

ON-LINE ICU MANUAL

The target audience for this on-line manual is the resident trainees at Boston Medical Center. The goal is to facilitate learning of critical care medicine. In each folder the following items can be found:

1. Topic Summary –1-2 page handout summary of the topic. This is written with a busy, fatigued resident in mind. Each topic summary is designed for use in conjunction with the relevant didactic lecture given during the rotation.
2. Original and Review Articles – Original, and review articles are provided for residents who seek a more comprehensive understanding of a topic. We recognize that residency is a busy time, but we hope that you will take the time to read articles relevant to the management of your patients.
3. BMC approved protocols – For convenience BMC approved protocols, when available, are included in relevant folders.

This manual is just one component of the ICU educational curriculum. In order to facilitate learning at many levels, several other educational opportunities are available. These include:

1. Didactic lectures – Essential core topics in critical care medicine will be introduced during each ICU rotation. Many, but not all, of the topics addressed in this manual will be covered.
2. Tutorials – These are 20-30 minute sessions offered during the rotation that will provide the resident with hands on experience (e.g. mechanical ventilators, ultrasound devices, procedure kits).
3. Morning rounds – Housestaff are expected to take ownership of assigned patients. The goal of morning rounds is to develop treatment plans that can be defended by the best available scientific evidence. In addition, morning rounds are an opportunity for residents to test their knowledge, gauge their progress in critical care education, and recognize the limits of the current medical practice.

The faculty and fellows of Boston University Pulmonary and Critical Care section hope that you enjoy your rotation in the medical intensive care unit.



BOSTON MEDICAL CENTER

ICU MANUAL 2008

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Table of Contents

Chapters on Oxygen Delivery Devices, Airways and Mechanical Ventilation

- A. [Oxygen Delivery Devices and Goals of Oxygenation](#) / [Literature](#)
- B. [Modes of Mechanical Ventilation](#) / [Literature](#)
- C. [Acute Respiratory Distress Syndrome and Ventilator-Associated Lung Injury](#) / [Literature](#)
- D. [Discontinuing Mechanical Ventilation](#) / [Literature](#)
- E. [Noninvasive Mechanical Ventilation](#) / [Literature](#)
- F. [Management and Optimal Timing of Tracheostomy](#) / [Literature](#)

Chapters on Cardiopulmonary Critical Care

- G. [How to Read a Portable CXR](#) / [Literature](#)
- H. [Acid Base Disorders](#) / [Literature](#)
- I. [Treatment of Severe Sepsis & Shock: Part I \(Fluids and Antibiotics\)](#) / [Literature](#)
- J. [Treatment of Severe Sepsis & Shock: Part II \(Steroids, Glucose, Xigris\)](#) / [Literature](#)
- K. [Vasopressor & Inotropic Therapy](#) / [Literature](#)
- L. [Venous Thromboembolism: Prophylaxis and Treatment](#) / [Literature](#)
- M. [Sedation and Analgesia](#) / [Paralytics](#) / [Literature](#)
- N. [Diagnosis and Management of Delirium Tremens](#) / [Literature](#)
- O. [Pneumonia: Community-Acquired, Nosocomial and Ventilator-Associated Pneumonia](#) / [Literature](#)
- P. [Asthma](#) and [COPD](#): Treatment / [COPD Literature](#) [Asthma Literature](#)
- Q. [Nutrition in the ICU](#) / [Literature](#)
- R. [Ischemic Stroke](#) / [Literature](#)
- S. [Subarachnoid Hemorrhage](#) / [Literature](#)
- T. [Seizures](#) / [Literature](#)
- U. [Hypertensive crisis](#) / [Literature](#)
- V. [Prognosis after Anoxic Brain Injury and Diagnosis of Brain Death](#) / [Literature](#)
- W. [Management of Severe Electrolyte Abnormalities](#) / [Literature](#)
- X. [Renal Replacement Therapy](#) / [Literature](#)
- Y. [Acute Pancreatitis](#) / [Literature](#)
- Z. [Gastrointestinal Bleeding and Massive Transfusion](#) / [Variceal Literature](#), [nonvariceal](#)
- AA. [Compartment Syndromes](#) / [Literature](#)
- BB. [Massive Hemoptysis](#) / [Literature](#)
- CC. [Shock](#) and [Advanced Hemodynamic Monitoring](#) / [Literature](#)
- DD. [Hypothermia](#) and [Hyperthermia](#) / [Literature](#)
- EE. [Toxicology](#) / [Literature](#)
- FF. [Carbon Monoxide, Cyanide and Methemoglobin Toxicity](#)
- GG. [Diabetic Ketoacidosis](#) and [HHNK](#) / [Literature](#)
- HH. [End of Life Care](#) / [Literature](#)
- II. [ACLS](#) / [Literature](#)
- JJ. [Anaphylaxis](#) / [Literature](#)
- KK. [Blood Products in the ICU](#) / [Literature](#)

LL. Miscellaneous: [Acute Chest Syndrome](#) / [Acute Chest Literature](#)

[Cardiac Biomarkers in ICU Lit.](#)

[Fulminant Hepatic Failure/ Literature](#)

[Stress Ulcer prophylaxis](#)

MM. [PA Catheter and Pulmonary Hypertension](#) / [Literature](#)

A. Oxygen Delivery Devices and Goals of Oxygenation

- I. **Oxygen cascade:** Describes the process of declining oxygen tension from atmosphere to mitochondria. At sea level, atmospheric pressure is 760mmHg. Oxygen makes up 21% of atmospheric gases ($760\text{mmHg} \times 0.21$) so the partial pressure of oxygen in the atmosphere is 159mmHg. During respiration air is humidified reducing atmospheric pressure by 47mmHg to 713mmHg so the maximal inspired partial pressure of oxygen is 149mmHg. Once air enters the lungs it meets up with carbon dioxide, which further dilutes oxygen concentration (see alveolar air equation, part VI). Therefore, the maximal oxygen concentration in the alveolar space depends on barometric pressure, the fraction of oxygen in inspired air, and the concentration of CO₂ in the alveolar space.
- II. **Causes of low blood oxygen.**
 - a. Atmospheric causes
 - i. Decreased fraction of inspired oxygen.
 - ii. Decreased barometric pressure
 - b. Cardiopulmonary causes
 - i. V/Q mismatch
 - ii. Shunt
 - iii. Diffusion defect
 - iv. Decreased cardiac output
- III. **Oxygen carrying capacity**
 - a. $[1.34 \times \text{Hb} \times (\text{SaO}_2/100)] + 0.003 \times \text{PO}_2$
 - b. Oxygen is carried in blood in two forms.
 - i. Bound to hemoglobin (largest component) - Each gram of hemoglobin can carry 1.34ml of oxygen. Hemoglobin has 4 binding sites for oxygen, and if all are occupied then the oxygen capacity would be saturated. Under normal conditions, the hemoglobin is 97% to 98% saturated. Assuming a hemoglobin concentration of 15g/dl O₂ content is approximately 20ml/100ml. With a normal cardiac output of 5 l/min, the delivery of oxygen to the tissues at rest is approximately 1000 ml/min: a huge physiologic reserve.
 - ii. Dissolved in blood - Dissolved oxygen follows Henry's law – the amount of oxygen dissolved is proportional to the partial pressure. For each mmHg of PO₂ there is 0.003 ml O₂/dl (100ml of blood). If this was the only source of oxygen, then with a normal cardiac output of 5L/min, oxygen delivery would only be 15 ml/min.
- IV. **Oxygen Delivery:**
 - a. $\text{DO}_2 = [1.39 \times \text{Hb} \times \text{SaO}_2 + (0.003 \times \text{PaO}_2)] \times \text{C.O.}$
 - b. The Delivery of oxygen (DO₂) to the tissues is determined by:
 - i. The amount of oxygen in the blood
 - ii. The cardiac output
- V. **Oxygen Extraction:**
 - a. Fick equation: This is computed by determining the amount of oxygen that has been lost between the arterial side and the venous side and multiplying by the cardiac output. In the following equation, VO₂ is the oxygen consumption per

minute, CaO_2 is the content of oxygen in arterial blood, and CvO_2 is the content of oxygen in venous blood:

$$\text{i. } \text{VO}_2 = \text{C.O.} \times (\text{CaO}_2 - \text{CvO}_2) \text{ mL O}_2/\text{min}$$

VI. What is the alveolar air equation?

a. $\text{PAO}_2 = \text{PiO}_2 - (\text{PaCO}_2 / R)$

i. What is the highest PaO_2 you can achieve on RA? Assuming a CO_2 40.

Answer 100

ii. Barometric pressure - is the pressure at any point in the Earth's atmosphere.

