroid myopathy
- Neuromuscular junction problems: organophosphate poisoning, myasthenia gravis, botulism, Lambert-Eaton myasthenic syndrome, acute quadriplegic myopathy syndrome from neuromuscular blockers (see page 189)
- Peripheral nerve problems: Acute Inflammatory Demyelinating Polyneuropathy (AIDP, Guillain-Barré Syndrome), Chronic Inflammatory Demyelinating Polyneuropathy (CIDP), Metabolic causes (hypokalemia, hypophosphatemia, hypocalcemia, hypomagnesemia), drug-induced neuropathy, porphyria, B1 deficiency (beri-beri), heavy metal poisoning, Critical Illness Neuropathy, neuromuscular blockers, tick paralysis

Myasthenia Gravis (MG)/ Myasthenic Crisis

Pathophysiology
- Autoimmune disorder caused by antibodies against skeletal muscle acetylcholine receptors
- Exacerbations (myasthenic crises) may be caused by infection, anti-cholinesterase medication, initiation of corticosteroids or other medications, or other unidentified factors

Medications implicated in worsening of Myasthenia Gravis
- Definite: Penicillamine, corticosteroids
- Probable: Aminoglycosides, ciprofloxacin, phenytoin, Beta-blockers, lithium, procainamide
- Possible: Anticholinergics, ampicillin, erythromycin, verapamil, chloroquine, neuromuscular blockers

Intubation criteria
- VC < 15 ml/kg; wet, gurgling, or stridorous voice

Extubation criteria
- Weaning trials when VC > 10 ml/kg, NIF better than -20 cm H$_2$O, and positive expiratory force > 40cm H$_2$O; consider extubation for > 4 hrs of stable VC > 10 ml/kg or T-piece tolerated for > 4 hrs

Treatment/Medical Management
- Cardiac monitoring (14% of patients with myasthenic crisis have some degree of arrhythmia)
- Once the patient is intubated, the anticholinesterase medication is usually stopped
- Resume anticholinesterase medication at half the previous dose when starting ventilator wean
- Therapeutic plasma exchange (TPE), 2-3 L qod x 5-6 treatments
- Alternatively, IVIg 2 g/kg total dose over 2-5 days may be less effective than TPE
- Improvement seen with TPE or IVIg is transient; longer-term therapies must be continued:
  - Prednisone 1 mg/kg/day x 4 weeks, then slow (2.5mg/week) taper over months to lowest effective dose OR
  - Azathioprine (unclear when to start, dose); OR cyclosporine; OR mycophenolate mofetil
- Thymectomy may be beneficial in those patients with thymoma + MG, but not during a myasthenic crisis

Guillain-Barré Syndrome (GBS): Acute Inflammatory Demyelinating Polyneuropathy

Pathophysiology
- Most commonly caused by post-infection antibodies (to Campylobacter, CMV, EBV, Haemophilus, Mycoplasma, etc.) that cross-react with gangliosides in peripheral nerves

Diagnosis
- Clinical criteria, required for diagnosis:
  - Acute rapidly progressive symmetrical weakness with or without sensory disturbance (pain, numbness) beginning in the legs or legs and arms and progressing proximally
  - Areflexia or hyporeflexia
- Clinical criteria, supportive of diagnosis: Progression of symptoms from days to 4 weeks; symmetry of symptoms; relatively mild sensory symptoms; cranial nerve involvement; autonomic dysfunction; pain (often present)
- CSF criteria: Protein > 45 mg/dL (may be normal initially, but should be high by 3 weeks); acellular CSF (if high CSF WBCs, consider poliomyelitis, HIV, Lyme, West Nile, etc.)
- EMG criteria: Nerve conduction velocity < 80% of normal and/or absent or prolonged F waves
- Features that should raise doubt as to the diagnosis: Severe pulmonary dysfunction with limited limb weakness at onset, severe sensory signs with limited weakness at onset, bladder or bowel dysfunction at onset, fever at onset, sharp sensory level, slow progression with limited weakness without respiratory involvement (consider subacute inflammatory demyelinating polyneuropathy or CIDP), marked persistent asymmetry of weakness, persistent bladder or bowel dysfunction, increased number of mononuclear cells in CSF (>50×10⁶/L), polymorphonuclear cells in CSF

Management
- IVIg or Therapeutic Plasma Exchange (TPE) preferably started within first 2 weeks:
  - IVIg: 400 mg/kg daily x 5 days
  - TPE: Five 50ml/kg exchanges over 8 to 13 days
  - If patient is ambulatory (with or without assistance) without autonomic instability (“mild” disease), may consider observation alone
- Check Vital Capacity (VC) and Negative Inspiratory Force (NIF) q 4-8 hours until sustained improvement is seen
- When Vital Capacity < 30 ml/kg, start pulmonary toilet and strengthening exercises
  - Incentive Spirometer 10 times per hour while awake
  - Chest physiotherapy with EZ-Pap or Intermittent Positive Pressure Breaths q 4 hours
- Elective Intubation for: VC < 20ml/kg, NIF < -30, decline of VC or NIF >30% in 24 hours, or aspiration/ inability to protect airway; consider for difficulty swallowing
  - Start ventilator weaning when VC 8-10 ml/kg
  - Consider extubation when VC 20 ml/kg, NIF > -35 and meets usual extubation criteria
- ICU admission for: intubation criteria, autonomic instability (e.g. blood pressure and pulse lability, ileus, pupillary changes), rapid progression of weakness, planned TPE, difficulty swallowing

Prognosis
- Maximum weakness usually by 2 weeks, always by 4 weeks
- Plateau phase of weakness: several weeks to months
- If admitted to hospital unable to walk, 25% will require mechanical ventilation
- Despite IVIg or plasma exchange, 20% of severely affected patients cannot walk after 6 months
- Some patients will deteriorate after initial improvement; repeating the IVIg is often helpful in this situation.

Critical Illness Polyneuropathy/ Myopathy (CIP/M)

Clinical presentation
- Symmetric limb muscle weakness, often with sparing of the cranial nerve musculature
- There may be reduced or absent deep tendon reflexes and sensory loss
- Nerve conduction studies: reduction of the amplitude of compound motor and sensory nerve action potentials without changes in latency or conduction velocity = sensorimotor axonal polyneuropathy
- Electromyography shows fibrillation and positive sharp waves consistent with denervation changes
- Muscle biopsy often shows myopathic change with critical illness myopathy

Risk factors
- Usually occurs in the setting of multi-organ failure/sepsis; most patients are already intubated
- Risk factors include female gender, increased number of days with multi-organ failure, longer duration of mechanical ventilation, hyperglycemia (tight glycemic control may prevent), and use of corticosteroids, neuromuscular blockers, aminoglycosides, catecholamines, and parenteral nutrition.

Prognosis
- Mortality rate may be up to 50%; chance of complete recovery up to 50%
- Duration of intubation prolonged in patients with CIP/M to an average of 5 weeks in 1 study
- There is no specific treatment; treatment is supportive once the syndrome develops

Wound Botulism

Definition
- Progressive descending flaccid paralysis caused by the neuroparalytic botulinum toxin released by Clostridium botulinum infection of wounds (may also taint food products such as honey = botulism)

Clinical Characteristics
- Weakness begins with cranial nerve palsies (ptosis, diplopia, dysarthria) and progresses distally
- Most often occurs with injection of black-tar heroin (“skin-popping”)
- Most patients will have an infected wound, though some may not have an obvious site of infection.
- CSF studies are normal
- EMG testing shows augmentation of muscle action potentials on repetitive stimulation

Management
- Early (<24 hr.) administration of anti-toxin (prior to or during debridement of wounds) is paramount
  - Prior to administration of anti-toxin, draw 30ml of whole blood into red top tubes labeled ‘pre-antitoxin serum’ and send to the Ventura County Department of Public Health, who will facilitate the release of anti-toxin from the CDC (call public health directly if anti-toxin needed)
  - Indicate if the patient has received neostigmine bromide, neostigmine methyl sulfate, pyridostigmine bromide, mepinovin/timespan (used in tensilon test), ambenonin chloride, or IVIg prior to the administration of anti-toxin
  - May repeat anti-toxin in 3 to 5 days if continued neurologic deterioration
- Debridement of all wounds, including un-infected injection sites that may harbor the bacteria/toxin
- If concern for food botulism, consider gastric lavage and/or charcoal
- Penicillin G 3 million units q 4 hours (or metronidazole for penicillin-allergic patients)
- Consider broader spectrum antibiotics for suspected poly-microbial infections
- Avoid aminoglycoside antibiotics and magnesium for risk of potentiating effects of the toxin
- Vaccinate against tetanus if not up to date
- Admit to ICU if any concern for ability to protect airway (e.g. absence of gag), cranial nerve involvement, or any complaints of shortness of breath; progression to respiratory failure may be rapid
- Formal assessment of swallow function prior to feeding if concern for weakness
- Intubation indicated for inability to protect airway, lack of gag reflex, or VC < 30% of predicted

Analgesia and Sedation in the ICU

What’s the goal of sedation? (Make patients tolerate their ET Tube? Treat Agitation? Ensure No Memory of Painful/difficult things? Usually RASS -2 to -3 is ideal for intubated patients)

**Richmond Agitation/Sedation Score**

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
<th>Detailed Description</th>
<th>Score</th>
<th>Description</th>
<th>Detailed Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>+4</td>
<td>Combative</td>
<td>Combative, violent, immediate danger to self</td>
<td>-1</td>
<td>Drowsy</td>
<td>Not fully alert, but has sustained awakening to voice (eye opening &amp; contact &gt; 10 sec)</td>
</tr>
<tr>
<td>+3</td>
<td>Very agitated</td>
<td>Pulls or removes tube(s) or catheter(s); aggressive</td>
<td>-2</td>
<td>Light sedation</td>
<td>Briefly awakens to voice (eye opening and contact &lt; 10 sec)</td>
</tr>
<tr>
<td>+2</td>
<td>Agitated</td>
<td>Frequent nonpurposeful movement, fights ventilator</td>
<td>-3</td>
<td>Moderate sedation</td>
<td>Movement or eye opening to voice (but no eye contact)</td>
</tr>
<tr>
<td>+1</td>
<td>Restless</td>
<td>Anxious, apprehensive but movements are not aggressive or vigorous</td>
<td>-4</td>
<td>Deep sedation</td>
<td>No response to voice, but movement or eye opening to physical stimulation</td>
</tr>
<tr>
<td>0</td>
<td>Alert and Calm</td>
<td></td>
<td>-5</td>
<td>Unarousable</td>
<td>No response to voice or physical stimulation</td>
</tr>
</tbody>
</table>

What is the goal of analgesia? (Usually to control pain while minimizing side effects)

**Ventura County Medical Center Observational Pain Scale (VOPS)**

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
<th>Detailed Description</th>
<th>Score</th>
<th>Description</th>
<th>Detailed Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Relaxed, neutral:</td>
<td>No muscular tension observed</td>
<td>1</td>
<td>Tense:</td>
<td>Presence of frowning, brow lowering, orbit tightening, &amp; levator contraction</td>
</tr>
<tr>
<td></td>
<td>Grimacing:</td>
<td>All of the facial expressions for 1 point + eyelids tightly closed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Absence of Movements</td>
<td></td>
<td>2</td>
<td>Restlessness:</td>
<td>Pulling at tube, attempting to sit up, moving limbs or thrashing, not following commands, striking at staff, trying to climb out of bed</td>
</tr>
<tr>
<td>2</td>
<td>Relaxed:</td>
<td>No resistance to passive movement</td>
<td></td>
<td>Very Tense or Rigid:</td>
<td>Strong resistance to passive movements, inability to complete them</td>
</tr>
<tr>
<td></td>
<td>Fighting Ventilator:</td>
<td>Coughing but tolerating the ventilator: Alarms stop spontaneously OR Sighing, moaning</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Tense, Rigid:</td>
<td>Resistance to passive movements</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fighting Ventilator:</td>
<td>Asynchrony; blocking ventilation; alarms frequently activated OR Crying out, sobbing, tearing</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Modifiers:**

- Known mildly painful procedure or condition (see list next page): +1
- Known moderately to severely painful procedure or condition (see list next page): +2
- Unexplained elevated blood pressure, heart rate, or respiratory rate over baseline: +1
- Unexplained **markedly** elevated BP, heart rate, or respiratory rate over baseline: +2

The scale is to be recorded hourly with the vital signs. Scores of ≥10 are recorded as 10.

* - VCMC Observational Pain Scale is utilized if a patient cannot self-report pain; desire a VOPS score <3
Adapted from the Critical Care Pain Observation Tool in American Journal of Critical Care. 2006; 15(4):420-427
‡ - Note: This scale does not apply to patients who are receiving neuromuscular blockers
## Common Causes of Acute Pain

<table>
<thead>
<tr>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suctioning</td>
</tr>
<tr>
<td>Incisional pain</td>
</tr>
<tr>
<td>Pleuritic Chest Pain</td>
</tr>
<tr>
<td>Immobility</td>
</tr>
<tr>
<td>Patient turning</td>
</tr>
<tr>
<td>Dressing changes</td>
</tr>
<tr>
<td>MI or myocarditis</td>
</tr>
<tr>
<td>Line placement</td>
</tr>
<tr>
<td>Invasive Procedures</td>
</tr>
<tr>
<td>Presence of tubes (ETT/chest tubes/NGT/OGT)</td>
</tr>
</tbody>
</table>

## Common Causes of Acute Anxiety

<table>
<thead>
<tr>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep disturbance</td>
</tr>
<tr>
<td>Head Injury</td>
</tr>
<tr>
<td>Visceral pain</td>
</tr>
<tr>
<td>Neuropathies</td>
</tr>
<tr>
<td>Invasive Procedures</td>
</tr>
</tbody>
</table>

### Sedative Table

<table>
<thead>
<tr>
<th>Agent</th>
<th>Half-Life/ Metabolism</th>
<th>Intermittent IV Dosing</th>
<th>Continuous Infusion</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sedatives</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Propofol</strong></td>
<td>26-32min/ Renal</td>
<td>40mg q 10 seconds up to 2-2.5mg/kg</td>
<td>5-80 (max 300) mcg/kg/min</td>
<td>Short-acting; easily titratable; good prior to extubation</td>
<td>Hypotension, metabolic acidosis, ↑triglycerides; bradycardia, inflammation</td>
</tr>
<tr>
<td><strong>Ketamine</strong></td>
<td>0.25-2.5h/ Hepatic</td>
<td>1-2mg/kg IV over 5 min</td>
<td>0.1-5mg/min†</td>
<td>Analgesia; amnesia; anxiolysis; ↑BP; no resp. depression</td>
<td>↑ICP/BP/Pulse/ocular pressure; emergence reactions; hypersalivation; laryngospasm (rare)</td>
</tr>
<tr>
<td><strong>Midazolam</strong></td>
<td>3-11h/ Hepatic</td>
<td>0.02-0.08mg/kg q 0.5-2 h</td>
<td>0.04-0.2 mg/kg/hr</td>
<td>All: Anxiolysis, Amnesia, Sedation Lorazepam; has no prolonged sedation</td>
<td>All: Hypotension, Respiratory depression Diazepam/Midazolam drip; Prolonged sedation Lorazepam/Diazepam drip; Propylene glycol toxicity (acidosis, renal failure, high osmolar gap)</td>
</tr>
<tr>
<td><strong>Lorazepam</strong></td>
<td>8-15h/ Hepatic</td>
<td>0.02-0.06mg/kg q 2-6 h</td>
<td>0.01-0.1 mg/kg/hr</td>
<td>All: Sedation Diazepam/Midazolam drip: Prolonged sedation Lorazepam/Diazepam drip; Propylene glycol toxicity (acidosis, renal failure, high osmolar gap)</td>
<td></td>
</tr>
<tr>
<td><strong>Diazepam</strong></td>
<td>40-100 h/ Hepatic</td>
<td>0.03-0.1mg/kg q 0.5-6 h</td>
<td>N/A</td>
<td>All: No respiratory depression; good for EtOH/ drug withdrawal</td>
<td>Hypotension; high cost; bradycardia; dry mouth; adrenal suppression; afib</td>
</tr>
<tr>
<td><strong>Dexmedetomidine</strong></td>
<td>2h/ Hepatic</td>
<td>N/A</td>
<td>0.2-0.7 mcg/kg/hour</td>
<td>All: Analgesia, sedation, reversibility Fentanyl: rapid onset, short duration, less hypotension</td>
<td>All: GI Hypomotility Respiratory depression Hypotension (esp. Morphine) Morphine: Itching Fentanyl: rigid chest wall</td>
</tr>
<tr>
<td><strong>Analgesics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Fentanyl</strong></td>
<td>1.5-6h/ Hepatic</td>
<td>0.35-1.5mcg/kg q 1/2-1h</td>
<td>0.6-10 mcg/kg/hr</td>
<td>All: Analgesia, sedation, reversibility Fentanyl: rapid onset, short duration, less hypotension</td>
<td>All: No respiratory depression; good for agitation</td>
</tr>
<tr>
<td><strong>Hydromorphone</strong></td>
<td>2-3h/ Hepatic</td>
<td>10-30mcg/kg q 1-2h</td>
<td>7-15 mcg/kg/hr</td>
<td>All: Analgesia, sedation, reversibility Fentanyl: rapid onset, short duration, less hypotension</td>
<td>All: Seizures Haloperidol (especially IV): Prolonged QT</td>
</tr>
<tr>
<td><strong>Morphine</strong></td>
<td>3-7h/ Hepatic</td>
<td>0.01-0.15mg/kg q 1-2h</td>
<td>0.07-0.5 mg/kg/hr</td>
<td>All: Analgesia, sedation, reversibility Fentanyl: rapid onset, short duration, less hypotension</td>
<td>All: Seizures Haloperidol (especially IV): Prolonged QT</td>
</tr>
<tr>
<td><strong>Antipsychotics/Neuroleptics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Haloperidol</strong></td>
<td>21-24h/H</td>
<td>0.5-10mg IM/IV q 1-4 h</td>
<td>N/A</td>
<td>All: No respiratory depression; good for agitation</td>
<td>All: Seizures Haloperidol (especially IV): Prolonged QT</td>
</tr>
<tr>
<td><strong>Zyprexa</strong></td>
<td>21-54h/H</td>
<td>IM:10mg q12h</td>
<td>N/A</td>
<td>All: No respiratory depression; good for agitation</td>
<td>All: Seizures Haloperidol (especially IV): Prolonged QT</td>
</tr>
</tbody>
</table>