VII. What is A-a gradient?

a. $\text{A-a gradient} = \text{PAO}_2 - \text{PaO}_2$

b. What is the highest PaO_2 you can achieve on RA? Assuming a CO_2 40 and an A-a gradient of 10. *Answer 90*

c. Normal A-a gradient = $(\text{Age} + 10) / 4$

VIII. How much oxygen should I administer to a hypoxic patient?

a. Only marginal increases in oxygen content occur with saturations above 88-90% so this should be your goal. In the severely hypoxic pt always start with 100% oxygen, and wean FiO_2 as tolerated. Remember: short-term risk of low oxygen is greater than short-term risk of administering too much oxygen.

IX. Oxygen Toxicity: Initial concern for oxygen toxicity came from the discovery that therapeutic oxygen causes blindness in premature babies with respiratory distress syndrome. Observational studies in adults suggest that high inspired oxygen may lead to acute lung injury. These observations are supported by animal models of oxygen-induced lung toxicity. In animal models, the extent of injury appears to depend on 1. The FiO_2 , 2. The duration of exposure, 3. The barometric pressure under which exposure occurred. It appears that the critical FiO_2 for toxicity is above 60. Since oxygen is a drug, the goal should always be to minimize FiO_2 .

X. Oxygen Delivery Devices- Oxygen can be delivered to the upper airway by a variety of devices. The performance of a particular device depends: 1) flow rate of gas out of the device, and 2) inspiratory flow rate created by the patient. In the ideal device, gas flow exceeds the patient's peak inspiratory flow so as not to entrain air from the atmosphere.

a. Variable performance devices:

i. Nasal cannula: The premise behind nasal cannula is to use the dead space of the nasopharynx as a reservoir for oxygen. When the patient inspires, atmospheric air mixes with the reservoir air in the nasopharynx. The final FIO_2 depends on the flow of oxygen from the nasal cannula, the patient's minute ventilation and peak flow. For most patients, each addition 1 litre per minute of O_2 flow with nasal cannula represents an increase in the FIO_2 by 3%. So 1 liter is 24%, 2 liters is 27% and so on. At 6 liters (40%), it is not possible to raise the FIO_2 further, due to turbulence in the tubing and in the airway. There are a couple of problems with nasal cannula: 1) they need to be positioned at the nares, 2) effectiveness is influenced by the pattern of breathing - there appears to be little difference whether the patient is a mouth or a nose breather, but it is important that the patient exhale through their mouth. The advantage of nasal cannula is patient comfort.

- ii. Face mask: Standard oxygen masks provide a larger reservoir than the nasopharynx. In individual patients FIO₂ can vary greatly depending on flow oxygen into the mask and the flow rates generated by the patient.
- iii. High-flow oxygen and non-rebreather face masks. Oxygen enters these masks at a very high flow rate. For non-rebreather masks a large reservoir is attached to the mask to store oxygen. Theoretically these devices could provide 100% FIO₂ to the patient; however, because patients using these devices tend to have very high inspiratory flow rates and the seal of the mask around the patients mouth is never complete FIO₂ is often significantly less than 100% (usually in 70-80% range).

B. Mechanical Ventilation

1. Initiating Mechanical ventilation

Aim: Provide adequate ventilation and oxygenation without inducing barotrauma/volutrauma. Allow respiratory muscles to rest.

After intubation:

Confirm ETT placement by:

1. Auscultation: Listen for bilateral breath sounds (Unilateral BS consider right mainstem bronchus intubation or pneumothorax)
2. End tidal CO₂ monitor
3. CXR -

Order ABG in 20 minutes (as long as Pulse OX >93-95%)

Order Sedation

Initial Settings:

Mode Typically start with volume control mode (sIMV OR AC)

TV 6-8 ml/kg (may use higher TV if no lung disease (eg CVA or overdose) but this should be your goal in most patients)

FiO₂ Start with 100%

Rate 12-14 b/min (higher rates if prior metabolic acidosis or ARDS, lower rates with severe obstructive lung disease)

PEEP Initial level 5cmH₂O

PS If sIMV mode place PS 10 cmH₂O (titrate PS to ensure spontaneous TV are 6-8 ml/kg)

What to watch out for:

1. High airway Pressures: Peak Pressures > 35 cmH₂O.
 - a. Find out plateau pressure
 - i. If high: problem with lung compliance:
 1. ARDS
 2. CHF
 3. PTX
 4. Pulmonary Hemorrhage
 5. Large effusion
 6. Right mainstem intubation
 - ii. If low: problem with airway:
 1. Obstructive lung disease (asthma,COPD)
 2. Kink in tubing
 3. Mucus plug
 2. Unstable hemodynamics: Hypotension is common after intubation—probably multi-factorial including pre-intubation hypovolemia which is increased by peri-intubation

analgesia and anesthesia, immediate effects of positive pressure ventilation on venous return; acidosis (hyperventilate pre-intubation). Usually responds to fluids – if persistent and life threatening consider air-trapping or pneumothorax (temporary hypoventilation at rate of 4 or disconnect vent from ETT to assess if BP improves / obtain CXR)

3. Agitation: Don't forget that if paralytic agent has been used ensure patient also receives an anxiolytic/anesthetic agent like benzodiazepine.

2. Daily Assessment

1. Oxygen requirement:

- If decreasing: wean FIO₂
- If increasing:

Methods to improve oxygenation:

1. Increase Alveolar O₂ concentration: Increase FiO₂, Decrease CO₂ (hyperventilate).

2. Ventilator maneuvers to facilitate alveolar recruitment:

- i. PEEP: PEEP increases functional residual capacity (FRC) by recruiting and stabilizing alveoli that may have been collapsed at normal end-expiratory pressures. This improves V/Q matching allowing better gas mixing.

- A. Optimal PEEP - difficult to assess even with sophisticated techniques

Pressure Volume Curve (compliance curve)

Estimate Lung Compliance (TV mls / Pressure)

- B. Potential Complications

Decrease venous return- hypotension

Barotrauma

- ii. Sighs: Intermittent high volume breaths to recruit gas exchange units

- iii. Pressure Control Ventilation (see below)

Uses Square Pressure wave form-hypothetically allows for recruitment of alveolar gas exchange units by maintaining inspiratory pressures for longer periods.

- iv. Lengthen inspiratory time (inverse ratio ventilation)

Normal I:E ratio is set at 1:2 on ventilator. Prolonged I time can increase recruitment of alveolar units.

3. Prone position:

Lung involvement in ARDS is heterogeneous but dependent areas are more affected than non-dependent regions. Turning patient to prone position results in recruitment of previously collapsed alveoli- The majority of patients respond within 30 minutes. 50% maintain improvement when turned supine again (usually after 2 hours). Typically prone position is only a temporizing measure.

4. Increase Oxygen Delivery {O₂ Content x 10} x CO

$$\text{O}_2 \text{ Content} = \text{Hb} \times \text{O}_2 \text{ Sat} \times 1.36 + [0.003 \times \text{pO}_2]$$

Although in cardiac disease optimizing O₂ delivery appears to be beneficial this may not be the case in septic patients. In fact, attempts at increasing cardiac output in sepsis may be associated with worse outcomes.

2. Ventilatory requirement

- Alveolar Minute Volume = RR x {TV-dead space}
- Normal MV is 6L/min, but we tolerate <10 L/min when assessing whether a patient is ready to wean from the ventilator.

3. Patient–Ventilator Synchrony

- Perfect synchrony is virtually impossible i.e. duration of neural inspiration should equal mechanical inflation and neural expiration should equal mechanical inactivity.
- There are many potential reasons for tachypnea on ventilator:
 - Pain, Anxiety, Sepsis..... but poor interaction with delivered breaths may play a role
 - a. Is patient getting enough Minute Volume- Pco₂, Ph.
 - b. Is patient having difficulty triggering the Ventilator
 - Mode: AC may be better tolerated than IMV. On IMV add Pressure Support.
- Trigger: Threshold of negative pressure required to trigger breath- RT can lower the triggering threshold. Auto-PEEP raises the triggering threshold but Applied PEEP does not.
- Flow Rates: Some patients need higher flow rates Ask RT 80-120L.min.

4. Barotrauma: Signs include decrease breath sounds, hypotension, increase O₂ requirements, chest pain.

Barotrauma takes two forms:

- a. Alveolar Injury (aka ARDS)
- b. Pneumothorax.

- Aim to keep plateau pressure less than 30cmH20.
- Clinical evidence:
 - High plateau pressures are associated with lung injury (baro or volutrauma) in experimental animals.
 - RCT showed that low volume / low pressure ventilation resulted in decreased mortality in ARDS (some confusion in literature reflects heterogeneous studies- mortality benefit only seen when control group has plateau pressure exceeding 30cmH20). Keep plateau less than 30.
 - Increased peak w/o increased plateau unlikely to cause lung injury, but no evidence to support this statement

5. Air-trapping

- AUTO-PEEP (Dynamic hyperinflation)
 - Clinical Situations: Reflects inadequate time for expiration.

- a. Prolonged Expiration- Bronchospasm.
- b. Shortened Expiratory Time (high RR or Prolonged Inspiratory time e.g. ARDS)
- o Measure: Expiratory Pause Pressure
(occlude expiratory port of ventilator at end expiration- if persisting airflow at end-expiration a pressure will register).
- o Problems:
 - Hemodynamic Comprise (Decreased venous return)
 - Hypoventilation (airtrapping implies less gas mixing and exchange)
 - Difficulty triggering ventilator.