† Midazolam usually given with Ketamine drips to avoid emergence reactions; Ratio ketamine:midazolam = 25:1 to 40:1

(Drip Usually Administered: Ketamine 500mg + midazolam 25mg in NS 250mg titrated to RASS -2 to -3)

Metabolism: H=Hepatic

Ventura County Medical Center Guideline for Sedation and Analgesia in Ventilated Patients

Is pt comfortable and at target RASS level?
- Yes: Continue current care
  - Perform daily awakening trial (see reverse for contraindications to daily awakening trial)
- No: Any reversible cause of pain or anxiety? (see back page)

PAIN
- Is pain level >3?
  - Yes: Fentanyl 0.5-1 mcg/kg (20-100 mcg) IV q3min prn OR Hydromorphone 0.25-2 mg IV q3 min prn
  - No: Opiate drip at 50% total bolus dose every hour
    - If pain uncontrolled at 60 min, bolus 50% drip rate (to max 100 mcg) and ↑ drip by 50% (max ↑ 100 mcg/hr)
    - If oversedated, hold drip until target RASS score then decrease drip by 50%
- Is VOPIS score >2?
  - Yes: Fentanyl or Hydromorphone as above
  - No: Dexmedetomidine (Precedex)
    - DO NOT BOLUS
    - Initiate drip at 0.5 mcg/kg/hour
    - Titrate between 0.2-1.4 mcg/kg/hr every 30-60 min; caution if CrCl<50mL/min
    - Maximal duration of use is 5 days
    - Avoid in AV block/severe bradycardia

ANXIETY
- Is pt anxious?
  - Yes: Propofol 0.5 mg/kg IV load then start drip at 20 mcg/kg/min
  - No: Ketamine 1 mg/kg IV bolus over 2-3 min; then start drip at 0.25-1 mg/kg/hour
    - Start midazolam 1 mg IV q4h (hold for excessive sedation)
    - Maximal duration of use is 3 days
    - Avoid if increased ICP/IOP, severe hypertension, psychosis
- Is RASS score >0?
  - Yes: Lorazepam or midazolam 1-2 mg IV q10min titrated to target RASS then q2h prn
    - If benzos needed >q2h, start midazolam infusion at 1-2 mg/hr (AVOID lorazepam drip)
    - If undersedated in 60 min, bolus with 50% drip rate and increase drip by 50%
    - If oversedated, hold drip until target RASS score then decrease drip by 50% or restart intermittent dosing q2h prn
    - Max duration of midazolam drip is 72h; 24h if BMI>30, liver failure or renal failure (CrCl<30 mL/min)
  - No: Haloperidol 5-10 mg PO/IV q12h q4h prn (1-2 mg q12h if elderly) (avoid if prolonged QT interval >500 msec)
    - Olanzapine 5-10 mg PO/IM daily-bid (2.5-5 mg daily-bid if elderly) (max 20mg/day)
    - Continue antipsychotics for 24 hours past delirium
    - Sleep aids: Ambien 5-10 mg PO qhs or alternative
    - Hold antipsychotics and sleep aids for over-sedation

DELIRIUM
- Is pt delirious? (CAM-ICU)
  - Yes: Control ambient noise
    - Bundle nighttime care
    - Early mobilization
    - Hearing aids
    - Avoid dehydration
  - OR: Turn off lights
    - Frequent reorientation
    - Remove unnecessary lines
    - Glasses
    - Ear muffs and eye shades at night
    - BP cuff check q4 h in hemodynamically stable sleeping patients
Procedural Sedation

Indications for procedural sedation:
- Patient factors: anxiety, pre-existing pain
- Procedure factors: Painful, requires motionless patient, duration

Common inpatient procedures that may require procedural sedation
- Non-emergent chest tube placement
- Bone marrow biopsy and aspiration
- Synchronized cardioversion
- Biopsy or I&D procedures
- Deep line placement
- Laceration Repair
- Foreign Body removal
- Shoulder, hip or elbow dislocations
- CT or MRI scan sedation
- Any procedure that MAY cause pain or anxiety

<table>
<thead>
<tr>
<th>Sedation Level</th>
<th>Level of Consciousness</th>
<th>Response to Verbal</th>
<th>Response to Tactile</th>
<th>Airway Patency</th>
<th>Ventilation &amp; Oxygenation</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>Fully aware</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>P</td>
</tr>
<tr>
<td>Light</td>
<td>Sedated</td>
<td>P-L</td>
<td>P</td>
<td>P</td>
<td>P</td>
</tr>
<tr>
<td>Moderate</td>
<td>Somnolent</td>
<td>L-A</td>
<td>P-L</td>
<td>P-L</td>
<td>P-L</td>
</tr>
<tr>
<td>Deep</td>
<td>Obtunded</td>
<td>A</td>
<td>L (noxious)</td>
<td>L-A</td>
<td>L</td>
</tr>
<tr>
<td>General Anesthesia</td>
<td>Unconscious</td>
<td>A</td>
<td>A</td>
<td>A</td>
<td>L-A</td>
</tr>
</tbody>
</table>

P= present; L = limited/ mildly abnormal; A = absent/ inadequate; * may need supplemental oxygen

Procedural sedation for Moderate – Deep sedation
- No clear liquids for ≥ 2 hours or food for ≥ 6 hours
- Monitor continuous heart rate, oximetry, and end tidal CO2 levels
  - Absolute number not as important as a trend; if trend up in end tidal CO2, corresponds to increased PCO2 and decreased ventilation; airway manipulation/ insertion of nasal trumpet or oral airway may be necessary
- Monitor blood pressure and level of consciousness every 5-10 minutes until level of sedation returns to ‘light’ or ‘none’
- Equipment readily available: suction equipment, supplemental oxygen, oral airway, nasal trumpet, bag-valve mask equipment, emergency airway cart, crash cart/ defibrillator

Adapted with permission from Joseph Esherick, MD
Neurology: Neuromuscular Blockade

Neuromuscular Blocking Agents (NMBAs)

### Indications for Sustained Neuromuscular Blockade
- Ventilator-patient dyssynchrony when all other modalities have been exhausted
- Severe refractory ARDS when all other modalities have been exhausted
- Tetanus
- Elevated Intracranial pressure when all other modalities have been exhausted

### Non-depolarizing Agents

<table>
<thead>
<tr>
<th>Agent</th>
<th>Loading Dose</th>
<th>Infusion Rate</th>
<th>Duration</th>
<th>Elimination</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aminosteroidal NMBAs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pancuronium</td>
<td>0.06-0.1mg/kg</td>
<td>N/A</td>
<td>90-100 m</td>
<td>45-70%R</td>
<td>Tachycardia; active metabolites</td>
</tr>
<tr>
<td>Pipecuronium</td>
<td>0.85-0.1mg/kg</td>
<td>N/A</td>
<td>90-100 m</td>
<td>50+%R</td>
<td></td>
</tr>
<tr>
<td>Vecuronium</td>
<td>0.08-0.1mg/kg</td>
<td>N/A</td>
<td>35-45 m</td>
<td>50%R; 35-50%H</td>
<td>Active Metabolites</td>
</tr>
<tr>
<td>Rocuronium</td>
<td>0.6-1mg/kg</td>
<td>N/A</td>
<td>30 min</td>
<td>33%R; &lt;75%H</td>
<td>Tachycardia at higher doses</td>
</tr>
<tr>
<td>Benzylisoquinolinium NMBAs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>d-tubocurarine</td>
<td>0.1-0.2mg/kg</td>
<td>N/A</td>
<td>80 min</td>
<td>45%R; 10-40%H</td>
<td>Histamine release, hypotension</td>
</tr>
<tr>
<td>Atracurium</td>
<td>0.4-0.5mg/kg</td>
<td>4-12mcg/kg/min</td>
<td>40-60 m</td>
<td>E</td>
<td></td>
</tr>
<tr>
<td>cis-atracurium</td>
<td>0.1-0.2mg/kg</td>
<td>2.5-3mcg/kg/min</td>
<td>90 min</td>
<td>E</td>
<td></td>
</tr>
<tr>
<td>Doxacurium</td>
<td>0.025-0.05mg/kg</td>
<td>0.3-0.5mcg/kg/m</td>
<td>120-150m</td>
<td>70%R;</td>
<td></td>
</tr>
<tr>
<td>Mivacurium</td>
<td>0.15-0.25mg/kg</td>
<td>9-10mcg/kg/min</td>
<td>10-20 min</td>
<td>R+H, unclear</td>
<td></td>
</tr>
</tbody>
</table>

R=Renal Metabolism; H= Hepatic Metabolism; E=Hoffman Elimination

### Management of Neuromuscular Blockade
- Ensure adequate sedation
- Monitor train-of-four ratio
  - One or two twitches when 4 twitches are administered
- Protect eyes (eye lubricant (e.g. Lacrilube), tape eyes shut)
- Position patient to protect pressure points
- Ensure no disconnection from the ventilator as the patient will not be able to breathe
- Reassess every 12-24 hours for continued indication for neuromuscular blockade

### Complications of NMBAs
- Risk of generalized deconditioning, skin breakdown, peripheral nerve injury
- Tachyphylaxis (if significant tachyphylaxis develops, switching to another NMBA is reasonable)
- Acute Quadriplegic Myopathy Syndrome (AQMS)
  - Acute Paresis, myonecrosis with increased creatinine phosphokinase (in ~50% of patients), abnormal electromyogram (EMG); characterized by severely reduced (low-amplitude) compound motor action potential (CMAP) and evidence of acute denervation; Global motor deficit in upper and lower extremities; extracocular motor function is usually preserved; normal or near-normal sensory nerve conduction studies
  - Worse with co-administration with steroids (up to 30% risk) (consider serial CPK checks if on steroids with NMBAs), aminoglycosides, cyclosporine, hyperglycemia, renal and hepatic dysfunction, fever, severe electrolyte or metabolic disorders
  - Muscle biopsy indicated for diagnosis (myonecrosis, type 2 fiber atrophy)
  - Drug holidays may decrease the incidence of AQMS
- Prolonged Recovery from Neuromuscular Blocking Agents
  - Steroid-based NMBAs have active metabolites
  - Worse with spinal cord injury, prolonged use
- Myositis Ossificans (heterotopic ossification) of connective tissue of muscles, ligaments, tendons, fascia, aponeuroses, joint capsules

## Alcohol Abstinence Syndromes

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Time from last drink</th>
<th>Clinical Presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Withdrawal tremulousness</td>
<td>6-36 hrs (typically 6-12 hrs)</td>
<td>Tremulousness; anxiety; insomnia; headache; palpitations; nausea; anorexia; &amp; palpitations</td>
</tr>
<tr>
<td>Withdrawal hallucinosis</td>
<td>12-48 hrs (typically 12-24 hrs)</td>
<td>Visual&gt;auditory or tactile hallucinations; orientation and sensorium usually maintained</td>
</tr>
<tr>
<td>Withdrawal seizures</td>
<td>6-48 hrs (typically 24-48 hrs)</td>
<td>Generalized, tonic-clonic and typically self-limited</td>
</tr>
<tr>
<td>Delirium tremens</td>
<td>48-96 hrs (peaks at 120 hrs)</td>
<td>Hallucinations; disorientation; sensorium clouded; and marked autonomic instability</td>
</tr>
</tbody>
</table>


### Clinical Institute Withdrawal Assessment for Alcohol (CIWA-Ar) Scale*

<table>
<thead>
<tr>
<th>Clinical Symptom</th>
<th>0 points</th>
<th>1 point</th>
<th>2 points</th>
<th>4 points</th>
<th>7 points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea/emetis</td>
<td>None</td>
<td>Mild nausea</td>
<td></td>
<td>Occ. nausea/ dry heaves</td>
<td>Constant nausea and vomiting</td>
</tr>
<tr>
<td>Tremor</td>
<td>None</td>
<td>Can be felt</td>
<td></td>
<td>Moderate tremor</td>
<td>Severe tremor</td>
</tr>
<tr>
<td>Diaphoresis</td>
<td>None</td>
<td>Palms moist</td>
<td></td>
<td>Beads of sweat on forehead</td>
<td>Drenching sweats</td>
</tr>
<tr>
<td>Anxiety</td>
<td>None/calm</td>
<td>Mild anxiety</td>
<td></td>
<td>Moderate anxiety</td>
<td>Severe, or panic state</td>
</tr>
<tr>
<td>Agitation</td>
<td>None</td>
<td>Slight</td>
<td></td>
<td>Moderate; fidgety, restless</td>
<td>Severe, pacing, thrashing about</td>
</tr>
<tr>
<td>Tactile disturbance</td>
<td>None</td>
<td>Mild itching or paresthesias</td>
<td></td>
<td>Moderate occ. Hallucinosis</td>
<td>Continuous hallucinosis</td>
</tr>
<tr>
<td>Auditory disturbance</td>
<td>None</td>
<td>Very mild sounds</td>
<td></td>
<td>Moderate occ. Hallucinosis</td>
<td>Continuous hallucinosis</td>
</tr>
<tr>
<td>Visual Disturbance</td>
<td>None</td>
<td>Mild sensitivity to light</td>
<td></td>
<td>Moderate occ. Hallucinosis</td>
<td>Continuous hallucinosis</td>
</tr>
<tr>
<td>Headache or Head Fullness</td>
<td>None</td>
<td>Very mild headache</td>
<td></td>
<td>Moderate headache</td>
<td>Extremely severe</td>
</tr>
<tr>
<td>Level of Orientation</td>
<td>Oriented + can do serial additions</td>
<td>Unsure of date; or unable to add</td>
<td>Date disorientation by ≤ 2 days</td>
<td>Disoriented to person or place</td>
<td></td>
</tr>
</tbody>
</table>

* CIWA-Ar score is generally appropriate for non-ICU patients up to moderately-severe alcohol withdrawal.

### Suggested Treatment Regimen for Alcohol Abstinence Syndrome

<table>
<thead>
<tr>
<th>CIWA-Ar Score</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-9</td>
<td>Lorazepam 1 mg IV</td>
</tr>
<tr>
<td>10-19</td>
<td>Lorazepam 2 mg IV; chlordiazepoxide 25 mg or diazepam 5 mg PO</td>
</tr>
<tr>
<td>20-29</td>
<td>Lorazepam 3 mg IV; chlordiazepoxide 50 mg or diazepam 10 mg PO</td>
</tr>
<tr>
<td>30-39</td>
<td>Lorazepam 4 mg IV; chlordiazepoxide 75 mg or diazepam 15 mg PO</td>
</tr>
<tr>
<td>&gt;40</td>
<td>Lorazepam 6 mg IV q1h until score&lt;30; may need continuous infusion</td>
</tr>
</tbody>
</table>

- Assess CIWA-Ar score q4 hrs if score <20; q2h for score 20-30; and q1h if score >30
- Minimal withdrawal if score<8; Mild withdrawal if score 8-15; and moderate symptoms for score 16-29; severe symptoms for score 30-39 and extremely severe for score≥40.

References: Adapted from CIWA-Ar scale in Brit J Addiction 1989; 84: 1353; J Addictive Diseases 2006; 25: 17
Protocol for ICU Management of Severe Alcohol Withdrawal: MINDS Score

For MINDS Score > 20
1. If less than 16 mg of lorazepam have been given in the last 12 hours, give lorazepam 4 mg IV now and recheck MINDS score and RASS score in 15 minutes.
2. If 16 mg lorazepam or more have been given in last 12 hours but no infusion is running, give lorazepam 4 mg IV now, start dexmedetomidine infusion at 0.5 mcg/kg/hr and recheck MINDS score and RASS score in 15 minutes.
3. If dexmedetomidine infusion is running, then increase infusion by 0.2 mcg/kg/hr every 15 minutes, continuing to increase drip by 0.2 mcg/kg/hr every 15 minutes to a maximum infusion rate of 1.4 mcg/kg/hr.
4. If dexmedetomidine infusion is at rate of 1.4 mcg/kg/hr, notify ICU physician, who should consider adding alternative agents.
5. Continue to check MINDS score and RASS score every 15 minutes.

For MINDS Score 15 to 19
1. Check MINDS score and RASS score every 1 hour.
2. If not on infusion, give lorazepam 4 mg IV every 1 hour as needed for tremor or agitation.
   Hold for RASS score -2, -3, -4 or -5.
3. If on dexmedetomidine infusion, continue at current rate.
4. Continue to check MINDS score and RASS score every 1 hour.

For MINDS Score < 15
1. Check MINDS score and RASS score every 2 hours.
2. If not on infusion, give lorazepam 2 mg IV every 1 hour as needed for tremor, agitation. Hold for RASS score -3, -4 or -5.
3. If on dexmedetomidine infusion, decrease infusion rate by 0.2 mcg/kg/hr.
4. Continue to check MINDS score and RASS score every 2 hours.

**NOTE:** For pulse less than 50 or SBP < 90, or RASS -3, decrease dexmedetomidine rate by 50% and call House Officer
For pulse <45 or SBP < 85 or RASS -4 or -5, turn off dexmedetomidine and call House Officer

**Valium:** For prevention of seizures and reduction in need for, expert opinion endorses concurrent benzodiazepine while being treated with dexmedetomidine for alcohol withdrawal:
- Valium 5 mg PO q 8 hours (may give IV if patient unable to take PO) (recommended for MINDS score ≥20)
- Valium 5 mg PO q 12 hours (may give IV if patient unable to take PO) (recommended for MINDS score 15-19)
- Valium 2.5 mg PO q 8 hours (may give IV if patient unable to take PO) (recommended for MINDS score <15)

Status Epilepticus

Definition

- A MEDICAL EMERGENCY. Usually defined as continuous seizure activity lasting 30 minutes
- Others have proposed: continuous generalized convulsive seizure lasting >5 minutes, or two or more seizures during which the patient does not return to baseline consciousness
- The longer the seizure lasts beyond 5 minutes:
  - the less likely it is to stop spontaneously
  - the more difficult the seizure is to control with antiepileptic medications
  - the greater degree of neuronal damage
- Refractory status epilepticus: seizures lasting > 2 hours, or seizures recurring at a rate of 2 or more per hour without recovery to baseline between episodes; others have proposed that refractory status epilepticus is status epilepticus that does not respond to first-line therapy
- Seizures may be: (generalized convulsive is the most common)
  - Generalized or partial
  - Convulsive (motor seizures) or non-convulsive

Stages of Status Epilepticus

- Stage I: First 30 minutes: Increased cerebral blood flow, increased cerebral metabolic demands, with an increase in autonomic activity that results in hypertension, hyperglycemia, sweating, salivation, and hyperpyrexia.
- Stage II: After ~30 minutes: Failure of cerebral autoregulation, decreased cerebral blood flow, increased intracranial pressure, and systemic hypotension. Electromechanical dissociation may then occur (non-convulsive status epilepticus, clinically, may only see minor twitching)

Etiology

- Known seizure disorder (spontaneously, poor compliance with medications, increased medication clearance)
- Alcohol-related (usually withdrawal)
- Cerebrovascular accidents
- Drug toxicity (i.e. cephalosporins, penicillins, quinolones, tacrolimus, cyclosporine, imipenem, antipsychotics, tramadol, theophylline, cocaine, etc.)
- CNS infections (meningitis, encephalitis)
- CNS tumors
- Metabolic disturbances (e.g. electrolyte abnormalities (sodium, calcium), sepsis, uremia)
- Head Trauma
- Anoxic/hypoxic brain injury
- Hypoglycemia/hyperglycemia
### Treatment

**General measures**
- Ensure adequate airway, provide respiratory support if needed
  - Most patients, despite cyanosis, breathe enough if their airway is clear
  - Consider oral airway when the seizure has ceased
- Position patient so they do not harm themselves
- Check Blood Sugar; consider Glucagon IM if low and no IV access
  - With IV access, consider Thiamine 100mg before 1 Amp D50
- IV Access
- Keep body temperature <40ºC
- Rule out reversible causes (see Etiology above)

---

**Lorazepam 0.1mg/kg IV x 1**

Seizure continues

If no rapidly-treatable precipitating factor:
- Phenytoin 20mg/kg (up to 1000mg) or fosphenytoin 15-20 mg/kg Phenytoin Equivalent (PE) IV load

Seizure stops

**Refractory Status Epilepticus:**
- Intubate the patient (may or may not need sedative)
  - (if paralytic needed, use Rocuronium 1mg/kg)

Seizure stops

**IV infusion of Propofol † OR midazolam‡**
- (Continuous EEG monitoring is preferred)

Seizure stops

Observe on cardiac monitor, seizure precautions

If the patient remains comatose after seizure activity has apparently ceased:
- Consider intubation
- If patient not intubated, consider NG Tube to prevent aspiration
- Observe for minor twitching; consider EEG to rule out non-convulsive status epilepticus

---

**Brain imaging with CT with contrast or MRI Lumbar puncture after imaging if no mass lesion**

† midazolam 0.2mg/kg load, then 0.1-0.5mg/kg/hr. to produce seizure suppression by continuous EEG
‡ Propofol 3-5mg/kg load, then 30-100mcg/kg/min titrated to produce seizure suppression by EEG; gradually titrated down by 50% over next 12 hours, then to 0% over subsequent 12 hours.
* other options may include high-dose thiopentone or pentobarbital, IV valproate, topiramate, tiagabine, ketamine, isoflurane, and IV lidocaine; levetiracetam may be an excellent option, effective in 16 of 18 patients with benzodiazepine-refractory status in an uncontrolled study (2008)

---

### Prognosis
- Mortality rate up to 76% in elderly patients
- Complications include metabolic and autonomic derangements, neurogenic pulmonary edema, hyperthermia, rhabdomyolysis, and aspiration pneumonia/pneumonitis
- Permanent neurologic damage occurs with prolonged uncontrolled convulsive activity

---

Serotonin Syndrome (SS)

Clinical Presentation
- Triad of CNS changes (confusion, delirium, agitation or seizures); neuromuscular changes (hyperreflexia, clonus, shivering and muscular rigidity); autonomic hyperactivity (fever; diaphoresis; HTN, ↑ HR/RR, & mydriasis; & nausea/vomiting, diarrhea
  - Spontaneous/inducible clonus of legs>arms>eyes is most important clue for SS diagnosis
  - Develops acutely over 24 hours and usually resolves within 24-48 hours
- Serotonin syndrome typically develops from the use of or overdose of ≥2 serotonergic meds
  - Serotonergic medications: amantadine, amphetamines, bromocriptine, buspirone, clomipramine, cocaine, dextromethorphan, dietary supplements (ginseng, St. John’s Wort and tryptophan), duloxetine, granisetron, hallucinogens (LSD and MDMA), imipramine, levodopa, linezolid, lithium, MAO inhibitors, metoclopramide, mirtazapine, nefazodone, ondansetron, opioids (fentanyl, meperidine and tramadol), ritonovir, SSRIs, sibutramine, trazodone, tricyclic antidepressants, triptans, valproic acid, venlafaxine, and wellbutrin

Lab Findings in Severe Cases
- Metabolic acidosis; ↑ transaminases, CK and creatinine; +/- DIC

Treatment
- Discontinuation of offending medications, aggressive hydration and supportive care
- Intubation with neuromuscular paralysis for life-threatening SS (avoid succinylcholine)
- Lorazepam 1 to 2 mg IV q30 min for agitation, muscle rigidity, myoclonus, and seizures
- Beta-blockers for blood pressure management
- Serotonin antagonists: cyproheptadine 12 mg PO x 1 then 4-8 mg PO q4-6h up to 32 mg/d titrated to effect
  - Olanzapine 10 mg SL or chlorpromazine 50-100 mg IM added for refractory cases

Neuroleptic Malignant Syndrome (NMS)

Clinical Presentation
- high fevers, “lead pipe rigidity”, autonomic instability, and AMS
- Onset over days-to-weeks, slower resolution than SS and no midriasis or hyperreflexia
- Risk factors: dehydration, catatonia, mood disorders and organic brain syndrome
- Most common with high-potency antipsychotics (e.g., haloperidol), but can occur with atypical antipsychotics, metoclopramide, promethazine, prochlorperazine or droperidol

Lab Findings
- Elevated CK, WBC and liver transaminases; metabolic acidosis

Treatment
- Discontinue offending meds, aggressive hydration, normalize electrolytes & antipyretics
- Dopamine agonists: PO bromocriptine 2.5 mg q8h or amantadine 100 mg q8h x 10-14 d
- Dantrolene 2-2.5 mg/kg IV q6h for T≥40°C, coma, respiratory failure, renal failure or extensive rhabdomyolysis until symptoms controlled, then 1 mg/kg PO q6h x 10 days
- Lorazepam 1-2 mg IV q30-60 min for autonomic instability, rigidity and agitation

Ischemic Stroke

Etiology
- Thrombotic or Embolic occlusion of one or more blood vessels supplying the brain

Clinical Presentation
- Acute onset of neurologic deficit

<table>
<thead>
<tr>
<th>Distribution</th>
<th>Clinical Presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardioembolic or Thrombotic in a Carotid Artery Distribution</td>
<td>Anterior Cerebral Artery</td>
</tr>
<tr>
<td>Cardioembolic or Thrombotic in a Posterior Circulation Distribution</td>
<td>Posterior Cerebral Artery</td>
</tr>
<tr>
<td></td>
<td>Brainstem</td>
</tr>
<tr>
<td></td>
<td>Cerebellum</td>
</tr>
<tr>
<td></td>
<td>Basilar artery</td>
</tr>
<tr>
<td></td>
<td>Lateral Medullary Infarct</td>
</tr>
<tr>
<td>Lacunar Infarction</td>
<td>Pure motor lacunar</td>
</tr>
<tr>
<td></td>
<td>Pure sensory lacunar</td>
</tr>
<tr>
<td></td>
<td>Ataxia hemiparesis lacunar</td>
</tr>
<tr>
<td></td>
<td>Pons</td>
</tr>
<tr>
<td></td>
<td>Posterior IC and Thalamus</td>
</tr>
<tr>
<td></td>
<td>Internal Capsule</td>
</tr>
</tbody>
</table>

Differential Diagnosis with Clinical Presentation
- Conversion disorder: Lack of cranial nerve findings, neurological findings in a nonvascular distribution, inconsistent examination
- Hypertensive encephalopathy: Headache, delirium, significant hypertension, cerebral edema, papilledema
- Hypoglycemia: History of diabetes, serum glucose low, decreased level of consciousness
- Complicated migraine: History of similar events, preceding aura, headache
- Seizures: History of seizures, witnessed seizure activity, postictal period

Initial Workup of Suspected Ischemic Stroke
- Complete evaluation and decide treatment within 60 minutes of reaching the Emergency Department
- Noncontrast brain CT or brain MRI (CT may remain negative for >48 hours despite ischemic stroke)
- Blood glucose
- Serum electrolytes/renal function tests, CBC
- EKG, Markers of cardiac ischemia
- Prothrombin time/international normalized ratio (INR), Activated partial thromboplastin time
- Oxygen saturation
- For Selected patients, may consider: Hepatic function tests, Toxicology screen, Blood alcohol level, Pregnancy test, Arterial blood gas tests (if hypoxia or hypercarbia is suspected), Chest radiography (if
lung disease is suspected), Lumbar puncture (if subarachnoid hemorrhage is suspected and CT scan is negative for blood), Electroencephalogram (if seizures are suspected)

- Subsequent workup should include Echocardiogram and Carotid Doppler

General Management of Ischemic Stroke

- Airway, Ventilatory Support, Supplemental Oxygen
- Achieve and Maintain Normo-thermia (fever is associated with worse neurologic outcome)
- Cardiac Monitoring and Treatment of arrhythmias or other issues
- Euglycemia (goal 80-150, with poorer neurologic outcomes seen with blood glucose persistently >200)
- Avoid hypotension (consider volume expansion, treatment of inciting arrhythmias, and consider dopamine if persistent SBP<100mmHg or DBP<70mmHg)
- Pharmacologic DVT Prophylaxis is indicated, with low-risk of bleeding; the ideal timing of this is not known
- AVOID HYPOTONIC IV FLUIDS AS THESE CAN INCREASE BRAIN EDEMA

Blood Pressure Elevation in Ischemic Stroke

- Elevations in blood pressure >160 mm Hg are detected in >60% of patients with acute stroke
- Both elevated and low blood pressures are associated with poor outcome after stroke
- For every 10-mm Hg increase >180 mm Hg, the risk of neurological deterioration increased by 40% and the risk of poor outcome increased by 23%
- The elevation in blood pressure may be secondary to the stress of the cerebrovascular event, a full bladder, nausea, pain, preexisting hypertension, a physiological response to hypoxia, or a response to increased intracranial pressure.
- Much less commonly, a hypertensive emergency is causing the neurologic deficits (often associated with headache, confusion, and papilledema)

Blood Pressure Management in Ischemic Stroke

- In a majority of patients, a decline in blood pressure occurs within the first hours after stroke even without any specific medical treatment
  - Spontaneous fall when the patient is moved to a quiet room, the patient is allowed to rest, the bladder is emptied, or the pain is controlled
  - Treatment of increased intracranial pressure may result in a decline in blood pressure
- With treatment, drops in either systolic or diastolic blood pressure of >20 mm Hg were associated with early neurological worsening, higher rates of poor outcomes or death, and larger volumes of infarctions
- Treatment is controversial; Pending more data, the consensus of the panel is that emergency administration of antihypertensive agents should be withheld unless the diastolic blood pressure is >120 mm Hg or unless the systolic blood pressure is >220 mm Hg.
- When treatment is indicated, lowering the blood pressure should be done cautiously (reasonable goal is to lower the blood pressure between 15-25% within the first day)
  - Labetalol 10 to 20 mg IV over 1 to 2 minutes, may repeat x 1, OR
  - Nitropaste 1 to 2 inches, OR
  - Nicardipine infusion, 5 mg/h, titrate up by 2.5 mg/h at 5- to 15-minute intervals, maximum dose 15 mg/h; when desired blood pressure attained, reduce to 3 mg/h
  - Note: avoid beta blockers or calcium channel blockers in the face of sympathomimetics (e.g. cocaine, methamphetamines) as they can worsen vasospasm (see “Hypertensive Crisis” section
- If the patient has been on anti-hypertensive medication as an outpatient, it is considered safe to restart that medication at 24 hours post stroke if the patient has pre-existing hypertension and there are no contraindications to the therapy.
- Medications recommended for secondary stroke prevention: Thiazide diuretics and ACE inhibitors.
Treatment

- If the stroke is embolic in nature, anticoagulants such as heparin may be considered after 1 week if there are no contraindications; caution is advised early on to prevent hemorrhagic transformation of the ischemic area
- Aspirin 325mg po or pr within 48 hours of ischemic stroke is the only approved antiplatelet therapy for ischemic stroke; the other antiplatelet agents (clopidogrel, dipyridamole) are approved for secondary prevention but not for treatment of acute ischemic stroke
- Consider thrombolytics if ≤ 3 hours to 4.5 hours from symptom onset (see “Thrombolysis for Acute Ischemic Stroke Protocol”, page 199)

Prognosis/Subsequent Management

- 25% of patients with acute stroke will have worsening within 24-48 hours of presentation
- Assessment of swallow function prior to initiating feeding is indicated
- Early mobilization with Physical Therapy, and Occupational Therapy, are indicated

Complications

- Ischemic Cerebral Edema
  - Risk Factors for edema and poorer neurologic outcome: Females; patients with more than one vascular territory infarct; cerebellar infarcts (VERY high risk for edema leading to compressive hydrocephalus); early (<12 hours after onset of symptoms) CT Scan Hypodensity in >50% of MCA distribution; mass effect seen on CT with MCA stroke
  - Clinical signs of edema/worse outcome:
    - bilateral ptosis, involvement of the nondominant hemisphere
    - history of hypertension, heart failure
    - elevated white blood cell count
    - need for early mechanical ventilation
    - Clinical signs are often absent, edema is very difficult to predict
  - “Malignant” edema = large territorial infarct that swells within 24 hours (usual swelling is maximum at 4 days post CVA)
  - Early management (not often associated with elevated intracranial pressure)
    - Avoid hypo-osmolar fluid
    - Correct hypoxemia, hypercarbia, hyperthermia
    - Elevate head of bed to 30° to improve venous return
    - Avoid anti-hypertensives that may lead to cerebral venodilation
    - Avoid tight cervical collar
  - Hyperventilation, Osmotic Diuretics, Drainage of CSF, Decompressive Surgery may all be considered; Mannitol 0.25-0.5 g/kg IV q 6 hours may temporize until surgery
  - For Cerebellar strokes, decompressive surgical evacuation may be necessary to prevent herniation of the cerebellum upward
  - Prognosis: Despite aggressive therapy, mortality is 50-70%

- Hemorrhagic Transformation
  - ~5% of ischemic CVAs develop frank hemorrhagic transformation
  - Higher risk with anticoagulants and thrombolytics. Early aspirin may also increase risk slightly
  - Data regarding management is very limited

- Seizures
  - 2-23% incidence; primarily in the first 24 hours; usually partial, with or without secondary generalization; late seizures often occur in patients with dementia
  - Data regarding management is very limited and patients are usually managed as with routine seizure disorders