Measures to Decrease Auto-PEEP

- a. Decreasing RR is more helpful than lowering tidal volume.
- b. Increase Inspiratory Time (higher flow rates)
- c. Bronchodilators
- d. PEEP match

C. Acute Respiratory Distress Syndrome (ARDS)

Definition: Acute lung injury leading to increased vascular permeability and impaired gas exchange. ARDS criteria include:

1. Widespread bilateral radiographic infiltrates
2. $\text{PaO}_2/\text{FiO}_2$ ratio ≤ 200 mm Hg (regardless of PEEP Level)
3. No evidence of elevated left atrial pressure (wedge < 18 mm Hg)

There are over 60 documented causes of ARDS. The most common causes include:

- Sepsis
- Aspiration of gastric contents
- Pneumonia
- Severe trauma
- Burns
- Massive blood transfusion
- Lung and bone marrow transplantation
- Drugs
- Leukoagglutinin reactions
- Near drowning
- Pancreatitis

Pathophysiology of ARDS

Inflammatory injury to the alveoli produces diffuse alveolar damage. Inflammatory mediators such as TNF-alpha, IL-1, and IL-6 are released leading to inflammatory cell (neutrophils thought to be primary mediator of injury) recruitment, which lead to damage to the capillary endothelium and the alveolar epithelium. Protein-rich fluid escapes into the alveolar space and interstitium leading to impaired lung compliance and gas exchange.

Pathologic Stages of ARDS

4. Exudative phase: diffuse alveolar damage, usually first week of illness.
5. Proliferative phase: pulmonary edema resolves, Type II alveolar cells proliferate, there is squamous metaplasia and myofibroblasts infiltrate the interstitium and begin laying down collagen
6. Fibrotic stage: normal lung architecture is not seen. There is diffuse fibrosis and cyst formation.

Clinically:

- Patients usually develop syndrome 4-48 hours after precipitant injury, and may persist for days to weeks.
- Severe hypoxemia, with rapidly worsening tachypnea, dyspnea, increasing oxygen requirements and worsening lung compliance.
- CXR will demonstrate bilateral alveolar infiltrates.
- Differential diagnosis includes:
 - cardiogenic pulmonary edema
 - diffuse alveolar hemorrhage
 - acute eosinophilic pneumonia.
 - Hamman-Rich syndrome

- Most patients require mechanical ventilatory support because of the severe hypoxemia, high minute ventilation requirements, and poor lung compliance.

Pulmonary goals in ARDS

1. Improve oxygenation
2. Decrease the work of breathing
3. Avoid ventilator-induced lung injury

Ventilation in ARDS: utilize a lung-protective strategy to reduce risk of further lung injury

1. Low tidal volumes 6 ml/kg
2. Use of PEEP to prevent cyclic atelectasis
3. Keep plateau pressures < 30 cm H2O
4. Hypercapnia may be need to ventilate with low TV (permissive hypercapnea)

Oxygenation in ARDS:

1. Increase FIO₂
2. Increase PEEP
3. Pressure control ventilation may be needed to keep peak pressures <30.
4. Lengthening inspiratory time (Inverse ratio) to allow recruitment of more alveoli may be needed to improve oxygenation.
5. Prone positioning: improves blood flow to better ventilated lung units and promotes expansion of collapsed lung units.
6. Deep sedation +/- paralytics.
7. Suppress fever

Complications of ARDS

1. Barotrauma: (13%)
2. Nosocomial infection
3. Myopathy from NMB and/or critical illness

Mortality

1. Estimated at 35-40%
2. Long term survivors of ARDS are usually asymptomatic from a pulmonary standpoint, but may have mild abnormalities seen on pulmonary function testing

ARDSNet Protocol (THE Guide for ARDS vent management) Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. The Acute Respiratory Distress Syndrome Network. *N Engl J Med* 2000; 342:1301-8.

1. **Initial ventilator settings:**

- Calculate ideal body weight (IBW):
 - Male=50+2.3[height(inches)-60]
 - Female=45.5+2.3[height(inches)-60]
 - Set mode to assist-control ventilation (ACV) and set initial tidal volume to 8 cc/kg (IBW). Reduce to 7 cc/kg (IBW) after 1-2 hours and then to 6 cc/kg (IBW) after 1-2 hours.
4. The **plateau pressure (P_{PL})** goal is ≤ 30 cm H₂O. Adjust the tidal volume to reach this goal:
- Ask RT to check P_{PL} with a 0.5 second inspiratory pause q4h and after each change in tidal volume or PEEP.
 - If $P_{PL} > 30$, decrease tidal volume to 5 cc/kg IBW or even 4 cc/kg IBW if necessary.
 - If $P_{PL} < 25$ and the tidal volume < 6 cc/kg IBW, increase tidal volume until $P_{PL} > 25$ or tidal volume = 6 cc/kg.
 - If the patient is breath stacking or has severe dyspnea, tidal volume may be increased to 7 or 8 cc/kg IBW as long as the $P_{PL} \leq 30$.

5. **Oxygenation goal** = PaO_2 55-80 mmHg or O_2 sat 88-95% in order to avoid oxygen-induced lung injury. Basically, you'll want to use a high level of PEEP for any given F_iO_2 setting:

F_iO_2	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7	0.7	0.8	0.9	0.9	0.9	1.0
PEEP	5	5	8	8	10	10	10	12	14	14	14	16	18	20-24

6. **pH goal** = 7.30 - 7.45:

- If pH 7.15 - 7.30, increase the set rate until pH > 7.30 or $\text{PaCO}_2 < 25$ (max rate = 35). If the set rate = 35 and the pH is still < 7.30, consider giving NaHCO_3 .
- If pH < 7.15, set rate to 35. If the set rate = 35 and pH is still < 7.15, consider NaHCO_3 . In addition, increase tidal volume at 1 cc/kg IBW increments until pH > 7.15. It is okay to go above the target P_{PL} at this point.
- If pH > 7.45, decrease set rate until patient's respiratory rate < set vent rate. Minimum set rate=6.

7. The goal **I:E ratio** is 1:1 - 1:3. Adjust flow rate and inspiratory flow wave-form to achieve this goal.
8. Conduct a **weaning trial** daily if the patient meets **all** of the following criteria:
- $\text{F}_i\text{O}_2 \leq 0.4$ and PEEP ≤ 8 (as long as these values are \leq values from previous day).
 - Patient can take spontaneous breaths (turn down the set vent rate and see).
 - Systolic BP ≥ 90 mmHg without pressors.
9. For more specifics on the weaning protocol go to <http://www.ardsnet.org> or <http://hedwig.mgh.harvard.edu/ardsnet/>.

D. Discontinuation of Mechanical Ventilation

- I. **Definitions:** concepts of “Weaning”, “Liberation”:
 - a. Like everything in ICU: generate hypothesis (this patient is ready to wean) and test hypothesis (perform spontaneous breathing trial)
- II. **Steps in discontinuation of mechanical ventilation:**
 - a. Assessing Readiness to Wean: General Rules
 - i. Underlying cause of ventilator requirement is improving
 - ii. Neurologic
 - 1. Can clear secretions
 - 2. No excessive sedation or obtundation, ie. Follows commands
 - iii. Cardiovascular
 - 1. No hypotension or unstable arrhythmia
 - 2. No active coronary ischemia
 - iv. Metabolic
 - 1. No major electrolyte disturbance (eg., K+ normal, phosphorus>1.0)
 - 2. No signs of adrenal insufficiency
 - v. Pulmonary
 - 1. Oxygenation requirement:
 - a. PEEP ≤8
 - b. sat >90% on 0.4FiO₂ (pO₂/FiO₂ ratio >200)
 - 2. Ventilation requirement:
 - a. Minute ventilation <12
 - b. No significant respiratory acidosis (change from baseline)
 - c. RR<35
 - d. RSBI {RR/TV(L)} is <105
 - e. If consideration of neuromuscular Dz, MIP <-20
 - b. **Perform Spontaneous Breathing Trial if above Criteria are Met:**
 - i. Stop pressure support and PEEP
 - 1. If ETT is <7 may consider PS 5 or automatic tube compensation to decrease ETT resistance
 - 2. PEEP of 5 is OK, or can use no PEEP
 - ii. Watch the patient for 30 minutes (no difference from 120min SBT in randomized trial Perren A et al. Intens Care Med 2002)
 - iii. If patient still meets ‘readiness to wean’ criteria, and has passed SBT they should be ready to extubate.
 - iv. 13% of patients passing SBT vs 40% not getting SBT need to be re-intubated (zeggwagh AA. Intes Care med 1999)
 - v. Place back on supportive vent setting once SBT passed (or not passed!)
 - c. **A Failed SBT**
 - i. This heralds a difficult to wean patient
 - ii. **MUST EVALUATE CAUSE OF SBT FAILURE**
 - 1. Pulmonary
 - a. Lack of resolution of underlying dz

- b. Muscle fatigue (increasing RR, decreasing TV)? See also neurologic causes below if no clear pulmonary issue.
 - 2. Neurologic
 - a. Uncontrolled anxiety, delirium
 - b. Inadequate central respiratory drive (sedation?)
 - c. Inadequate peripheral muscle strength (low NIF, steroids, NMBs)
 - 3. Cardiovascular
 - a. Did pulmonary edema develop after PEEP removal?
 - b. Unstable arrhythmia, angina, hypo/hypertension during SBT
 - 4. Other: metabolic (metabolic acidosis, adrenal insufficiency), nutrition, glycemic control
 - iii. If cause is addressed, perform daily SBT
 - iv. Always place back on supportive vent mode after weaning attempt is complete.
- Different strategies:
- 1. Can use AC mode with daily SBT or
 - 2. Can use gradual PSV wean
 - 3. Avoid SIMV
 - 4. Just make sure you do a daily attempt!
 - v. So, your patient has passed a SBT...Extubation
 - 1. Not so fast!
 - 2. Patients intubated for > 2 days should have cuff leak test performed to assess risk of post-extubation stridor/laryngeal edema
 - 3. Ideally this test should be done AT ONSET OF WEANING (no evidence for this, but it makes sense)
- vi. The Cuff Leak Test**
- 1. Make sure cuff is inflated.
 - 2. Suction above cuff so secretions aren't aspirated
 - 3. Proper cuff leak test: set vent to AC 8cc/kg, and make sure patient is getting proper TV
 - 4. Deflate cuff and measure expired TV on six breaths, take average of lowest three breaths.
 - 5. Qualitative tests: deflate cuff and listen for turbulent air without stethoscope, and/or occlude ETT with your thumb
 - 6. An 'adequate' cuff leak is defined as <75% inspired TV measured by the vent (a >25% cuff leak), turbulent flow heard without a stethoscope, or ability to breath with ETT occluded.
 - a. 2% of patients with cuff leak >25% will have post-extubation stridor, compared with 30% without a cuff leak.
 - 7. Solumedrol 40IV reduces cuff leak volume after 6hrs and reduces post-extubation stridor (no evidence for reduced need for reintubation)
 - 8. Francois Lancet 2007: Solumedrol 20mg x1 12 hours prior to extubation for everyone intubated >36h → only strategy which reduces reintubation for laryngeal edema (8% vs 54%)
- vii. Patient is extubated and is not doing well**
- 1. Consider NIPPV-especially for pure hypercarbic failure
 - 2. Can treat laryngeal edema with steroids, heliox, racemic epi
 - 3. LOW threshold for immediate re-intubation

E. Noninvasive Mechanical Ventilation

Definition: The delivery of mechanical ventilation to the lungs without an endotracheal tube or tracheostomy in the airway

Modes of noninvasive ventilation:

Negative pressure:

Mechanism of negative pressure ventilation: delivery of sub-atmospheric pressure around chest and abdomen (creating a vacuum effect), which results in the expansion of the chest and air being drawn into the lungs through the mouth and nose. Expiration will occur passively when the pressure around the chest walls returns to normal atmospheric pressure. Negative Pressure ventilation attempts to simulate normal breathing.

- Drawbacks with negative pressure ventilation:
 - 1) Worsening of obstructive sleep apnea
 - 2) Problems with correct fitting and portability
 - 3) Difficulty in application and removal of the device-requiring attendants
 - 4) Must sleep in supine position
- Indications for negative pressure ventilation: (Not used very often since the development of positive pressure nasal/face interfaces)
 - 1) Chronic respiratory failure secondary to neuromuscular disease- polio, muscular dystrophy. Generally used for nocturnal ventilatory support, with the patient breathing spontaneously during the day.
 - 2) Acute respiratory failure- there are 2 different studies which examined the use of the iron lung and poncho wrap (respectively) in COPD patients with acute respiratory failure. Both studies demonstrated the effectiveness of negative pressure ventilation to correct CO₂ retention.
- Types of negative Pressure Ventilation”
 - Iron lung: Used primarily during the polio epidemic in the 1950's
 - Cuirass/shell: A shell or cage surrounds the chest and is connected to a portable ventilator
 - Raincoat/poncho: A tight fitting suit connected by hoses to a portable ventilator
 - Pneumowrap
 - Rocking bed: Patient is placed on a bed which rocks rapidly flat to upright which also induces diaphragmatic motion as the abdominal contents shift
 - Pneumobelt: A device designed as a belt with a bladder which inflates and deflates with air in a cyclic pattern. The diaphragm moves in response to changes in intra-abdominal pressure

Positive pressure

- Mechanism of positive pressure ventilation: delivery of either a supra-atmospheric pressure or a preset tidal volume which then inflates the lungs. Exhalation is also a passive event, relying on the elastic recoil of the lung to deflate the lung until equilibration with atmospheric pressure or PEEP.
- The most common mode of noninvasive ventilation utilized presently. The interface with the patient can be a full face mask, a nasal mask, or nasal pillows.

- Benefits of positive pressure noninvasive ventilation
 - 1) Avoid intubation and the associated risks and complications
 - 2) Preservation of swallowing and speech
 - 3) Preservation of cough reflex
 - 4) Improve gas exchange
 - 5) Reduction of work of breathing by resting respiratory muscles

Absolute/Relative contraindications:

- 1) Decreased mental status
- 2) Uncooperative
- 3) Unstable hemodynamics
- 4) Copious secretions and unable to protect airway.
- Candidates for NIPPV: Respiratory failure from almost any cause including:
 - 1) Acute exacerbations of COPD- careful pt selection, may be able to avoid intubation
 - 2) Acute pulmonary edema
 - 3) Exacerbations of cystic fibrosis, asthma, or restrictive lung disease
 - 4) Pneumonia
- Drawbacks to positive pressure ventilation:
 - 1) Interface difficulties- discomfort from mask, headgear, or straps
 - 2) Air leak
 - 3) Nasal pain, erythema, or skin breakdown from mask
 - 4) Nasal congestion or dryness
 - 5) Nasal bridge ulceration
 - 6) Eye irritation from air leak blowing into eyes
 - 7) Aspiration
- Types of Positive Pressure:
 - 1) BiPap
 - 2) Portable ventilator (LP-6, LP-10)

Initiation of NIPPV:

- Portable ventilator (LP-6, LP-10, LTV)
 - 1) Set up a volume targeted strategy- tidal volumes need to be higher than invasive ventilation.
 - 2) Tidal volume 10-15cc/kg is used. This compensates for air leak through the mouth and around the mask
 - 3) A respiratory rate can be chosen as in standard ventilation. Check adequacy of ventilation/oxygenation with ABG.
 - 4) Increase the tidal volume or the respiratory rate if the minute ventilation needs to be increased. Similarly, decrease the tidal volume or the respiratory rate if the patient is being overventilated.
 - 5) Oxygen supplementation is provided in line with the circuit.
- BiPAP
 - 1) Uses a pressure targeted strategy:

- 2) Inspiratory pressures (IPAP) can be set from 8-20 cm H₂O of pressure (Think of IPAP as pressure support). As the pressure increases, the more uncomfortable it will feel for the patient. Generally start between 8-11 cm H₂O.
 - 3) Expiratory pressure (EPAP) is set at 3-5 cm H₂O. Think of this as PEEP.
 - 4) The difference or “step” between the IPAP and EPAP is the amount of support the patient is getting. If the patient requires more ventilation, gradually increase the IPAP level.
 - 5) The ventilator rate can also be set- a back-up rate can be chosen below the patient’s spontaneous rate to be assured the patient will not develop apnea. One can choose a higher ventilator rate to prevent periods of prolonged apnea and allow rest of respiratory muscles.
- 6) If oxygenation needs to be improved, one can either increase the amount of oxygen in the circuit, or one can increase the EPAP level. Remember if EPAP level is increased TV will decrease. To offset this, one can increase the IPAP level the same increment as the increase in the EPAP.

- Patients when initiated on NIPPV are often anxious and initially uncomfortable. They usually require 1:1 assistance by a respiratory therapist to become acclimated to the technique and make fine tuning adjustments to the flow rate and pressures. It may take an hour for the patient to become comfortable. Monitoring of the heart rate, respiratory rate and ABGs will determine the effectiveness of NIPPV in correcting acute respiratory failure. If at any point, the patient is worsening conversion to endotracheal tube should be considered.

To wean a patient from noninvasive ventilation:

- 1) Improved oxygen saturation on a low oxygen flow rate
- 2) Respiratory rate < 24/min
- 3) Interrupt for short periods for talking, eating, drinking and assess tolerance

See Review in Chest 2007.