Adapted from write-up by Joseph Esherick, MD with his permission.
<table>
<thead>
<tr>
<th>Item</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level of consciousness</td>
<td>0=Alert&lt;br&gt;1=Lethargic&lt;br&gt;2=Responds to vigorous or noxious stimuli&lt;br&gt;3=Unresponsive</td>
</tr>
<tr>
<td>Level of consciousness questions</td>
<td>0=Answers both correctly&lt;br&gt;1=Answers one correctly&lt;br&gt;2=Answers neither correctly</td>
</tr>
<tr>
<td>Level of consciousness commands</td>
<td>0=Performs both tasks correctly&lt;br&gt;1=Performs one task correctly&lt;br&gt;2=Performs neither task correctly</td>
</tr>
<tr>
<td>Best Gaze</td>
<td>0=Normal&lt;br&gt;1=Partial gaze palsy&lt;br&gt;2=Complete gaze palsy</td>
</tr>
<tr>
<td>Visual Fields</td>
<td>0=No visual field deficits&lt;br&gt;1=Partial hemianopsia&lt;br&gt;2=Complete hemianopsia&lt;br&gt;3=Bilateral hemianopsia</td>
</tr>
<tr>
<td>Facial Palsy</td>
<td>0=No palsies&lt;br&gt;1=Minor facial paralysis&lt;br&gt;2=Partial facial paralysis&lt;br&gt;3=Complete facial paralysis</td>
</tr>
<tr>
<td>Motor arm</td>
<td>0=No drift&lt;br&gt;1=Drift before 10 seconds&lt;br&gt;2=Falls before 10 seconds&lt;br&gt;3=No effort against gravity&lt;br&gt;4=No movement</td>
</tr>
<tr>
<td>Motor leg</td>
<td>0=Lifts leg to 30° position for 5 seconds&lt;br&gt;1=Drift down before 5 seconds&lt;br&gt;2=Falls before 5 seconds&lt;br&gt;3=No effort against gravity&lt;br&gt;4=No movement</td>
</tr>
<tr>
<td>Ataxia</td>
<td>0=Absent&lt;br&gt;1=One limb&lt;br&gt;2=Two limbs</td>
</tr>
<tr>
<td>Sensory</td>
<td>0=Normal&lt;br&gt;1=Mild loss&lt;br&gt;2=Severe loss</td>
</tr>
<tr>
<td>Language</td>
<td>0=Normal&lt;br&gt;1=Mild aphasia&lt;br&gt;2=Severe aphasia&lt;br&gt;3=Mute or global aphasia</td>
</tr>
<tr>
<td>Dysarthria</td>
<td>0=None&lt;br&gt;1=Mild dysarthria&lt;br&gt;2=Severe dysarthria</td>
</tr>
<tr>
<td>Extinction/inattention (Testing for neglect)</td>
<td>0=Normal&lt;br&gt;1=Mild deficits&lt;br&gt;2=Severe deficits</td>
</tr>
</tbody>
</table>

Total score based on adding up all the individual scores
NIH Stroke Scale available in Cerner via Power Forms: found on the “Ad Hoc” tab, then “Additional Assessments”

Adapted from the NIHSS form available at [http://www.ninds.nih.gov/doctors/NIH_Str...](http://www.ninds.nih.gov/doctors/NIH_Str...).
Thrombolysis for Acute Ischemic Stroke: tPA (alteplase)

CLINICAL USE GUIDELINES:
Strict adherence to this protocol is required. Only 2-4% of patients presenting with ischemic stroke will qualify for this therapy. The sooner the tPA is administered within the 3-hour window the better the results. There is a 6.4% absolute increased risk of intracranial hemorrhage and no benefit in long-term mortality with this therapy, but there is a 12% absolute increase in the number of patients with little or no neurological impairment at 3 months following the ischemic stroke.

SELECTION CRITERIA (NOTE: ALL CRITERIAL MUST BE MET):
1. Patient age ≥ 18 years and
2. Well-defined onset of stroke symptoms <3 hours prior to tPA administration (or, may be extended to well-defined onset of stroke symptoms <4.5 hours prior to tPA administration if age<80, NIH score≤25, non-diabetics, and not on anticoagulation) and
3. Diagnosis of acute ischemic stroke with measurable and significant neurological deficits based on the NIH Scale (see Table 1) and
4. Patient or family members understand potential risks and benefits of treatment.

EXCLUSION CRITERIA: tPA is contraindicated if any of the following are present:
1. Onset of stroke symptoms >3 hours from initiation of tPA therapy, or UNCERTAIN TIME.
2. Minor, isolated or rapidly improving stroke symptoms.
3. Seizure at onset of stroke or postictal neurological impairments.
4. Non-contrast head CT scan NOT done or if CT scan shows evidence of ICH.
5. Stroke symptoms suggestive of subarachnoid hemorrhage despite negative CT scan.
6. CT scan shows a multilobar infarction (hypodensity > 1/3 cerebral hemisphere).
7. Caution should be exercised in treating a patient with major deficits (NIHS score >22 predicts greater risk of intracranial hemorrhage).
8. Active bleeding or trauma.
9. History of stroke, serious head trauma, intracranial surgery or myocardial infarction in last 3 months.
11. History of GI or urinary tract hemorrhage in previous 21 days.
12. History of major surgery or serious trauma within last 14 days.
13. Arterial puncture at non-compressible site or lumbar puncture within 7 days.
14. Intracranial pathology (i.e. neoplasm, AV-malformation, aneurysm, etc.)
15. Abnormal serum glucose: <50 mg/dL or >400 mg/dL or Platelet count <100,000/mm³.
16. Uncontrolled blood pressures: SBP>185 or DBP >110 mmHg.
17. Recent anticoagulant therapy with elevated prothrombin INR >1.5 seconds or elevated aPTT.

DOSAGE and ADMINISTRATION:
1. Alteplase Dose = 0.9 mg/kg body weight, maximum 90 mg.
2. Dosing: Administer 10% of the total calculated dose as an IV bolus over 1 minute, followed by infusion of the remaining 90% of the dose over 60 minutes.
3. Admit patient to ICU.
4. Perform neurological assessment every 15 minutes during infusion; every 30 minutes thereafter for the next 6 hours, then hourly until 24 hours after treatment.
5. If patient develops severe headache, acute hypertension, nausea or vomiting, stop infusion and obtain emergency CT scan.
6. Measure BP every 15 minutes for the first 2 hours, then every 30 minutes for the next 6 hours, then hourly until 24 hours after therapy.
7. Increase the frequency of BP measurement if SBP ≥180 mmHg or if DBP ≥105 mmHg; treat BP to keep BP below 185/110 mmHg.
8. No placement of NG tubes bladder catheters or intra-arterial lines.
9. Obtain follow-up CT at 24 hours before starting anticoagulants or anti-platelet drugs.

Return to Table of Contents
Arterial Hypertension Treatment Algorithm with Thrombolysis

BP management prior to thrombolysis

Systolic BP > 185 mmHg or diastolic BP > 110 mmHg
- Labetalol 10-20 mg IV over 1-2 minutes, may repeat X1
  Or
- Nitropaste 1 to 2 inches
  Or
- Nicardipine infusion 5 mg per hour, titrate up to 0.25 mg/h @ 5-10 minute intervals to a maximum dose 15 mg/h. If goal reached, then decrease dose by 3 mg/hour.

BP management during or after thrombolysis

Measure the BP every 15 minutes for the first 2 hours, then every 30 minutes for the next 6 hours, then hourly until 24 hours after therapy.

If SBP 180-230 mmHg or DBP 105-120 mmHg:
- Labetalol 10 mg IV over 1-2 minutes, may repeat every 10-20 minutes to max dose 300 mg.
  Or
- Labetalol 10 mg IV followed by infusion @ 2-8 mg/min.

If SBP >230 mmHg or DBP 121-140 mmHg
- Labetalol 10 mg IV over 1-2 minutes, may repeat every 10-20 minutes to max dose 300 mg.
  Or
- Labetalol 10 mg IV followed by infusion @ 2-8 mg/minute.
  Or
- Nicardipine infusion 5 mg per hour, titrate up to 0.25 mg/h @ 5-10 minute intervals to a maximum dose 15 mg/hour.
If BP not controlled consider sodium nitroprusside.

* Based upon the National Institute of Neurological Disorders (NIND) tPA in acute ischemic stroke study (NINDS. NEJM 1995; 333:1581) and the AHA/ASA Guideline for Early Management of Adults with Ischemic Stroke (Stroke 2007; 38:1655-1711) Department of Medicine 10/2007. Updates from AHA/ASA Recommendation from Stroke 2009 (March 28th advisory released June 10, 2009.)
Hemorrhagic Stroke/Intracerebral Hemorrhage (ICH)

Definition
- Bleeding directly into the brain parenchyma
- Classified as primary (unrelated to congenital or acquired lesions), secondary (directly related to congenital or acquired conditions), and/or spontaneous (not secondary to trauma or surgery)
- Accounts for ~10% of all strokes

Risk Factors
- More common in males, increasing age (rate doubles every 10 years after the age of 35), African American, Japanese, Hispanic ancestry, Heavy alcohol consumption, Tobacco use, LOW cholesterol

<table>
<thead>
<tr>
<th>Risk Factors for Primary ICH (in approximate descending order)</th>
<th>Risk Factors for Secondary ICH (in approximate descending order)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic hypertension is the underlying cause in~75% of all ICH</td>
<td>Vascular Malformations (Arteriovenous (AV) malformation, Dural AV fistula, cavernous malformations)</td>
</tr>
<tr>
<td>Cerebral Amyloid Angiopathy</td>
<td>Aneurysms (Saccular, Mycotic, Fusiform)</td>
</tr>
<tr>
<td>Anticoagulant/fibrinolytic use, Antiplatelet use, Bleeding diathesis</td>
<td>Tumors (primary brain, or brain metastases)</td>
</tr>
<tr>
<td>Drug use (cocaine, methamphetamines, phenylpropanolamine)</td>
<td>Hemorrhagic transformation of ischemic infarction</td>
</tr>
<tr>
<td></td>
<td>Cerebral Venous Thrombosis leading to venous infarction with hemorrhage</td>
</tr>
<tr>
<td></td>
<td>Moyamoya disease</td>
</tr>
</tbody>
</table>

Clinical Presentation/Course
- Depends on the site of bleeding, size of the hemorrhage, degree of edema
- Hematoma expansion is common (up to 26% of patients in the first hour after admission, and another 12% by hospitalization hour 20 in 1 study); may increase the size of bleed by up to 40% and is associated with poor prognosis; may be associated with SBP>200 or hyperglycemia

Management
- Consider cerebral angiography for young patients with no clear source of hemorrhage who may be surgical candidates; angiography not indicated in hypertensive older adults in locations typical for hypertensive bleeding
- See Management of Patients with Intracranial Hemorrhage on page 203

Predictors of Outcome
- Size of hematoma most correlates with outcome (= length x width x depth in cm divided by 2); a comatose patient with a hematoma volume >60cm³ has a 91% 30-day mortality rate
- Poor prognosis also associated with advanced age, hydrocephalus, deep location of ICH, elevated blood pressure on hospital admission, need for mechanical ventilation, fever

Prognosis
- Patients with edema do worse; edema peaks at 3-7 days post-hemorrhage due to lysis of RBCs
- 30-day mortality 30-40%; up to 2/3 of patients with intracranial hemorrhage do not return to independence

Subarachnoid Hemorrhage (SAH)

Definition
- Hemorrhage into the subarachnoid space, usually from a ruptured aneurysm (may also be from pituitary apoplexy, arterial dissection, cerebral venous thrombosis, hypertensive encephalopathy, idiopathic)

Clinical Presentations
- Sudden death occurs in 10% of patients from massive increase in intracranial pressure
- Another 10-20% arrive at the Emergency Department comatose and in need of emergency respiratory support
- Majority of patients present with excrutiating headache (“thunderclap”=split-second onset, extremely overwhelming headache that fails to subside), confusion, or abnormal behavior
- Other presenting signs and symptoms may include cranial neuropathy (3rd or 6th nerve most common), nuchal rigidity, other localized neurologic findings (aphasia, hemiparesis), though major focal neurologic deficits are usually not seen

Diagnosis
- CT Scan is 98% sensitive
- Xanthrochromia by lumbar puncture [sensitivity>99%] usually present by 6 hours
- CT Angiogram should be performed on all patients with SAH
- Grading system for SAH (World Federation of Neurosurgical Societies [WFNS])

<table>
<thead>
<tr>
<th>WFNS Grade</th>
<th>Glasgow Coma Scale Score</th>
<th>Motor Deficit</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>15</td>
<td>Absent</td>
</tr>
<tr>
<td>II</td>
<td>14-13</td>
<td>Absent</td>
</tr>
<tr>
<td>III</td>
<td>14-13</td>
<td>Absent</td>
</tr>
<tr>
<td>IV (“poor grade”)</td>
<td>12-7</td>
<td>Present or Absent</td>
</tr>
<tr>
<td>V (“poor grade”)</td>
<td>6-3</td>
<td>Present or Absent</td>
</tr>
</tbody>
</table>

Complications (see Management of Patients with Intracranial Hemorrhage, page 203)
- Re-rupture of aneurysm
  - Highest risk within the first 48 hours
- Acute hydrocephalus
  - Develops in 20% of patients; may cause acute neurologic deterioration
  - More common with intracerebral extension of hemorrhage, posterior circulation aneurysm, and reduced Glasgow Coma Scale score on admission
  - Ventriculostomy CSF drainage indicated; some patients may need permanent shunting
- Early cerebral vasospasm
  - Prevention: maintain euvoemia or mild hyervolemia (AVOID fluid restriction)
  - Treatment may involve more aggressive intravascular volume expansion (to goal urine output >250ml/hour), induced hypertension (with phenylephrine, dobutamine and/or Levophed to goal MAP>25% above baseline or MAP>120mmHg), and/or more invasive hemodynamic monitoring
- Seizures
- Hyponatremia
  - Consider treatment with fludricortisone 0.3mg/day

Prognosis
- Poorer prognosis with age>65, decreased neurologic status at admission, posterior distribution aneurysms, development of cerebral vasospasm or cerebral infarction
- 30% of patients with poor outcome; 90% mortality with Grade IV or V SAH

### Management of Patients with Intracranial Hemorrhage (SAH and ICH)

| **History/exam, Onset of symptoms** |
| **GCS score** |
| **CBC, chemistry panel, PT, PTT** |
| **Noncontrast head CT scan** |
| **Consider EKG, Cardiac Panel, Chest X-Ray** |

#### For GCS≤8 or increased ICP:
- Intubate → PaCO₂ 35 +/- 2 mmHg
- Head of bed elevated to 30-45°
- Isotonic fluids until euvolemic
- Consider mannitol 0.5-1 gm/kg IV
- Consider intracranial pressure monitoring

- Maintain normothermia and euvolemia
- Keep glucose<180 mg/dL
- Sequential compression devices
- GI Prophylaxis
- Consider antiepileptic x 7 days for lobar hemorrhages
- Correct coagulopathy with FFP/PCC/Vitamin K (see Pages 111-112 and links)
- Platelet transfusion if Platelet count<50,000 or if on antiplatelet therapy (see page 125)

### Subarachnoid Hemorrhage (SAH)

**Medical mgmt**
- Blood pressure management is controversial
- Accept MAP≤130; if MAP >130:
  - Labetolol 20mg IV, OR
  - Esmolol 500mcg/kg IV, OR
  - Enalaprilat 0.625mg IV
- Nimodipine 60 mg PO q4h x 21d (does not reduce vasospasm; may be neuroprotective (unclear))
- Cerebral angiogram to locate aneurysm
  - 4 vessel cerebral angiogram
  - CT Angiogram with 3D reconstruction
- Surgical clipping or endovascular coiling within 72 hours

### Intracranial Hemorrhage (ICH)

**Medical management**
- Acute BP management
  - Keep MAP<130 mmHg if pre-existing hypertension
    - Options include Labetalol, hydralazine, nicardipine
  - Keep MAP≤110 mmHg or BP<160/90 if no h/o HTN or if post-craniotomy
- Recombinant Factor VII decreases the volume of expansion of hematomas but does not improve survival or functional outcome and is not recommended (based on FAST Trial, 2008 ¥)

**Indications for Surgical Evacuation**
- Infratentorial ICH >3cm or smaller with neurologic deterioration
- Superficial (<1cm) supratentorial ICH with neurological deficits (based on STICH trial, 2005 †)
- Young patient with lobar ICH and GCS≤13

### References:
Induced Hypothermia Protocol: DRAFT

- Induced hypothermia has been extensively studied in a wide array of clinical scenarios of neuronal hypoperfusion/hypoxia in the hope of preserving neurologic function
- The largest study to date of unconscious survivors of out-of-hospital cardiac arrest (n=939), the Targeted Temperature Management (TTM) trial, revealed no difference in outcome between patients maintained at 33º C vs. those maintained at 36º C
- It is generally accepted that Induced Hypothermia should be utilized after Ventricular Fibrillation cardiac arrest; other indications remain controversial. The degree of hypothermia should likely be 36º C (or slightly lower) for all patients being considered for therapeutic hypothermia regardless of cause, as lower temperature leads to more shivering and more potential for coagulopathy and other organ dysfunction and is more difficult to maintain

<table>
<thead>
<tr>
<th>Inclusion Criteria (must have ALL):</th>
<th>Exclusion Criteria:</th>
</tr>
</thead>
<tbody>
<tr>
<td>● Post cardiac arrest (any rhythm as cause is eligible), with post Ventricular fibrillation (V-fib) arrest being the most compelling indication</td>
<td>● Patient has DNR, POLST, poor baseline status, or terminal disease</td>
</tr>
<tr>
<td>● Return of Spontaneous Circulation (ROSC) &lt; 30 minutes from EMS/Code Team arrival</td>
<td>● Active bleeding or intracranial bleeding</td>
</tr>
<tr>
<td>● Time now &lt; 6 hours from ROSC</td>
<td>● Traumatic etiology of arrest</td>
</tr>
<tr>
<td>● Comatose (does not follow commands)</td>
<td>● Cryoglobulinemia</td>
</tr>
<tr>
<td>● MAP &gt; 65 on no more than one vasopressor</td>
<td>● Pregnancy (relative – consider OB consult)</td>
</tr>
</tbody>
</table>