F. Optimal Timing and Management of Tracheostomy

- I. **Introduction:** Tracheostomy is a procedure commonly performed on critical patients that will likely require prolonged mechanical ventilation. Controversy exists over the optimal timing of this procedure. Ideally, the procedure is performed only if benefits ascribed to the procedure outweigh the risks.
- II. **Benefits of tracheostomy:**
 - a. Reduce laryngeal ulceration.
 - b. Reduce vocal cord injury.
 - c. Improves patient communication.
 - d. Improves patient comfort (long-term)
 - e. Improves patient's ability to rehabilitate.
 - f. Requires less nursing care (Astrachan et al Laryngoscope 1988).
 - g. Lower incidence of nosocomial pneumonia
 - h. Less sedation required
 - i. Decreased airway resistance- easier to wean
- III. **Risks**
 - a. Bleeding
 - b. Pain
 - c. Stomal infections
 - d. Stomal hemorrhage,
 - e. PTX
 - f. Pneumomediastinum
 - g. Death
- IV. **Timing -**
 - a. Early - Within the 1st week.
 - b. Late – Greater than 14 days.
- V. **Outcomes:**
 - a. Pneumonia: mixed results, trend toward reduction with early tracheostomy (Rodriquez et al surgery 1990, Kluger et al *Eur J Emerg Med* 1996, Sugerman HJ, Wolfe L, Pasquale MD, et al. Multicenter, randomized, prospective trial of early tracheostomy. *J Trauma* 1997)
 - b. Mortality: No difference in mortality (Griffiths et al BMJ 2005)
 - c. Time in ICU: reduced with early tracheostomy (Griffiths et al BMJ 2005, Rodriquez et al surgery 1990, Rumbak et al Critical Care Med 2004)
 - d. Time on ventilator – reduced with early (Griffiths et al BMJ 2005, Rodriquez et al J Trauma 1997, Arabi et al Critical Care 2004, Rumbak et al Critical Care Med 2004)
- VI. **Conclusion:** Early tracheostomy appears to reduce time on vent and LOS in ICU but does not alter mortality. Early tracheostomy may reduce the incidence of nosocomial pneumonia. The optimal timing for tracheostomy in ICU needs further study.

G. How to Read a Portable CXR

5 Step approach to reading the portable CXR:

Step 1: Confirm patient's name, date of birth, and medical record number.

Step 2: Take notice of penetration: Too white (underpenetrated), too dark (overpenetrated).

Step 3: Take notice of inspiratory effort:

Step 4: Take notice of alignment:

Step 5: Begin systematic approach:

- A. Tubes and lines
- B. Bones
- C. Soft tissue structures
- D. Cardiac structures
- E. Trachea and airways
- F. Pleura and diaphragm
- G. Lung parenchyma

A few rules:

1. Right hilum is always higher than left.
2. 95% of the time the right hemidiaphragm is higher than left hemidiaphragm. A left hemidiaphragm that is greater than 1 cm higher than the right is abnormal.
3. Diaphragm should be smooth and costophrenic angles should be sharp.
4. Heart should be less than $\frac{1}{2}$ of hemithorax on a PA film. This does not hold true on portable AP film.
5. Left pulmonary artery should be less than $\frac{1}{2}$ of aortic knob.
6. Azygous vein should not be visible in an upright film.
7. Know your anatomy



Combat Docur

Reading the CXR

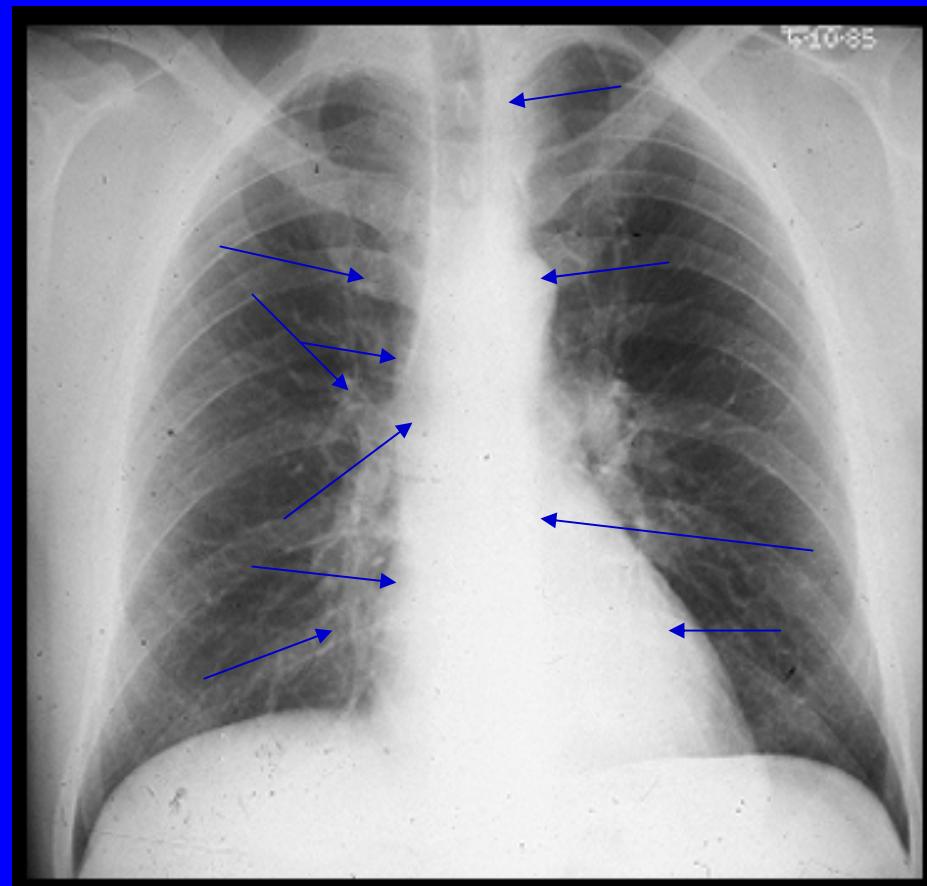
Approaching the CXR

- Always place the PA and lateral CXR in the same order.
- Look at the patients name, date of birth and note the type of film and patient position.
- How is the penetration of the film?
 - White is underpenetrated
 - Black is overpenetrated

Approaching the CXR

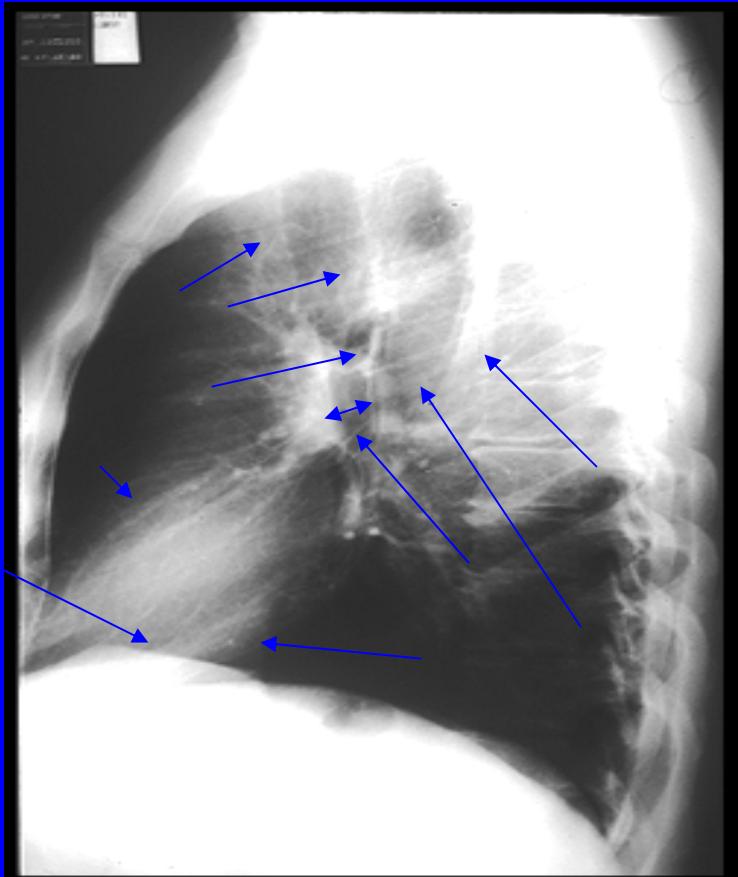
- Notice pt alignment.
 - Don't be fooled by kyphosis and scoliosis
- The systematic approach
 - Tubes
 - Bones
 - Cardiac
 - Trachea and lungs
 - Pleura and diaphragm
 - Soft tissue

Know Your Anatomy



1. Trachea
2. Right mainstem
3. Right atrium
4. Left atrium
5. Left ventricle
6. Aortic knob
7. Azygos vein
8. Right upper lobe PA
9. Pulmonary vein
10. 1st rib anteriorly