Prior to Protocol Initiation:
1. All potential cases must be discussed with the ICU Attending, who must agree with the plan for Induced Hypothermia
2. Ensure the following monitoring prior to initiation of the protocol:
   - Temperature: esophageal probe in mid-esophagus (~ 4cm above xiphoid via oral/nasal probe); or Foley cath with temperature probe, or rectal probe
   - Foley catheter to monitor urine output hourly
   - Central line with CVP (preferably IJ or subclavian)
   - Arterial line
3. Initial labs: CBC, CMP, Magnesium, Phosphorus, Lactic Acid, PT/PTT, Cardiac Panel, Amylase and Lipase, ABG with electrolytes, Type and Screen, Blood cultures x 2, Urine culture
4. Obtain echocardiogram, baseline EKG
5. Consider PCI in discussion with Cardiology Consult; may consider tPA if PCI unavailable or delayed

Protocol Induction:
1. Completely expose patient and place cooling blanket above and below the patient with nothing between
2. Hook both cooling blankets and the probe to the same ‘Blanketrol’ machine
3. Set temperature on hypothermia blanket to 35-36º
4. If initial Temperature is <36º C, allow patient to warm to 36º
5. Begin opioid infusion (fentanyl), titrate to “Ventura Observational Pain Scale” (VOPS) <3
6. Begin sedatives (propofol or dexmedetomidine preferred if blood pressure room, midazolam if no blood pressure room), titrate to RASS -3 to -4.
7. Infuse refrigerated crystalloid (4° C) preferably through large bore peripheral IV
8. Administer at ~100 ml/minute using pressure bag. Maximal initial infusion is 30 ml/kg
9. If patient not <36° C after this amount, wait 15 minutes before giving further 250 ml boluses q 10 minutes
10. Administer acetaminophen 650 mg via OG/NG tube unless patient allergic or LFTs 3 times the upper limit of normal
11. During induction, if patient has shivering unrelieved by above medications, vecuronium 0.1 mg/kg x 1 can be used
12. If MAP falls below 65, use pressors (preferable Levophed) to maintain MAP ≥ 65

Protocol maintenance:
1. If patient Temperature rises > 36°C, infuse 250 ml boluses of cold crystalloid q 10 minutes until Temperature < 36°C
2. Maintain Temperature 35-36°C for 24 hours
3. Assess for shivering q 15 minutes. If any signs of shivering, see below
4. Consider re-warming prior to 24 hours if significant bleeding or severe hemodynamic instability
5. Aggressively replete Magnesium IV, and keep Ionized Calcium high normal at all times
6. Maintain serum sodium 140-150
7. Maintain blood glucose 120-160 (with insulin drip if blood glucose > 180 x 2 checks)
8. Avoid hyperoxia
9. Serial labs:
   - ABG with electrolytes and lactate q 1 hour x 4, then q 4 hours
   - CMP, CBC, Magnesium and Phosphorus q 4 hours
   - Cardiac enzymes q 6 hours
   - EKG q 1 hour x 4

Rewarming:
1. Standard rewarming process should be gradual and take place ideally over 24 hours
   Target is 37° C over approximately 24 hours at a rewarming rate of 0.1° C/ hour
   Temperature setting on Blanketrol is to be manually increased by 0.1° C/hour
2. For patients with hemodynamically unstable arrhythmias, persistent hypotension despite pressors, or severe bleeding, a more rapid “active rewarming” process should take place at a maximum rate of 0.33° C
   Target is 37° C over approximately 9 hours at 0.33° C/ hour
   Temperature setting on Blanketrol is to be manually increased by 0.33° C/hour
   Once temperature of 37° C is reached, leave patient on Blanketrol set to 37° C for 24 h
Shivering Protocol After Induction

**Bedside Shivering Assessment (BSAS):**

0 = None (no shivering. Must not have shivering on EKG or palpation)

1 = Mild (localized to neck/thorax). May only be noticed on palpation

2 = Moderate (intermittent involvement of upper extremities +/- thorax)

3 = Severe (generalized shivering or sustained upper extremity shivering)

Management of Shivering:

- All patients to receive acetaminophen 650 mg via NG/OG tube q 6 hours unless allergy or LFTs greater than 3 times the upper limit of normal

  - Still shivering
    - If BSAS > 1, add fentanyl drip
      - Still shivering
        - If BSAS still >1, add propofol drop
          - Still shivering
            - If BSAS still > 1, administer Magnesium sulfate 2 grams IV bolus, then 0.5-1 gram/hour to a target serum Magnesium level of 3 mg/dL
              - Still shivering
                - If BSAS still > 1, apply Bair Hugger Device blanket to both of patient’s arms
                  - Still shivering
                    - If BSAS still > 1, administer ketamine 0.5 mg/kg IV push x 1
                      - Still shivering
                        - If BSAS still > 1 after titration of above medications, add cisatracurium 0.15 mg/kg IV q 1 hour prn shivering, while checking train of 4

Determination of Brain Death

Definition
- Brain death is defined as the irreversible loss of the clinical function of the whole brain, including the brainstem.
- Patients that are brain dead, despite spontaneous cardiac activity, are considered by the law to be dead

Causes of CNS Catastrophes Leading to Brain Death
- Head injury, intracranial bleed, hypoxic-ischemic brain injury, massive ischemic stroke, fulminant hepatic failure, severe meningoencephalitis, other

Clinical Criteria for Brain Death Declaration
- Core temperature > 95º F
- No effect of an CNS depressant drugs/medications or neuromuscular blocking agents
- Absence of any confounding metabolic or endocrine disorders
- Absence of cranial nerve function
  - Absence of the following reflexes: papillary light; corneal; oculocephalic (doll’s eyes); oculovestibular (cold caloric testing); sucking; rooting; gag reflexes
  - No swallowing, yawning, blinking, grimacing, or coughing
- Coma, with no motor response to noxious stimulation, excluding spinal reflexes
- Absence of spontaneous respirations as determined by an apnea test

Apnea testing
- Preoxygenate patient with 100% FiO2 for 20 minutes
- Start test with PaCO2~40 mm Hg and pH 7.35 to 7.45
- Disconnect ventilator and administer oxygen by tracheal cannula at 6-8 L/min (do not occlude ET tube, and do not extubate patient)
- Maintain SBP ≥ 90 mm Hg during the entire test (may use vasopressors if necessary)
- Observe for any spontaneous respirations
- Draw an ABG after 8-10 minutes and reconnect ventilator
- Positive test (brain death confirmed) if PaCO2 ≥ 60 or ↑ 20 mm Hg, pH≤7.3 and no spontaneous respirations noted

Alternative Methods to Confirm Brain Death
- Electroencephalogram reveals no electrocerebral activity for at least 30 minutes
- Cerebral scintigraphy study or cerebral angiogram demonstrates no cerebral blood flow
- Transcranial Doppler ultrasonography with absence of diastolic or reverberating flow

Legal Issues
- Declaration of brain death must be documented in the medical record by 2 physicians, each addressing the following in their note: time of declaration of brain death, cause/irreversibility of the condition, absence of brainstem reflexes, coma including absence of motor response to pain, and results of apnea testing
- Hospitals are required to contact organ procurement organizations prior to the withdrawal of life support for all individuals meeting criteria for brain death (in California: OneLegacy: 800-338-6112) (see Organ Donation)
- A physician is never to initiate a conversation about organ procurement with the family

TRAUMA IN THE ICU

Assessment of the Severity of Trauma

- Objective evaluation tools exist that help to standardize the evaluation, treatment, and prognosis of trauma patients
  - Anatomic Scoring Systems: Abbreviated Injury Score (AIS), Injury Severity Score (ISS)
  - Physiologic Scoring Systems: Revised Trauma Score (RTS)
  - Combined Scoring Systems: Trauma and Injury Severity Score (TRISS)
- To obtain accurate scoring, it is paramount to document in precise detail all injuries upon the patient’s admission to the hospital in your history and physical documentation

Anatomic Scoring Systems

<table>
<thead>
<tr>
<th>The Injury Severity Score (ISS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Each of 6 anatomical regions receives an AIS score for the most severe injury to that location:</td>
</tr>
<tr>
<td>• Head and neck</td>
</tr>
<tr>
<td>• Face</td>
</tr>
<tr>
<td>• Chest</td>
</tr>
<tr>
<td>• Abdomen and pelvic contents</td>
</tr>
<tr>
<td>• Extremities and pelvic girdle</td>
</tr>
<tr>
<td>• External (superficial)</td>
</tr>
<tr>
<td>2. The three highest scores out of the six regions are squared, then added to each other (e.g. for A, B, C as the highest region scores, ISS = A² + B² + C²)</td>
</tr>
<tr>
<td>3. An ISS of 75 is automatically given to a fatal injury</td>
</tr>
<tr>
<td>4. An ISS of 15 or greater is considered a severe injury</td>
</tr>
<tr>
<td>5. Mortality increases with age and higher ISS</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Abbreviated Injury Score (AIS):</th>
</tr>
</thead>
<tbody>
<tr>
<td>Each injury sustained by a patient is classified and scored as either:</td>
</tr>
<tr>
<td>Minor 1 point</td>
</tr>
<tr>
<td>Moderate 2 points</td>
</tr>
<tr>
<td>Serious 3 points</td>
</tr>
<tr>
<td>Severe 4 points</td>
</tr>
<tr>
<td>Critical 5 points</td>
</tr>
<tr>
<td>Fatal 6 points</td>
</tr>
</tbody>
</table>

The Revised Trauma Score

<table>
<thead>
<tr>
<th>Variable</th>
<th>Points</th>
<th>4</th>
<th>3</th>
<th>2</th>
<th>1</th>
<th>0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory Rate</td>
<td>10-29/min</td>
<td>&gt;29/min</td>
<td>6-9/min</td>
<td>1-5/min</td>
<td>0/min</td>
<td></td>
</tr>
<tr>
<td>Systolic BP</td>
<td>&gt;89 mmHg</td>
<td>76-89 mmHg</td>
<td>50-75 mmHg</td>
<td>1-49 mmHg</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Glasgow Coma Scale</td>
<td>13-15</td>
<td>9-12</td>
<td>6-8</td>
<td>4-5</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

Most affected = minimum score of 0; Least affected = maximum score of 12.

The Trauma and Injury Severity Score

- Utilizes the ISS, the RTS (weighted) and the patient’s age along with modifiers for blunt or penetrating trauma to predict the ‘age death rate’ and probability of survival (POS)
- The TRISS is being calculated for all trauma patients at VCMC by the Lancet 1 software by the Division of Trauma to continue to guide patient safety improvement measures

**Traumatic Brain Injury and Intracranial Pressure (ICP) Management**

**Indications for Intubation with Traumatic Brain Injury (TBI)**
- GCS ≤ 8; hemodynamic instability; respiratory instability; need for surgery

**Intracranial Pressure (ICP) Monitoring**
- Indicated for
  - GCS ≤ 8 and an abnormal CT scan, OR
  - GCS ≤ 8 with a normal head CT and 2 or more of the following: age > 40, motor posturing or focal lateralizing signs; or systolic blood pressure < 90 mmHg, OR
  - GCS 9-12 with abnormal CT scan and patient will undergo prolonged extra-cranial operative procedure
- ICP Bolt: pressure monitor with sensor on brain parenchyma; allows continuous measurement but no CSF drainage
- Ventriculostomy: pressure monitor with catheter in ventricular system; allows continuous measurement and CSF drainage to assist in controlling elevated ICP

**General Management Guidelines for Traumatic Brain Injury**
- Head of bed elevated to 30-45º; utilize reverse-Trendelenberg position if spinal precautions
- Keep neck straight; avoid tight cervical collar or tight dressings or tape on neck
- DVT Prophylaxis: sequential compression devices started immediately
  - May add heparin/LMWH once risk of intracranial bleeding is minimal
- Stress ulcer prophylaxis with proton pump inhibitor as high risk for Curling’s Ulcer
- Seizure prophylaxis with phenytoin or levetiracetam indicated for subarachnoid hemorrhage, subdural or epidural hematoma, penetrating injury, post-craniotomy, or witnessed seizure
  - Give for seven days unless patient had seizure or very high risk (e.g. penetrating injury)
- Selective gut decontamination for ventilated patients to prevent pneumonia
- Ventilated patients should have their pCO2 maintained ~ 35 cm H2O
- Sedate ventilated patients who have stable hemodynamics with propofol to allow for frequent neurological assessments; AVOID ketamine for risk of ↑ ICP
- Insert arterial line for blood pressure management with severe TBI
- Avoid BP < 90/60, PaO2 < 60 mmHg, SaO2<90%, fever, pain, anxiety or coughing
- Treat fever with cooling measures and acetaminophen; AVOID NSAIDs; treat infections
- Nutrition: needs 140% of resting metabolic expenditures if nonparalyzed (100% of resting metabolic expenditures if paralyzed); ≥ 15% protein; consider glutamine-containing formula
- Use only isotonic IV fluids (avoid LR, albumin, other hypotonic fluids); consider hypertonic fluids if difficult to maintain serum sodium ≥140

**Indications for Neurosurgery for Traumatic Brain Injury**
- Epidural hematomas: size > 30 ml; GCS ≤ 8 with anisocoria; worsening level of consciousness (LOC) with expanding hematoma
- Acute subdural hematomas: thickness > 10 mm or shift > 5 mm; ICP > 20 mm Hg; GCS decreases ≥ 2 points between injury and hospital arrival; or ↓ LOC with anisocoria
- Intraparenchymal hemorrhage: GCS 6–8 with contusion > 50 ml; or frontal/temporal contusions > 20 ml and shift > 4 mm OR cisternal compression
- Posterior fossa bleed/contusion and mass effect or new neurologic defect
- Open depressed skill fracture greater than the thickness of the skull
An Approach to the Management of Elevated Intracranial Pressure (ICP) > 20 cm H₂O and/or Low Cerebral Perfusion Pressure (CPP) < 60 mm Hg

Assure proper patient positioning, good ICP waveform, adequate sedation, normo-thermia

Improve compromised cerebral venous return

• Decrease Positive End Expiratory Pressure (PEEP) to 0 cm H₂O
• Loosen cervical collar or remove if C-spine cleared

If ventriculostomy present, drain CSF

Drain for 3-5 minutes, recheck

Consider continuous drainage with neurosurgeon approval

Mild hyper-ventilation to PCO₂ ~ 35 cm H₂O

• Only effective for ~ 12 hours
• Lower levels of PCO₂ may be deleterious

Sedative bolus

Hypertonic saline (3% NaCl): 0.1-1 ml/kg/hr slow IV infusion

Mannitol 20%; 0.25-2 gm/kg IV load, then 25 grams IV every 2 hours prn ICP > 20 cm H₂O

• Must be administered through a central venous catheter
• Check serum osmolality and serum sodium every 6 hrs.
• Hold hypertonic saline and call neurosurgery if serum osmolality >320 mosm/dL
• Goal serum sodium level ~150

Hemodynamic management to optimize Cerebral Perfusion Pressure (CPP)

Keep CPP > 60 mm Hg (CPP=MAP-ICP)

• Check serum osmolality and serum sodium every 6 hrs.
• Hold mannitol and call neurosurgery if serum osmolality is >320 mosm/dL.
• Osmotic diuresis may cause hypovolemia; favor hypertonic saline with hypovolemic patients

Trial of paralytic agent (see page 189)

Refractory ICP > 20 or CPP < 60 mm Hg

• Barbiturate coma (must have continuous EEG monitoring), or
• Decompressive craniectomy

Return to Table of Contents
Barbiturate Coma

- Inclusion criteria: severe traumatic brain injury with elevation of ICP refractory to maximum standard medical and surgical management (see page 209); presence of neurologic function; adequate cardiopulmonary reserve; continuous EEG monitoring available
- Medication: Pentobarbital sodium 10mg/kg IV load over 30 minutes, then 5mg/kg/hour x 3 hours, then 1mg/kg/hour; titrate up to 3mg/kg/hour as needed to maintain burst suppression and keep ICP < 20 cm H2O
- Monitoring: continuous EEG necessary to monitor for “burst suppression” (goal = 4-8 bursts/minute)
- Side Effects: hypotension, decreased clearance of pulmonary secretions, skin breakdown, hypothermia
- May stop barbiturate coma when ICP controlled for 24-48 hours, or if brain death ensues

Electrolyte Disorders Caused by Traumatic Brain Injury

Hyponatremia

- Syndrome of Inappropriate Antidiuretic Hormone secretion (SIADH)
  - Euvolemic hyponatremia caused by increased antidiuretic hormone (ADH)
  - Diagnosis: rule out hypothyroidism or hypoadrenalism; no clinical evidence of volume depletion; serum Na < 134; serum osmolality < 280; urine sodium > 20-40
  - Treatment: treat the underlying cause if any is found; supportive care and free water restriction being sure not to correct sodium level more than 8-10 mEq in 24 hours; for seizures thought to be due to hyponatremia, consider hypertonic saline administration
- Cerebral Salt Wasting (CSW)
  - Renal loss of sodium and decreased extracellular fluid leading to hypovolemia.
  - Diagnosis: Lab values similar to SIADH but patient will be volume depleted
  - Treatment: Volume replacement with isotonic or hypertonic saline. Avoid fluid restriction.