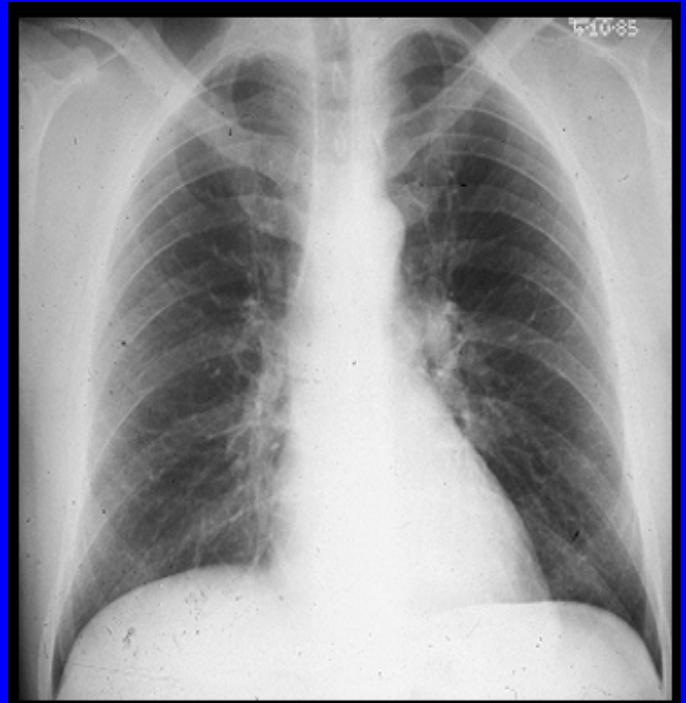
Know Your Anatomy



1. Scapula
2. IVC
3. Right ventricle
4. Right hemidiaphragm
5. Aortic arch
6. Trachea
7. Brachiocephalic vessels
8. Right upper lobe bronchus
9. Left upper lobe bronchus
10. Right and left pulmonary artery

Some Simple Rules

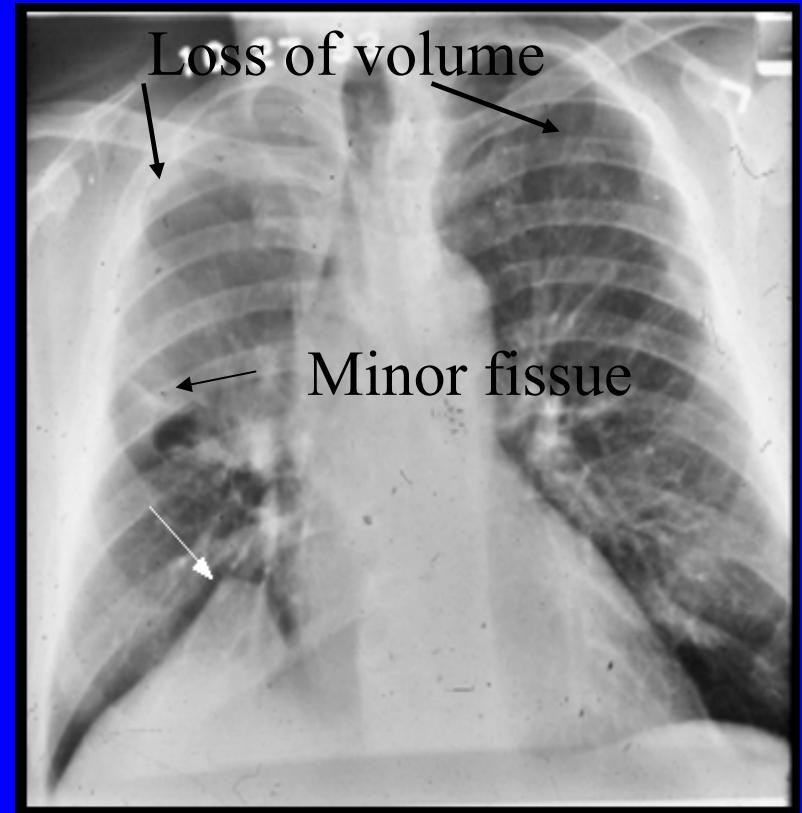
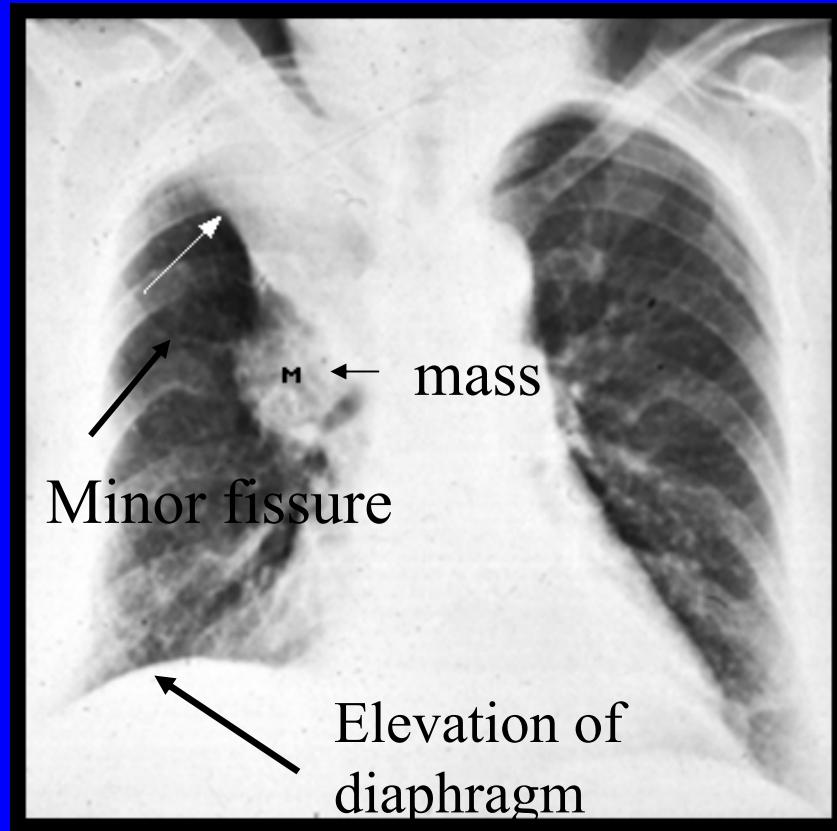
- Right hilum is higher than left
- Right hemidiaphragm is 1-2 cm higher than left
- Diaphragm should be smooth and you should be able to pick your teeth with the CPA
- Heart is less than 50% of hemithorax on a PA
- L PA should be less than $\frac{1}{2}$ of aortic knob
- Azygos vein should barely be visible in an upright film.



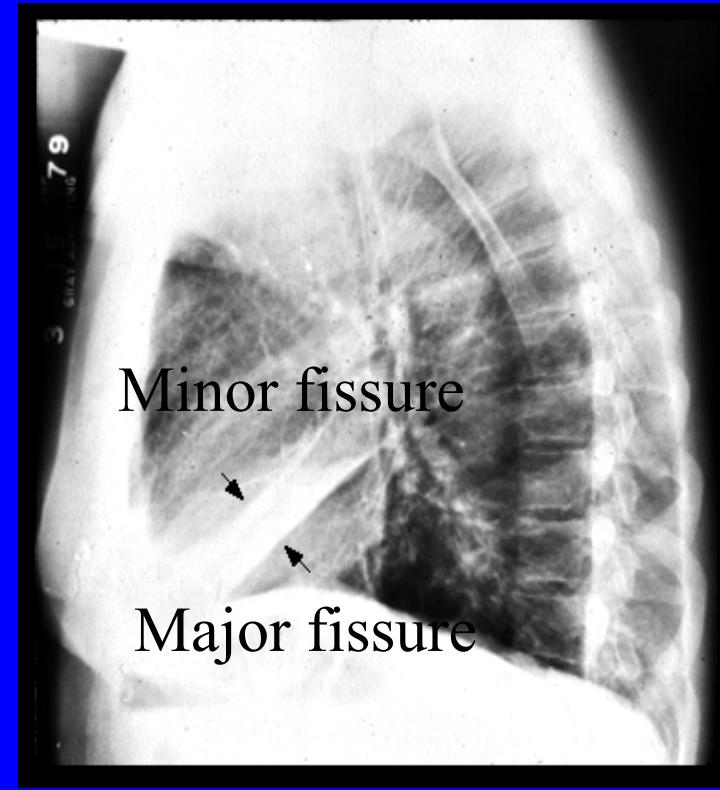
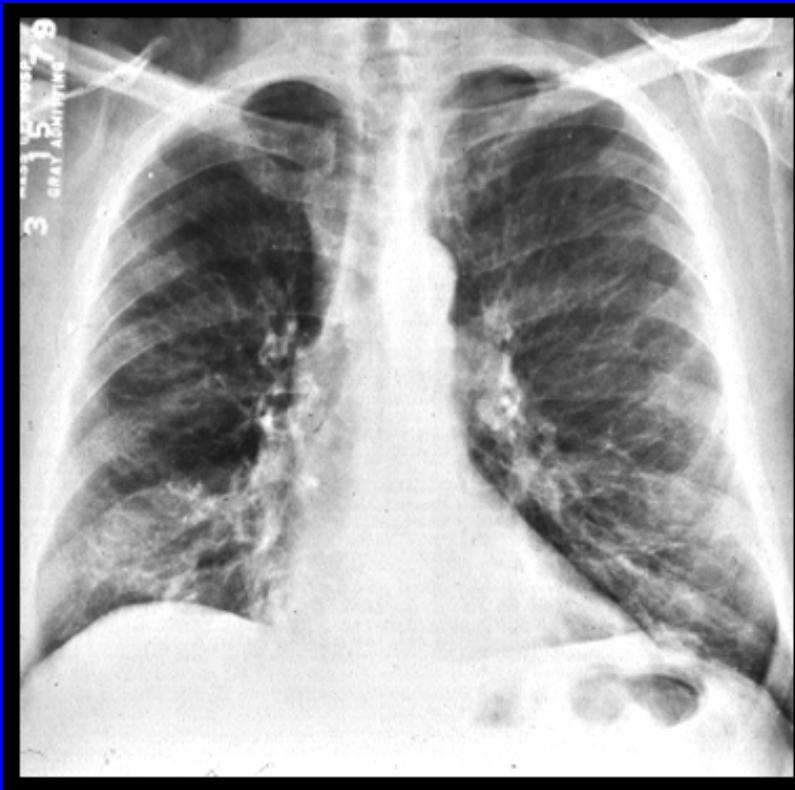
Common findings on CXR

- Atelectasis
- Pneumothorax
- CHF
- Pleural effusion

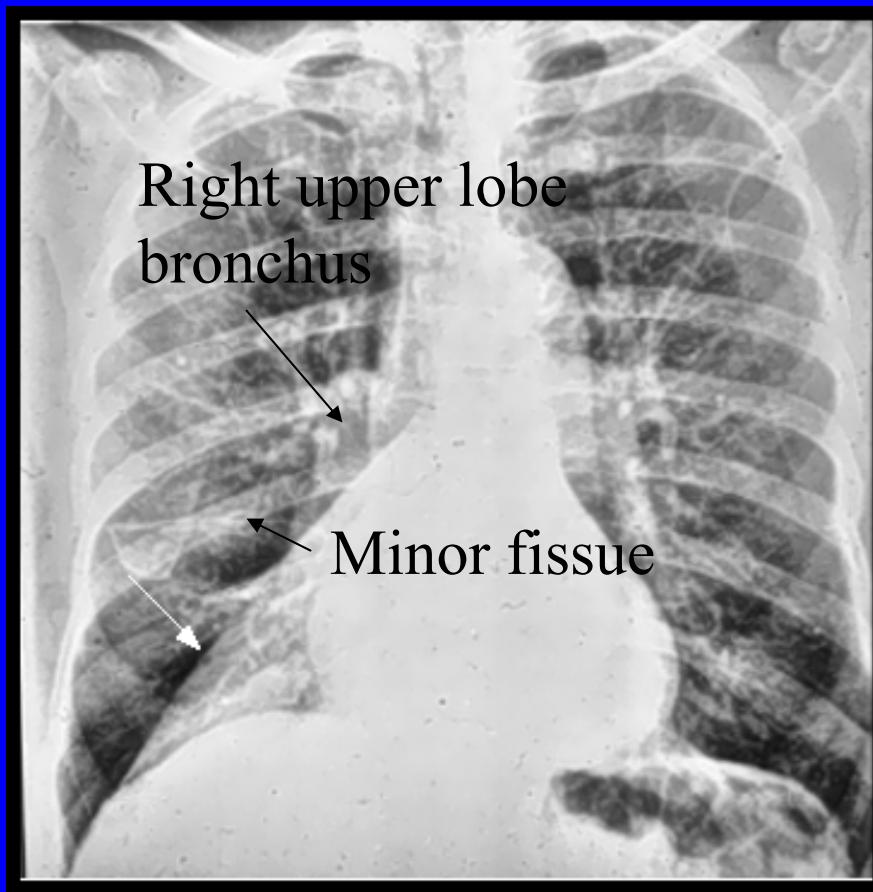
Right upper lobe atelectasis



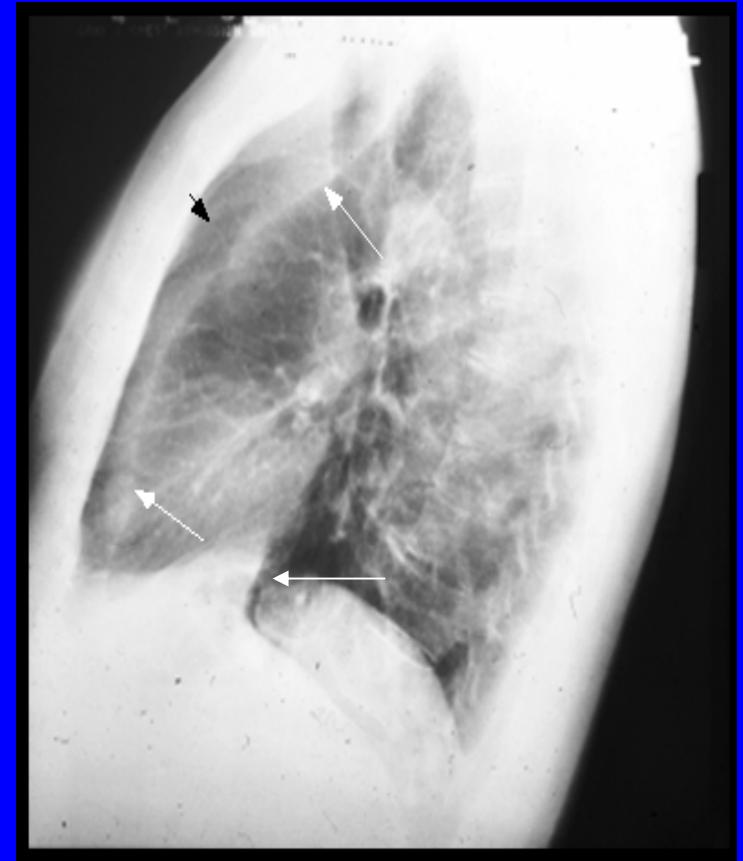
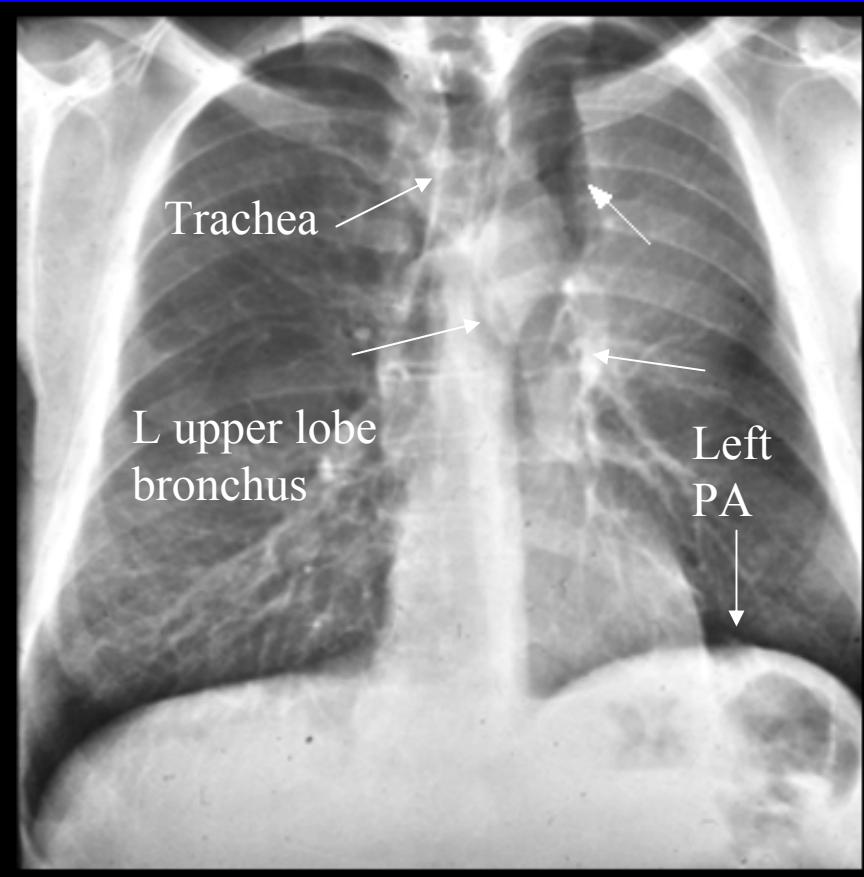
Right middle lobe atelectasis