Hypernatremia

- Diabetes Insipidus (DI)
  - Diminished ADH from the traumatized brain results in decreased water re-absorption in the renal collecting ducts and high output of dilute urine resulting in elevated serum sodium level
  - Diagnosis: suspect with urine output >250ml/hr, very dilute urine (urine specific gravity ≤1.005 and urine osmolarity ~ 50-150), rising serum sodium usually > 150; rule out adrenal insufficiency
  - Treatment:
    - Monitoring: follow Is/Os q 1 hour, electrolytes and serum osmolality q 4 hours
    - IV fluids: Normal saline until euvolemic, then D5W or free water per NG-tube hourly to match urine output
    - Pharmacologic ADH replacement with:
      - Desmopressin (DDAVP) 2-4 mcg (0.5-1.0 ml) IV/subcutaneous bid, OR
      - Pitressin (vasopressin) 5 Units IV/IM/subcutaneous q 4-6 hrs (max 60 Units/day)

Adapted with permission from James Herman, MD, Brian Kimbrell, MD, and Joseph Esherick, MD.
References: 2007 Brain Trauma Foundation Guidelines (www.braintrauma.org)
Spinal Cord Injuries

Evaluation:

- Perform a baseline neurological assessment on any patient with suspected spinal injury or spinal cord injury (SCI) to document the presence of SCI. If neurologic deficits are consistent with SCI, determine a neurological level and the completeness of injury.

- Perform serial examinations as indicated to detect neurological deterioration or improvement. In patients with SCI, be aware that bony imaging of the spinal column may be negative (i.e., “SCIWORA,” or SCI without radiological abnormality).

- In a patient with a stiff spine and midline tenderness, suspect a fracture. Consider MRI, bone scan, and/or computed tomography (CT) if the plain x-ray is negative for fracture, especially in the presence of spondylosis, ankylosing spondylitis (AS), or diffuse interstitial skeletal hyperostosis (DISH).
Neurological Syndromes of Incomplete Spinal Cord Injuries

| Syndrome          | Description                                                                                                                                       | Treatment/ Prognosis                                                                                   |
|-------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Bulbar-cervical   | A lesion above C4 that produces almost immediate cardiopulmonary arrest and death if CPR is not started within minutes. Ventilator dependent. Very poor prognosis and long-term survivability | No acute surgery unless highly unstable; wait for hemodynamic and autonomic stability                  |
| Central Cord      | A lesion, occurring almost exclusive in the central portion of the cervical spinal cord, that produces sacral sensory sparing and greater weakness in the upper limbs than lower limbs. Often pre-existing congenital or degenerative stenosis. Hyperpathia to sensory stimuli is common | • Classic teaching is to postpone surgery, to allow for cord edema and hematoma to pass  
• Delayed surgery to correct stenosis  
• Good chance of delayed leg function recovery                                                |
| Anterior Cord     | A lesion that produces dissociated loss of motor function and of sensitivity to pain and temperature while preserving proprioception. Bilateral paraplegia. May be result of either anterior spinal arterial ischemia or compression from disc or bone | • If compressive element seen early, early surgical decompression may be warranted  
• Worse prognosis, with only 20% motor recovery                                                      |
| Brown-Sequard     | A lesion that produces relatively greater ipsilateral proprioceptive and motor loss and contralateral loss of sensitivity to pain and temperature. Usually from penetrating trauma, epidural hematoma, radiation, large disc herniations, spondylosis. | • Best prognosis of incomplete lesions  
• 90% regain ability to ambulate independently  
• Rate indications for surgery except sometimes for debridement after penetrating trauma         |
| Cauda Equina      | Injury to lumbosacral nerve roots within the neural canal resulting in areflexic bladder, bowel, and lower limbs. Usually poor return of bowel/ bladder function. | • Surgery usually beneficial within 24-48 hours  
• Delayed root escape or improvement                                                               |

Management Principles:
• Initial Management (ABCs, Resuscitation)
  - Provide airway and ventilatory support in patients with high tetraplegia early in the clinical course.
    - Patients with motor-complete injury at a level rostral to C5 will almost invariably require ventilatory support.
    - The goal of intubation is to secure the airway with as little movement of the cervical spine as possible. The standard urgent or emergent intubating technique for someone with a presumed or known cervical spine injury is a rapid sequence induction with cricoid pressure and manual inline stabilization.
    - If a difficult intubation is anticipated, an awake fiberoptic intubation is an appropriate alternative (allows for no manipulation of the spinal column and assessment of neurologic function after intubation).
    - Anticipate bradycardia and hypotension during intubation of the tetraplegic patient.
    - Avoid the use of succinylcholine after the first 48 hours post–cord injury (may use in the first 48 hours after injury).
    - If intubation is not necessary, consider evaluation of baseline pulmonary function on admission with measurement of tidal volume, vital capacity, and negative inspiratory force ('NIF'; -30 or more negative is considered adequate)
Prevent and treat hypotension.

- Hypotension and shock are particularly deleterious to the injured spinal cord, contributing to cord hypoperfusion and perpetuating secondary cord injury
- Patients with injuries at or above T6 are at risk for hypotension caused by autonomic instability
- Standard hemodynamic parameters (blood pressure, pulse) do not adequately quantify the degree of shock and physiologic derangement in trauma patients, particularly in those with SCI. Initial base deficit or lactate level can be used to determine the severity of shock and the need for ongoing fluid resuscitation.
- Exclude other injuries before assigning the cause of hypotension to neurogenic shock (i.e. hemorrhage, pneumothorax, myocardial injury, pericardial tamponade, sepsis related to abdominal injury, and other traumatic and medical etiologies (like adrenal insufficiency; one study of patients with traumatic brain injury found a 50% incidence of at least transient adrenal insufficiency) (not an exhaustive list)).

Treatment:

- Fluid resuscitation is the mainstay of initial therapy
- Vasopressors should be chosen so as to minimize exacerbation of bradycardia. An ideal agent should have both alpha- and beta-adrenergic actions, such as dopamine, norepinephrine, or epinephrine, to counter the loss of sympathetic tone and provide chronotropic support to the heart. Pure alpha agents (phenylephrine) can potentiate bradycardia and may not be ideal for high thoracic or cervical spinal cord injuries
- Uncontrolled studies that used fluids and vasopressors to achieve a mean arterial pressure of 85 mmHg for a minimum of 7 days in patients with acute SCI have reported favorable outcomes (Levi et al., 1993; Vale et al., 1997)
- Recognize and treat neurogenic shock.
  - Neurogenic shock (reduced blood pressure from neurologic causes) is common in patients with acute tetraplegia or high-level paraplegia (T1–T4)
  - Occurs secondary to sympathetic denervation, resulting in arteriolar dilation and pooling of blood in the venous compartment, and interruption of cardiac sympathetic innervation (T1–T4) with unopposed vagal activity promotes bradycardia and reduced myocardial contractility.

Monitor and treat symptomatic bradycardia

- Acute cervical SCI may also result in bradydysrhythmas, which may lead to hypotension and asystole
- Bradydysrhythmas are more common in the first 2 weeks after injury.
- Bradycardia may also occur and is often associated with a noxious stimulus such as endotracheal suctioning or position changes
- Cardiovascular interventions, such as the use of vasopressors, atropine, aminophylline, or pacemakers, are more commonly required in high cervical injury patients

No clinical evidence exists to definitively recommend the use of any neuroprotective pharmacologic agent, including steroids, in the treatment of acute spinal cord injury in order to improve functional recovery.

Complete a comprehensive tertiary trauma survey in the patient with potential or confirmed spinal cord injury.

Surgical Management of Spinal Cord Injury

- Perform a closed or open reduction as soon as permissible on patients with bilateral cervical facet dislocation in the setting of an incomplete spinal cord injury. If traction reduction is not preferred or possible, then open reduction should be performed.
- Consider early surgical spinal canal decompression in the setting of a deteriorating spinal cord injury as a practice option that may improve neurologic recovery.
although there is no compelling evidence that it will. Consider early spinal stabilization where indicated.

- Pain and Analgesia Management
  - Following spinal cord injury, patients may immediately experience distressing pain and sensitivity relating to trauma to the cord (neuropathic pain at or below the level of the injury), the spinal nerves (at-level neuropathic pain), the spinal fracture (at-level musculoskeletal pain), or from other concomitant injuries.
  - Allodynia (hypersensitivity to dynamic touch) is a type of evoked pain that is more often seen in patients with cervical injuries, and follows shortly thereafter
  - Chronic pain affects approximately 70% of those with spinal cord injury

- Secondary Prevention
  - Skin Care
    - Assess areas at risk for skin breakdown frequently
    - Place the patient on a pressure-reduction mattress or a mattress overlay, depending on the patient’s condition. Use a pressure-reducing cushion when the patient is mobilized out of bed to a sitting position.
    - Provide meticulous skin care:
      - Reposition to provide pressure relief or turn at least every 2 hours while maintaining spinal precautions.
      - Keep the area under the patient clean and dry and avoid temperature elevation.
      - Inspect the skin under pressure garments and splints.
  - Prevention and Treatment of Venous Thromboembolism
    - Apply mechanical compression devices early after injury.
    - Begin low molecular weight heparin or unfractionated heparin plus intermittent pneumatic compression, in all patients once primary hemostasis is evident.
      - Intracranial bleeding, perispinal hematoma, or hemothorax are potential contraindications to the administration of anticoagulants, but anticoagulants may be appropriate once bleeding has stabilized.
    - Consider placing a vena cava filter only in those patients with active bleeding anticipated to persist for more than 72 hours and begin anticoagulants as soon as feasible.
  - Respiratory Management:
    - Monitor patients closely for respiratory failure in the first days following spinal cord injury.
      - Obtain baseline respiratory parameters (vital capacity, FEV1) and arterial blood gases when patients are first evaluated and at intervals until stable.
      - Consider mechanical ventilation for patients with tetraplegia.
      - Admit patients with complete tetraplegia and injury level at C5 or rostral to an intensive care unit.
    - Perform a tracheostomy early in the hospitalization of patients who are likely to remain ventilator dependent or to wean slowly from mechanical ventilation over an extended period of time, unless the treating center has special expertise in the use of noninvasive ventilation.
    - Treat retained secretions due to expiratory muscle weakness with manually assisted coughing (“quad coughing”), pulmonary hygiene, mechanical insufflation-exsufflation, or similar expiratory aids in addition to suctioning.
    - Initiate a comprehensive protocol to prevent ventilator-associated pneumonia in patients with acute SCI who require mechanical ventilation for respiratory failure.
  - Genitourinary Tract:
- Place an indwelling urinary catheter as part of the initial patient assessment unless contraindicated. If contraindicated, use emergent suprapubic drainage instead.
- Leave indwelling urinary catheters in place at least until the patient is hemodynamically stable and strict attention to fluid status is no longer needed.
- Priapism is usually self-limited in acute SCI and does not require treatment. There is no evidence to support avoidance of a urethral catheter in the presence of priapism secondary to acute SCI.

  o Gastrointestinal Tract:
    - Stress ulcer prophylaxis is to be continued for 4 weeks, due to high risk of bleeding with spinal cord injury.
    - The goal for patients with neurogenic bowel dysfunction is to have one scheduled bowel movement per day, with use of oral medications, suppositories, and digital stimulation as needed to trigger the bowel movement.

  o Nutritional Support:
    - Use enteral rather than parenteral nutrition whenever possible.
    - Feed a standard enteral formula initiated within 24 to 48 hours after admission, using the semirecumbent position when possible to prevent aspiration.

  o Rehabilitation:
    - Use nonpharmacologic and pharmacologic interventions for orthostatic hypotension as needed. Mobilize the patient out of bed to a seated position once there is medical and spinal stability. Develop an appropriate program for out-of-bed sitting. Limit in-bed and out-of-bed semireclined sitting, as it often produces excessive skin shear and predisposes to pressure ulcer formation.

  o Psychosocial and Family Issues:
    - Assess mental health in general and possible risk for psychosocial problems after admission and throughout acute care stay. Involve members of the health-care team as needed. Pay particular attention to the following factors: current major depression, acute stress disorder/posttraumatic stress disorder (PTSD), substance intoxication and withdrawal, social support network (or lack thereof), cognitive functioning and learning style, personal and cultural preferences in coping style and social support, concurrent life stressors, concomitant health problems, medical conditions, medications, and history of TBI; history of mental illness, including major depression, PTSD, substance abuse; use of psychiatric medications.
    - Foster effective coping strategies, health-promotion behaviors, and independence through a variety of ongoing interventions.
      - Use assistive devices such as head-controlled call bells, bed controls, prism glasses, and communication boards.
      - Acknowledge that feelings of gratitude, uncertainty, loss, and helplessness may be present simultaneously.
      - Provide medical and prognostic information matter-of-factly, yet at the same time leave room for hope.
      - Respect expressions of hope. Avoid direct confrontations of denial concerning probable implications of the injury.
      - Help the patient and family to identify effective coping strategies that have aided them in the past.
      - Develop a partnership of patient, family, and health-care team to promote involvement in the treatment plan and optimize patient outcomes.
OBSTETRICS IN THE ICU

Critical Care Cardiology in the Pregnant Patient

Cardiac Arrest in the Pregnant Patient
- CPR to be performed with a wedge under the right hip
- Remove all fetal monitoring leads prior to defibrillation
- Consider peri-mortem C-section within 4 minutes if initial resuscitation fails and there is a viable fetus.

Acute Coronary Syndrome in the Pregnant Patient
- Safe Medications in Pregnancy: Aspirin, clopidogrel, metoprolol, nitrates, morphine, heparin or low-molecular weight heparin
- PCI with bare metal stent placement is safe in pregnancy
- Thrombolytics are relatively contraindicated in pregnancy
- Postpone delivery for ≥ 2 weeks after MI if possible; vaginal delivery preferred

Hypertensive Emergencies in the Pregnant Patient
- MUST rule out pre-eclampsia (severe = BP≥ 160/110 on 2 occasions 6 hours apart, AND proteinuria ≥ 5 grams or 3+ or greater on two random urine specimens, AND end-organ damage [urine output <500ml/d, cerebral/visual disturbances, pulmonary edema, epigastric or RUQ pain, impaired liver function, thrombocytopenia, or fetal growth restriction]
- For true hypertensive emergencies (blood pressure > 160/110 mmHg with end-organ dysfunction): hydralazine 5-10mg IV q 15-20 minutes; labetalol 20-40 mg IV q 15 minutes (max 300 mg/day) or labetalol drip at 0.5-2 mg/min IV; or nicardipine 5-10 mg/hr
  - For refractory hypertensive emergencies: nitroprusside 0.5-4 mcg/kg/min
  - Nicardipine or labetalol are preferred for hypertensive encephalopathy
  - Nitroglycerine (5-100 mcg/min IV) preferred for myocardial ischemia

Preferred vasopressors During Pregnancy
- Dopamine or ephedrine

Congestive Heart Failure in the Pregnant Patient
- May be associated with tocolytics (+/- steroids)
- May also be associated with peri-partum cardiomyopathy (defined as Left Ventricular Ejection Fraction < 0.45 occurring ≥ 36 weeks gestation or within 5 months post-partum in the absence of other causes of heart failure)
- Treatment: discontinuation of tocolysis, furosemide, oxygen +/- non-invasive ventilation

Mitral Stenosis
- Bed rest, loop diuretics, and rate control with beta-blockers or digoxin
- Heparin or low-molecular weight heparin for atrial fibrillation/atrial flutter
- Balloon mitral valvuloplasty for hemodynamic compromise

Aortic Stenosis
- Usually presents as dyspnea, angina or syncope starting late 2nd to early 3rd trimester
- Consider percutaneous aortic balloon valvuloplasty for hemodynamic instability
- Use extreme caution with spinal/epidural anesthesia due to marked vasodilation
Critical Care Pulmonology in the Pregnant Patient

Amniotic Fluid Embolism
- Typically occurs during labor, immediately post-partum or after abdominal trauma
- Clinical presentation: sudden cardiovascular collapse, acute pulmonary edema; often disseminated intravascular coagulation (DIC), altered mental status and seizures
- Treatment: mechanical ventilation with 100% oxygen; fluids; inotropic support; for DIC see page 126

Pulmonary Embolism in the Pregnant Patient
- D-Dimer should be checked but may be elevated from pregnant state alone
- A CT pulmonary angiogram and a V/Q scan have similar radiation exposure to the fetus
- Duplex compression ultrasound of lower extremities to rule out DVT
- Treatment: Initiate IV heparin x 5 days, then transition to subcutaneous low-molecular weight heparin (until 6 weeks post-partum)
- Adjust low-molecular weight heparin based on anti-factor Xa levels
- Consider thrombolytics for massive pulmonary embolism with obstructive shock

Ventilator Management in Pregnancy
- Avoid hyperventilation (hypocapnea) as it will decrease utero-placental blood flow
- PCO2 may be allowed to rise up to 60 mmHg without detriment to the fetus
- In ARDS, deliver the baby as soon as possible once maternal conditions stabilizes

Miscellaneous Conditions in the Critically Ill Pregnant Patient

Eclamptic Seizures
- May occur pre-partum or up to a week or more post-partum
- Magnesium 4 grams IV load, then 2 grams IV/hour drip; deliver baby

HELLP Syndrome
- Hemolysis (LDH >600 IU/L, total bilirubin > 1.2 ng/dL), Elevated Liver enzymes (AST and ALT 200-700 IU/L), and Low Platelets
- Increased risk for ruptured liver hematoma
- Treatment: expeditious delivery of the baby, supportive care

Acute Fatty Liver of Pregnancy
- Occurs during third trimester of pregnancy
- Clinical presentation: right upper quadrant abdominal pain, nausea, vomiting, fatigue
- Labs: AST/ALT elevations up to 1,000 IU/L; elevated PT, PTT; decreased fibrinogen; renal failure; severe hypoglycemia; bilirubin 1-10 ng/dL (hyperbilirubinemia more marked in AFLP versus HELLP syndrome)

Trauma in the Pregnant Patient
- Standard ATLS procedure, but maintain left lateral tilt in the patient
- Workup: FAST ultrasound scan for free fluid in abdomen, Kleihauer-Betke prep to screen for feto-maternal transfusion, and standard ATLS diagnostic studies
- Placental abruption occurs in 25-50% of major trauma
- Give Rhogam 300 mcg IM to all Rh-negative women

**MISCELLANEOUS**

**End of Life Discussions in the ICU**

Physicians in the ICU are often responsible for conveying bad news to patients' families. How this is done can have significant impact on how the family copes with news, and the decisions they come to. It directly affects your patient's care.

One way to frame this discussion is the following:

1. Identify yourself and your role in caring for the patient.
2. Identify the family members and, if needing to come to a critical decision, ensure that all those who will want to be making decisions are present (and if not, when can they all be there?).
3. Present what is going on with their family member as much in ‘layman’s terms’ as possible.
4. Then say the following: "Because your [family member] is ill and in the ICU, we need to understand from you what he/she would want if his/her breathing or heart stops (you may choose to emphasize: “we're not asking you to make a decision, we're asking you to tell us what his/her decision would have been if we were having the conversation with them instead of you”). Another way this can be framed is to say, “if your family member was to wake up for 15 minutes, assess the situation, and then have to go back to it, what would they tell you they would want done?”
5. Then, "There are many things that people choose: from doing nothing, letting nature take its course and wanting to be kept as comfortable as possible; to using medications or shocks to try to correct an abnormal heart rhythm and wanting us to push on the chest if the heart stops, and attaching them to a breathing machine if they stop breathing. Many people are in-between. What most fits with what you think your family member would have wanted?"

The term “Allow Natural Death” is a very useful alternative term to use at this point.

Though subtle, framing things this way (which places the burden of decision on the critically ill patient as the decision maker, and only asks the family to tell us what the patient’s wishes would be could they tell us) may help to take away the feeling of responsibility about what happens to their family member and potentially avert the family feeling guilty that they are directly responsible for if their family member lives or passes away. Taking away guilt may be one of the kindest things that you can do for a family as they struggle with seeing their family member critically ill.

**Comment about “Do Not Resuscitate/Do Not Intubate” (DNR/DNI)”**

There has been an unfortunate confusion between “DNR/DNI” and “Comfort Measures Only”. Because someone has elected to not be intubated or resuscitated in the face of cardiopulmonary collapse does NOT mean that they do not want the best care available just short of that to try to make them better. Patients who are “DNR/DNI” should still be treated as you would treat patients who are “full code”, short of intubating/shocking/resuscitating them. “DNR/DNI” patients can be admitted to, and cared for in, the ICU.

For further reading, see [www.finalchoices.org](http://www.finalchoices.org), and the Physician Orders for Life-Sustaining Treatment (POLST) form.
End of Life Care in the ICU

It is paramount that a family and a patient feel that care is not being “withdrawn” at the end of life. The idea of continuing to provide care, but changing the GOAL of care from painful/curative to the GOAL of patient COMFORT is a subtle but extremely important nuance.

Prior to initiating comfort measures, ask the family / patient if they would like the hospital to contact a priest, rabbi, or other healer to administer the patient’s last rites in accordance with their desires. The nursing staff or nursing supervisor should have information on how to contact the appropriate person.

What to physically do with the patient when they are deemed to want to be comfortable?

- Monitors should be turned to “visitor status” (blank screen in the room, cardiac monitor able to be viewed at the nurse’s station to alert staff when the patient has passed away) and alarms turned off. The rationale: this will allow the family to focus on their family member and not on the monitor.
  - Note: If still intubated, you may ask the respiratory therapists to turn off the monitor, but most vent monitors do not turn off. In that case, covering the monitor with a bed sheet may serve the same purpose.
- If still vented, consider turning the vent down (in conjunction with Respiratory Therapy) to normal (and not supra-normal) vent settings. The patient may be extubated if the family so desires.
- Medications to ensure comfort:
  - Sedation/Analgesia: Morphine IV boluses vs. drip (communicate with your nurse as far as the best way to ensure patient comfort)
  - Anxiolysis: Ativan IV boluses vs. drip
  - Oxygen prn air hunger and patient comfort
  - For Copious secretions, Scopolamine 0.4mg patch behind the ear may be used q 3 days

Example of Orders:
1. D/C All Antibiotics, blood draws, Medications
2. Morphine drip 1 mg/hour; may increase drip rate 50-100% q 15 minutes prn patient discomfort, pain, or air hunger
3. Ativan 2mg IV q 1 hour prn anxiety
4. Oxygen by Nasal Cannula or facemask prn air hunger
5. Scopolamine 0.4mg transdermal behind the ear prn copious secretions

- Patients may be transferred to Definitive Observation Unit (DOU) status when the decision has been made to make them “Comfort Measures Only”, even if they remain intubated. However, if at all possible, the patient should not be physically moved to a new room for 12-24 hours after a “Comfort Measures” decision has been made unless extenuating circumstances (e.g. full ICU) happen. Comfort measures is often very nursing-heavy, and quickly transferring patients who are made “comfort measures” out of a Unit may make a family feel (fairly or unfairly) that they are being abandoned.
Organ Donation/ Procurement/ Transplantation

History of Organ Transplantation:
- First successful transplant performed in 1954 (kidney transplant, from one twin to another)
- Livers and hearts could only be transplanted from organ donors that had died
  - First liver transplant in 1967, and first successful heart transplant in 1968
- Introduction of cyclosporine in 1980 greatly improved survivability of transplantation and expanded the repertoire of organs that could be transplanted successfully
- The Uniform Declaration of Death Act (UDDA) was established by the National Conference of Commissioners on Uniform State Laws and ratified by the American Medical Association and American Bar Association and all 50 states in 1981
  - Defined death as either “1) irreversible cessation of circulatory and respiratory functions, or 2) irreversible cessation of all functions of the entire brain, including the brainstem. A determination of death must be made in accordance with accepted medical standards”
- National Organ Transplant Act (NOTA) of 1984 called for an Organ Procurement and Transplant Network to be run by a private, non-profit organization under federal contract
  - United Network for Organ Sharing (UNOS) (www.unos.org) manages the Organ Procurement and Transplant Network
  - Local “Organ Procurement Organization” (“OPO”) is “OneLegacy” based in Los Angeles

Organ Donation as it applies to care of critical patients:
- ~1% of deaths will qualify for organ donation
- Majority of donations will be done in brain dead donors (see Page 207, determination of brain death)
- “Donation After Cardiac Death” (“DCD”) (VCMC Administrative Policy 100.050)
  - The only criteria for donation (outside of living donor donation (i.e. a live person donating one kidney to another liver person)) prior to 1981; now uncommon
  - Patient must die within 1 hour of extubation or else their organs cannot be procured
    - “Wisconsin” scoring system and other scoring systems are used by “OPO”s to “score” the patient and determine the likelihood of death within 1 hour of extubation
    - Based on the score, the “OPO” will deem a patient eligible for “DCD” or not
    - If patient is eligible, extubation is often performed in the Operating Room with the Transplant Surgical team at the ready for when the patient is declared dead (usually 2-5 minutes after cessation of cardiopulmonary activity (2 minutes at VCMC))
  - Significant push from OneLegacy and other “OPO”s to increase rates of “DCD” in patients who are not brain dead—this is somewhat controversial

“Clinical Triggers” (reasons to call OneLegacy about a potential organ donor):
- “Ventilated patients with devastating injury or illness, including any of the following:
  - Brain/Neurologic injury (traumatic or non-traumatic) with loss of a brainstem reflex (pupils fixed, no cough, no gag, no response to painful stimuli, no spontaneous respirations)
  - Hemodynamic instability without chance of survivability”
  - OneLegacy would also like to hear about patients “prior to family discussion of DNR or withdrawal of ventilator” regarding eligibility for Donation After Cardiac Death (“DCD”).

Communication with families about organ donation:
- This is always an extremely difficult subject to broach, particularly when the family has a lot of hope for improvement of the patient, limited understanding of the patient’s illness, etc.
- It is the author’s opinion that families want to know that the medical staff treating the patient have the patient’s recovery as their only goal up until the point that it is deemed that recovery is impossible. The author does not discuss organ donation with families neither before nor during the discussion

Return to Table of Contents
about end of life issues (i.e. ‘separation of church and state’). The author is aware that this is a very
subjective and controversial subject and there are many ways to ‘skin the cat’.

- OneLegacy has experts ("Family Services Coordinators") who are trained to approach families in the
  most challenging of situations; approach of families about organ donation is to be performed by
  the OneLegacy Family Service Coordinator

- Treating providers have a number of different approaches to introducing the OneLegacy staff to the
  family at the appropriate time (usually at the end of an end of life discussion); options include:
  - “An end of life expert will now come and talk to you”, and have the OneLegacy
    representative talk to the family after you have concluded
  - Some centers have begun to couple the process of notification of brain death and the initial
    approach for donation, in that the treating physician and the family services coordinator from
    the organ donor network are present for both discussions.
    - More data needed, but may anecdotally increase the rate of conversion from potential
to actual donor

Management of the Potential Organ Donor

- Focus on supportive care for the body’s organs
  - Maintain hemodynamic stability as soon as possible
    - Vasopressin as an early pressor, if indicated
  - Preferential colloid administration for those who are already declared dead to minimize organ
    edema and improve blood flow; crystalloid prior to that point (subgroup analysis of SAFE
    Trial (2004) revealed higher mortality with head injured patients who received colloid)
  - Protective lung ventilation with consideration of Airway Pressure Release Ventilation
    (APRV) (see page 56)
- T4 protocol (“PHA T4 Protocol”)
  - Panhypopituitary state accompanies brain death and leads to refractory hypotension
  - With hormone replacement, 53% of hypotensive brain dead patients able to be weaned off of
    pressors
  - Hormones to be replaced:
    - Levothyroxine (T4)
      - Acts as a pressor
      - T4 bolus dose: 20 mcg IV x 1
        - Causes acute hyperkalemia—must be administered with insulin (10
          units regular IV) and glucose (D50 1 ampule) (unless blood glucose
          >300 mg/dL, then insulin alone) to drive potassium into cells
        - T4 infusion: 10 mcg/hour, titrated to ***SBP***, max dose 20 mcg/hour
        - Side effects: hypertension and tachyarrhythmias
          - Methylprednisolone at varying doses (1 gram IV bolus then 1 gram over 8 hours
daily is VCMC policy; others use 15 mg/kg IV daily) which improves potential for
lung donation and treats centrally mediated adrenal insufficiency
        - Insulin drip form starting at 1 unit / hour after initial bolus, titrated to euglycemia
        - Vasopressin at 0.5 units per hour IV

References:
Pronouncing Death

The following steps should be followed when pronouncing a patient dead:

- Identify the patient (name and ID number on their wrist band)
- Examine the patient for:
  - Response to verbal or tactile stimuli (none)
  - Spontaneous respirations (none)
  - Heart sounds and pulses (none)
  - Pupillary response (fixed and dilated)
- Document the time the patient was pronounced dead
- Notify the attending physician (if not already done by the nursing staff) and inquire if the family requests an autopsy
- Document findings in patient’s chart (i.e. “Called by charge nurse to pronounce Mr. Juan Garcia dead. Patient examined, unresponsive to verbal or tactile stimuli, no spontaneous respirations noted, heart sounds not audible, pulses absent, pupils fixed and dilated. Patient pronounced dead at 11:10pm. Attending physician notified. Next of kin notified.”)
- If you will be contacting the family to inform them of the death of their loved one, consider the following steps:
  - Familiarize yourself with the patient’s medical history and mode of death
  - Identify yourself to the family in a humble and caring manner and inform them that their family member has expired. Inform them of the time that the patient was pronounced dead and always try to comfort them that their relative died peacefully.
  - If it is not clear from the patient’s records, inquire if the family requests an autopsy
  - Ask the next of kin if the family will be coming to the hospital to view the body before it is transported to the hospital morgue. Notify the nurse of their decision.
- Dictate a brief death note, indicating cause of death if known
- Fill out discharge summary
- Write the order to “Release body to the morgue” if the family does not want to see the body
- A physician must call the Medical Examiner if the patient meets criteria as a Coroner’s Case:
  - Known or suspected homicides, suicides and accidents
  - Deaths involving criminal action or suspicion of a criminal act
  - Poisoning and deaths related to substance abuse.
  - All deaths in jail or in police custody
  - All deaths related to occupational diseases or hazards
  - All deaths wherein the deceased has not been attended by a physician within the 20 days preceding death
  - Deaths in which a physician is unable to reasonably state a cause of death (unwillingness does not apply)
  - Deaths involving suspected contagious diseases constituting a public hazard
  - Deaths of unidentified persons
  - Deaths occurring within 24 hours of admission to a hospital
  - Ventura County Medical Examiner: (805) 641-4400 (to be called by physician only)
- If the patient is accepted as a Coroner’s Case, do not remove any lines or tubes; cut them in-place or leave them in-place prior to releasing the body to the Coroner

Poisonings and Toxidromes (See “Approach to the Comatose Patient”, page 180)

<table>
<thead>
<tr>
<th>Toxidrome</th>
<th>Description</th>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-cholinergic</td>
<td>“red as a beet (flushed), dry as a bone (dry skin), hot as a hare (hyperthermia), blind as a bad (midriasis), mad as a hatter (delirium), full as a flask (urinary retention, ileus); and ↑ HR/BP, myoclonus or seizures</td>
<td>Amantadine, tricyclics, antihistamines, anti-parkinsonian meds, low-potency antipsychotics, antispasmetics, atropine, and jimson weed</td>
</tr>
<tr>
<td>Benzo OD</td>
<td>Coma, respiratory depression, nystagmus, hypotonia, ↓ BP</td>
<td>Carbamate, organophosphate insecticides, cholinesterase inhibitors</td>
</tr>
<tr>
<td>Cholinergic</td>
<td>SLUDGE (salivation, lacrimation, urination, defecation, GI cramps, emesis) and bradycardia, bronchoconstriction, miosis and rhinorrhea</td>
<td></td>
</tr>
<tr>
<td>Opiate OD</td>
<td>Coma, respiratory depression, miosis, pulmonary edema, ↓ HR/BP</td>
<td>Amphetamines, cocaine, ephedrine, pseudoephedrine, theophyllines</td>
</tr>
<tr>
<td>Sympathomimetic</td>
<td>Tachycardia, hypertension, fever, diaphoresis, midriasis, hyperreflexia, psychosis, potentially dysrhythmias or seizures</td>
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</tbody>
</table>

Antidotes for Specific Ingestions

<table>
<thead>
<tr>
<th>Ingestion or bite</th>
<th>Antidote/Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen</td>
<td>N-acetylcysteine 140mg/kg load, then 70mg/kg q4h</td>
</tr>
<tr>
<td>Anticholinergics</td>
<td>Physostigmine</td>
</tr>
<tr>
<td>Benzodiazepine</td>
<td>Flumazenil (avoid if chronic benzo use)</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>Atropine, glucagon, and calcium</td>
</tr>
<tr>
<td>Calcium channel blockers</td>
<td>Atropine, glucagon, and calcium</td>
</tr>
<tr>
<td>Carbon monoxide</td>
<td>Supplemental O₂ (hyperbaric in severe cases)</td>
</tr>
<tr>
<td>Cholinesterase inhibitors</td>
<td>Atropine, pralidoxime</td>
</tr>
<tr>
<td>Cyanide</td>
<td>Amyl nitrite, sodium nitrite, sodium thiosulfate</td>
</tr>
<tr>
<td>Digitalis</td>
<td>Digoxin immune Fab</td>
</tr>
<tr>
<td>Ethylene glycol</td>
<td>Ethanol, fomepizole, pyridoxine, thiamine</td>
</tr>
<tr>
<td>Heavy metals (arsenic, lead, mercury)</td>
<td>Dimercaprol, EDTA</td>
</tr>
<tr>
<td>Heparin (or LMWH)</td>
<td>Protamine sulfate</td>
</tr>
<tr>
<td>Iron</td>
<td>Deferoxamine</td>
</tr>
<tr>
<td>Isoniazid</td>
<td>Pyridoxine</td>
</tr>
<tr>
<td>Methanol</td>
<td>Ethanol, fomepizole, folinic acid, folate</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>Folinic acid</td>
</tr>
<tr>
<td>Methemoglobinemia</td>
<td>Methylene blue</td>
</tr>
<tr>
<td>Opioids</td>
<td>Naloxone</td>
</tr>
<tr>
<td>Organophosphates (&amp; other insecticides)</td>
<td>Atropine, pralidoxime</td>
</tr>
<tr>
<td>Salicylate overdose</td>
<td>Urine alkalization with Bicarb, dialysis if needed; AVOID INTUBATION IF AT ALL POSSIBLE</td>
</tr>
<tr>
<td>Snakebites (Crotalids)</td>
<td>Crotalidae Polyvalent Immune Fab</td>
</tr>
<tr>
<td>Sulfonylureas</td>
<td>Octreotide, glucagons and dextrose</td>
</tr>
<tr>
<td>Sympathomimetics</td>
<td>Benzodiazepines +/- phentolamine</td>
</tr>
<tr>
<td>Warfarin</td>
<td>Vitamin K</td>
</tr>
</tbody>
</table>

Adapted from Chest 2003; 123: 577.
Management of Acetaminophen Toxicity
- Clinical presentation: Stage 1: asymptomatic; Stage 2: nausea, vomiting, anorexia, RLQ pain, jaundice; Stage 3: renal failure, bleeding; Stage 4: encephalopathy → coma
- Treatment: N-acetylcysteine 140mg/kg po x 1, then 70mg/kg po q 4 hours x 17 doses

Management of Alcohol Intoxications (ethylene glycol, methanol)
- Clinical presentation: nausea, confusion, ataxia, slurred speech, sedation, seizures; severe cases: ARDS or cardiac failure; renal failure (ethylene glycol); blindness (methanol)
- Lab findings: anion gap acidosis, osmolar gap; ethylene glycol also causes hypocalcemia and urinary calcium oxalate crystals
- Indications for fomepizol or ethanol: serum ethylene glycol level > 20 mg/dL; ingested > 100 ml and osmolar gap > 10 mOsm/kg; or suspected ingestion and ≥ 2 of the following: pH<7.3, serum HCO₃ < 20 mEq/L, osmolar gap > 10 mOsm/kg, or urine oxalate crystals
- Hemodialysis if: worsening vitals; pH<7.25; refractory renal failure/electrolyte abnormalities

Management of Salicylate Toxicity
- Clinical presentation: nausea, vomiting → tinnitus, sweating, hyperpnea, delirium → lethargy, respiratory failure, seizures → cardiac failure and cerebral edema
- Labs: Anion gap acidosis, respiratory alkalosis, hypokalemia, salicylate level > 20mg/dL
- Treatment: Urinary alkalinization and potassium repletion
- Hemodialysis if: refractory acidosis or hypotension, seizures, pulmonary edema, rhabdomyolysis, renal failure, salicylate level > 100 mg/dL or if intubation is needed (prefer to dialyze rather than intubate if at all possible)

Management of Tricyclic Antidepressant Toxicity
- Clinical Presentation: anticholinergic toxidrome, sinus tachycardia, drowsiness → delirium, rigidity, prolonged PR/QRS/QT → seizures, hypotension → ventricular fibrillation/tachycardia, coma, and respiratory depression
- Best predictor of seizures or ventricular arrhythmias is a QRS duration > 0.16 seconds
- Treatment: urinary alkalinization, IV fluids and norepinephrine for hypotension, lorazepam for seizures, intubation for respiratory failure; monitor for arrhythmias

Hypothermia

Definitions
- Moderate Hypothermia: Core temperature 28-32°C
- Severe Hypothermia: Core temperature <28°C
- Frostbite: superficial if skin/subcutaneous tissues; deep if bones, joints or tendons

Risk Factors
- extremes of age, malnutrition, hypothyroidism, diabetes, adrenal insufficiency, sepsis, environmental temperatures under 0°C, high wind speeds, water immersion, alcohol use, meds (benzodiazepines, meperidine, clonidine or neuroleptics), immobility; risk of frostbite if wind chill index -25 or less

Clinical Presentation
- Delirium, amnesia or coma, bradycardia, arrhythmias, ileus, shock, renal failure, rhabdomyolysis, neuropathy, frostbite, skin blisters or gangrene

Labs
- CBC, chemistry panel, TSH, CK, urine drug screen, PT, PTT, and ABG
- Other data: CXR, ECG, and urinalysis with micro

Treatment
- ABCs, IV fluids, remove all cold clothing, cardiac monitoring, & a foley catheter
- Moderate Hypothermia
  - Passive rewarming: warming blanket, heat up ambient room temperature and hat
- Severe Hypothermia
  - Active rewarming: warm IV fluids and heated oxygen; gastric lavage and bladder lavage with heated fluids in more severe cases; peritoneal lavage, thoracic lavage or heated hemodialysis or cardiopulmonary bypass only in extreme cases
- Frostbite therapy: place in 40-42°C water x 15-30 min; splint & elevate extremity; keep blisters intact; give dTaP; consider escharotomy if vascular compromise

Near Drowning

Labs:
- CBC, chemistry panel, urine drug screen, ECG, CXR, and ABG

Treatment:
- ABCs, remove wet clothing, cardiac monitor, IV fluids, foley catheter and all passive and active rewarming methods as above if pt is hypothermic

Poor Prognosis with:
- Submersion>5 min, warm water, fresh water, pulseless at scene, ventricular fibrillation, GCS<8, arterial pH≤7, or initial PaO2<60 mmHg

Heat Stroke

Definition
- T>40°C (104°F) with CNS dysfunction (seizures, delirium or coma)

Risk factors
- age<15 or >65 yrs, obesity, severe exertion, high environmental heat and humidity, dehydration, alcohol, cocaine, ecstasy or amphetamine use, meds (pseudoephedrine, ephedrine, phenylpropanolamine, anticholinergics, antihistamines, benzodiazepines, β-blockers, calcium channel blockers, diuretics, laxatives, neuroleptics, phenothiazines, and tricyclic antidepressants)

Clinical presentation
- anhydrosis, CNS dysfunction, anorexia, dizziness, headache, nausea, weakness, visual disturbance, distributive shock, DIC, hepatic failure, renal failure, rhabdomyolysis, lactic acidosis, ARDS and cardiac arrhythmias

Labs
- CBC, chemistry panel, CK, urinalysis, urine drug screen, CXR and ECG
- Optional labs: ABG, lactic acid, D-dimer, PT, and PTT

Treatment
- ABCs, remove patient from heat, remove all clothing, IV fluids and foley catheter
- External cooling: wet skin, fan, cooling blanket, and ice packs to axilla, groin, neck and head; or ice water immersion with extremity massage for young pts
- Internal cooling: gastric and bladder cold-water lavage; peritoneal lavage, thoracic lavage and cardiopulmonary bypass are performed only in extreme cases
- No role for antipyretics, muscle relaxants, benzodiazepines or dantrolene

Malignant Hyperthermia

Definition
- A rare genetic myopathic disorder caused by an abnormal ryanodine receptor causing marked leakage of calcium from the sarcoplasmic reticulum of skeletal muscle cells resulting in extremely high intracellular calcium levels
- Precipitated by multiple drugs, especially inhalational anesthetics (e.g. halothane, sevoflurane, desflurane, isoflurane) and Succinylcholine

Clinical Manifestations
- Symptoms generally begin within an hour of the drug or anesthetic administration but may be delayed for hours: muscle rigidity (especially masseter stiffness), increased CO2 production, acidosis, sympathetic hyperactivity with hyperthermia (up to 113°F), and sinus tachycardia
- Patients may develop rhabdomyolysis, electrolyte abnormalities, dysrhythmias, hypotension/shock, disseminated intravascular coagulation, and death

Treatment
- Dantrolene 2.5mg/kg IV prn until episode controlled, then 1mg/kg IV q4-6h x 24-48h
- Mortality rate has decreased from 70% to less than 10% with intense medical therapy
Snake Bites

Clinical presentation
Local tissue injury, extremity swelling; rhabdomyolysis, nausea, vomiting, diaphoresis, tingling or numbness; severe: hypotension, delirium, acute renal failure, DIC, paralysis
Labs: CBC, chemistry panel, CK, PT, PTT, EKG, UA for blood (myoglobin)

Treatment
- Immobilize affected limb; clean wound; dTaP vaccination, opiates for pain control
- IV fluids for ↓ BP
- Intubation for shock, paralysis, or respiratory failure
- Consider fasciotomy for compartment pressures > 30 mmHg after antivenom given
- Antivenom: available for crotalids (rattlesnakes, copperheads and cottonmouths)
  Polyvalent Crotalid antivenom ovine Fab 4-6 vials IV, repeat q 1 hour until swelling, systemic symptoms and coagulopathy stable, then 2 vials IV q 6 hours x 2
- No role for tourniquet, aspiration of venom, excision of the puncture wounds, heparin, steroids, or antifibrinolytic agents

Severe Marine Envenomations

General Management
ABCs, dTaP vaccination, aggressive wound debridement

Specific Management
- Stingrays: submerse wound in hot water x 30-90 minutes, and copious irrigation of wound
- Scorpionfish or Stonefish: submerse wound in hot water x 30-90 minutes, surgical removal of embedded spines and antivenom for stonefish envenomation
- Jellyfish: wash wound with 5% acetic acid, remove attached tentacles; antihistamines
- Sea Urchins: hot water immersion, remove spines; X-ray area for retained spines

Borrowed with permission from Joseph Esherick, MD
Pressure Ulcers

Definition
- “an area of localized damage to the skin and underlying tissue caused by pressure, shear, friction or a combination of these”

Classification
- Grade I: nonblanchable erythema of intact skin. Discoloration of the skin, warmth, edema, induration, or hardness may also be used as indicators, particularly in individuals with darker skin.
- Grade II: partial thickness skin loss involving epidermis, dermis, or both; the ulcer is superficial and presents clinically as an abrasion or blister.
- Grade III: full-thickness skin loss involving damage to or necrosis of subcutaneous tissue that may extend down to, but not through, underlying fascia.
- Grade IV: extensive destruction, tissue necrosis, or damage to muscle, bone, or supporting structures with or without full thickness skin loss.
- “Braden Scale” appears to have the greatest sensitivity/specificity for assessing pressure ulcer risk

Risk Factors
- Loss of Sensory Perception (sedatives/anesthetics)
- Inability to shift in bed off of pressure spots (weakness, prolonged immobility)
- Malnutrition/negative nitrogen balance with loss of subcutaneous tissue (in one study, 75% of patients with a serum albumin below 3.5 g/dL developed pressure ulcers, compared to only 16% of patients with a higher serum albumin level)
- Moisture (increases pressure ulcers five-fold), fecal incontinence/diarrhea
- Increased illness severity/higher APACHE Score
- Use of steroids, vasoconstricting medications (e.g. Levophed)
- Non-blanchable erythema of the skin
- ICU Stay (2-3 times higher than the general hospitalized population; prevalence 14 to 41% in ICUs)

Prevention
- Patient rotation to the “30° tilt” every 2-3 hours
- Semi-Fowler position is best when supine in bed (30° elevation of head/trunk, 30° elevation of feet), pillow under the legs, heel protectors
- Special beds (foam pressure-reduction mattresses, low air-loss beds/mattresses, lateral rotation beds, air-fluidized beds)
- Reduce Excess Moisture

Management
- Eliminate source of pressure or friction
- Appropriate wound care
  - Debridement of necrotic tissue
  - Dressings to maintain a moist environment
- Nutrition (high protein intake is vital, upwards of 25% of the diet being protein; vitamin deficiencies need to be corrected; supplementation without deficiency is controversial)

PROPHYLAXIS

Summary of Recommendations
(for specifics, see the individual protocols)

Ventilator Associated Pneumonia (VAP) Prophylaxis (see page 65)
- Head of Bed > 30°- 45°
- Oral Care: Peridex solution 15ml bid
- Selective Gut Decontamination (trauma patients only)
  Neomycin 250mg
  Amphotericin 2mg per NG/OG tube q 6 hours, in mouth q 2 hours
  Bacitracin 500mg x 96 hours, then stop

Pressure Ulcer Prophylaxis (see page 229)
- Frequent Rotation in Bed
  - q 2 hour rotation
- Air Mattresses
  - Regular beds
  - Air Mattress Overlay
  - KCI Bed
  - Tridyne II Bed (for those needing rotation/percussion for pulmonary issues; costly to rent ($110/day))
- Minimizing Risk Factors

Deep Venous Thrombosis (DVT) Prophylaxis (see page 131)
- High Risk Patients – all should be pharmacologic unless there are specific contraindications
- Specific Contraindications:
  - Active bleeding
  - Within 24 hours of Spinal Anesthesia or Lumbar Puncture
  - Presence of Ventriculostomy
  - Presence of Intracranial or Intraocular Bleeding
  - Recent Major Bleeding (“Recent” time elapsed depends on clinical judgment as well as patient-related risk factors)
    - Severe thrombocytopenia with platelet count < 40,000

Stress Ulcer Prophylaxis (see page 86)
- Esomeprazole for very high risk patients
- Sucralfate for ICU admissions with only 1 minor risk factor

Catheter-Related Blood Stream Infection (CRBSI) Prophylaxis (see page 158)
- Daily examination of the insertion site to rule out erythema/purulence
- Removal of catheters when they are no longer needed
- Good handwashing whenever catheter assessed or accessed
- Chlorhexidine patch to cover the catheter
CHOICE OF CENTRAL LINE

Central Venous Catheters
- Site of Insertion
  - Awake/cooperative patient
    - Subclavian
    - Internal Jugular (slightly less preferable due to discomfort)
  - If need continuous Mixed Venous Oxygen Saturation (SvO₂) monitoring
    - Internal Jugular
    - Subclavian
  - If the patient has a coagulopathy or thrombocytopenia (compressible sites)
    - Internal Jugular
    - Femoral
  - If the patient is altered and not cooperative with line placement
    - Femoral
  - If the patient would not tolerate any risk of pneumothorax
    - Femoral
  - Dialysis catheter placement (Quintin®)
    - Internal Jugular
    - Femoral
- Type of Central Venous Catheter
  - Triple Lumen
    - Ok for most
  - SvO₂ Triple Lumen
    - If concern for sepsis
  - Cordis (or, in ER, may consider Trauma Line)
    - If the patient is in shock and in need of large amounts of fluid quickly
    - If CT contrast studies are indicated, unless triple lumen catheter is specifically made to be able to withstand the high pressures of rapid IV boluses
    - 2 large-bore IVs (18 gauge, 16 gauge, or 14 gauge) may be equally as effective
  - Swan-Ganz Catheter through the Cordis
    - Note: as of right now, our triple lumen SvO₂ monitors do NOT fit through a cordis

Arterial Line Catheters
- Site of Insertion
  - Radial Artery for most
  - Brachial Artery may be considered with Ultrasound guidance
  - Femoral or Dorsalis pedis are also viable options
- Type of Arterial Catheter
  - Femoral catheters are longer than radial catheters
    - Use the Radial Arterial line for radial or dorsalis pedis insertion
    - Use the Arterial Line “Box Kit” for femoral or brachial insertion
- Continuous Cardiac Output Arterial Lines
  - Inform your nurse if you would like the Continuous Cardiac Output monitor used, as the setup (tubing) is different than with the standard arterial line setup

Depth of central venous catheter insertion:
- Right subclavian/IJ: 13 cm
- Left subclavian/IJ: 17 cm
- Femoral: Full depth

(Note: for dialysis catheters, the subclavian vein is avoided to prevent scarring and narrowing of the subclavian vein pending long-term access)
**PHONE NUMBERS, REFERENCE NUMBERS, ETC.**

**Invasive Cardiologists:**
Consult the Schedule in the ICU or in the ER to find out which invasive cardiologist is on-call (you will not get the invasive cardiologist on-call via 6075)

**ICU Attendings:**
Page operator at (805) 652-6075  
Joseph Esherick: page first ➔ cell: (805) 218-8631  
David Fishman: (DO NOT PAGE) home first: (805) 445-9455 ➔ cell: (805) 377-7391  
Mark Lepore: Tiger Text first ➔ page ➔ cell: (617) 501-0874  
Tara Paterson: cell: (631) 766-4377 or pager  
Javier Romero: page first ➔ cell: (805) 302-3979  
Lisa Singh: cell first (612) 356-3867 ➔ Tiger Text ➔ page  
Israel Villanueva: Urgent: cell: (805) 587-9377; Non-urgent: Tiger Text till 11pm ➔ cell

**Procedure for transferring patients to higher levels of care:**
1. Contact Case Manager at (805) 652-6024 during weekday daytime, or the Nursing Supervisor (805) 652-6075 at any other time.
2. The appropriate institution will be selected depending on the patient’s payor source and medical need and in consultation with the Attending Physician.
3. Once the institution has been selected, the Case Manager/Nursing Supervisor should alert you to call for an accepting physician, with whom you should speak to determine their ability to accept the patient as well as to allow you to communicate all information related to the patient’s care/needs/current status.
4. Once an accepting physician has approved the transfer, the Nursing Supervisor/Case Manager will activate a bed request and take care of the transfer from there. If there is no bed available, there may be need to contact another hospital/physician depending on the patient’s needs.

**Hospitals to transfer patients to, for which indications:**
- Interventional Neuroradiology  
  - Cottage Hospital, Santa Barbara, Dr. Alois Zauner and colleagues  
- Ventilator Rehabilitation  
  - Barlow Hospital, Los Angeles  
- Acute Leukemia Care  
  - City of Hope  
  - Cottage Hospital, Santa Barbara  
- Hyperbaric Oxygen Therapy (stable non-ventilated patients only)  
  - St. John’s Pleasant Valley, Dr. Tessman and colleagues: (805) 389-5944

**Ventura County Communicable Disease Office:**
2240 East Gonzales Rd. Suite 220, Oxnard, CA 93036;  
Phone (805) 981-5201; Fax (805) 981-5200; after hours: (805) 656-9432

**Poison Control:** 800-411-8080 (California) or 800-222-1222 (National)

**One Legacy:** 800-338-6112