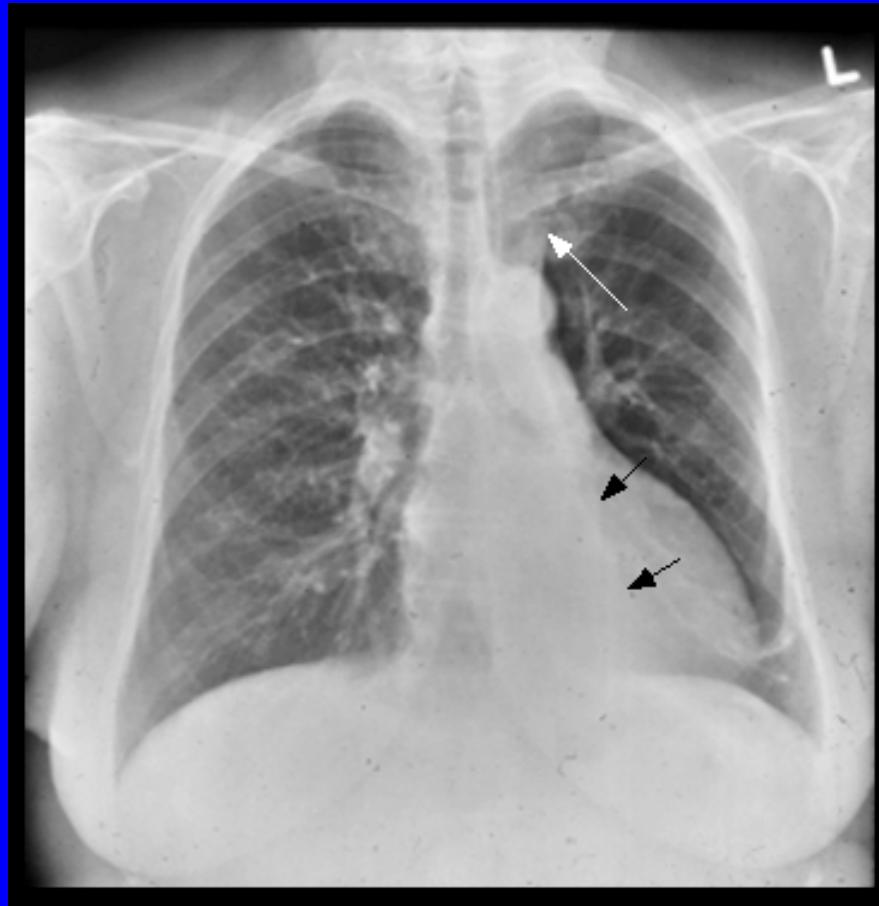
Right lower lobe atelectasis



Left upper lobe



Left lower lobe atelectasis



Top of the knob-
mediastinal shift

Pneumothorax

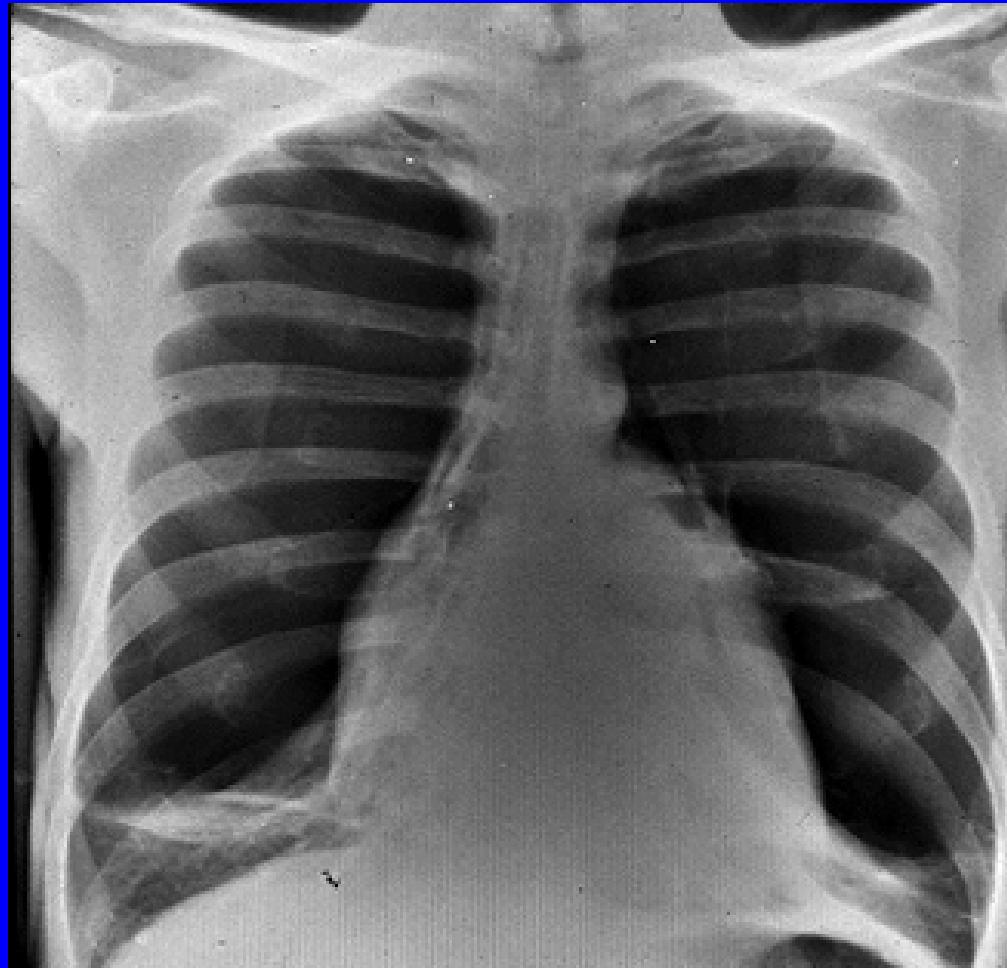
- Collection of air in pleural cavity
- Primary and secondary causes
- Upright position air rises and separates the lung from the chest wall creating a line. Don't be fooled by skin folds, clothing and bullae. Widening of rib spaces and contralateral shift of mediastinum can be seen.
- In the supine position air moves anteriorly. The lung will not be clearly separated from the chest wall. Look for widening rib spaces, deep sulcus sign, shift of mediastinum.

Pneumothorax

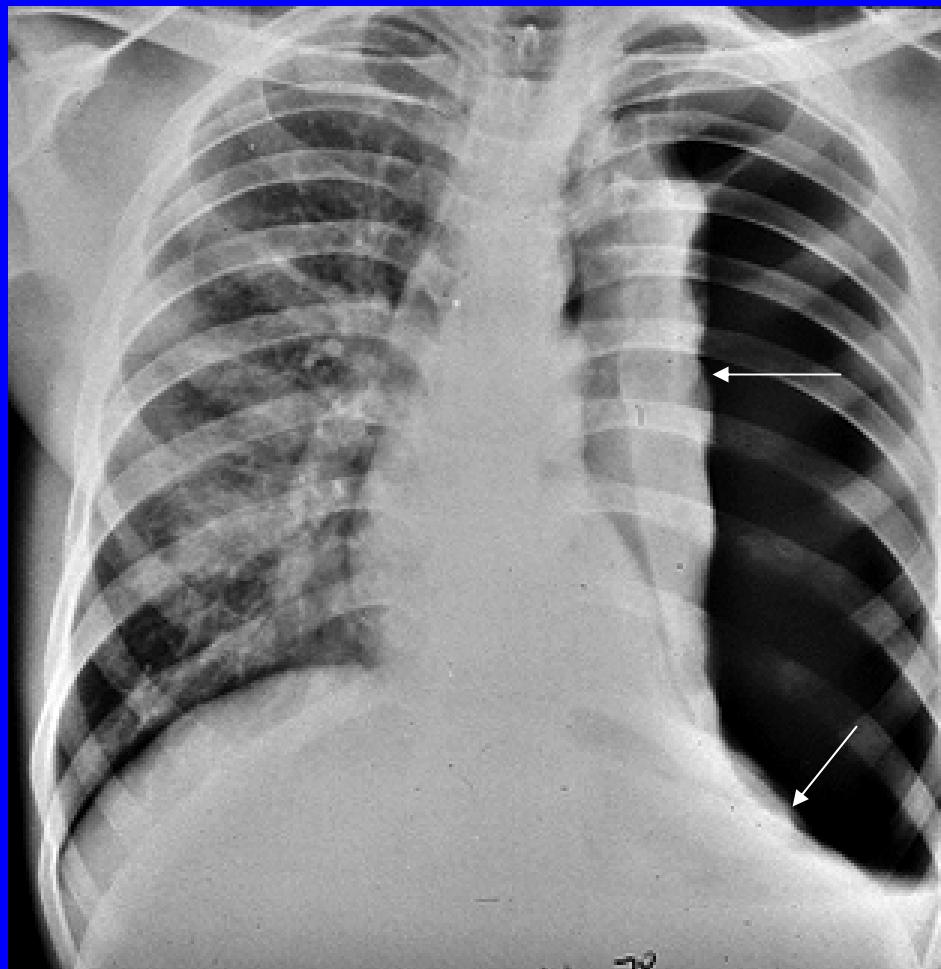


Not a pneumothorax

Watch out for bullae

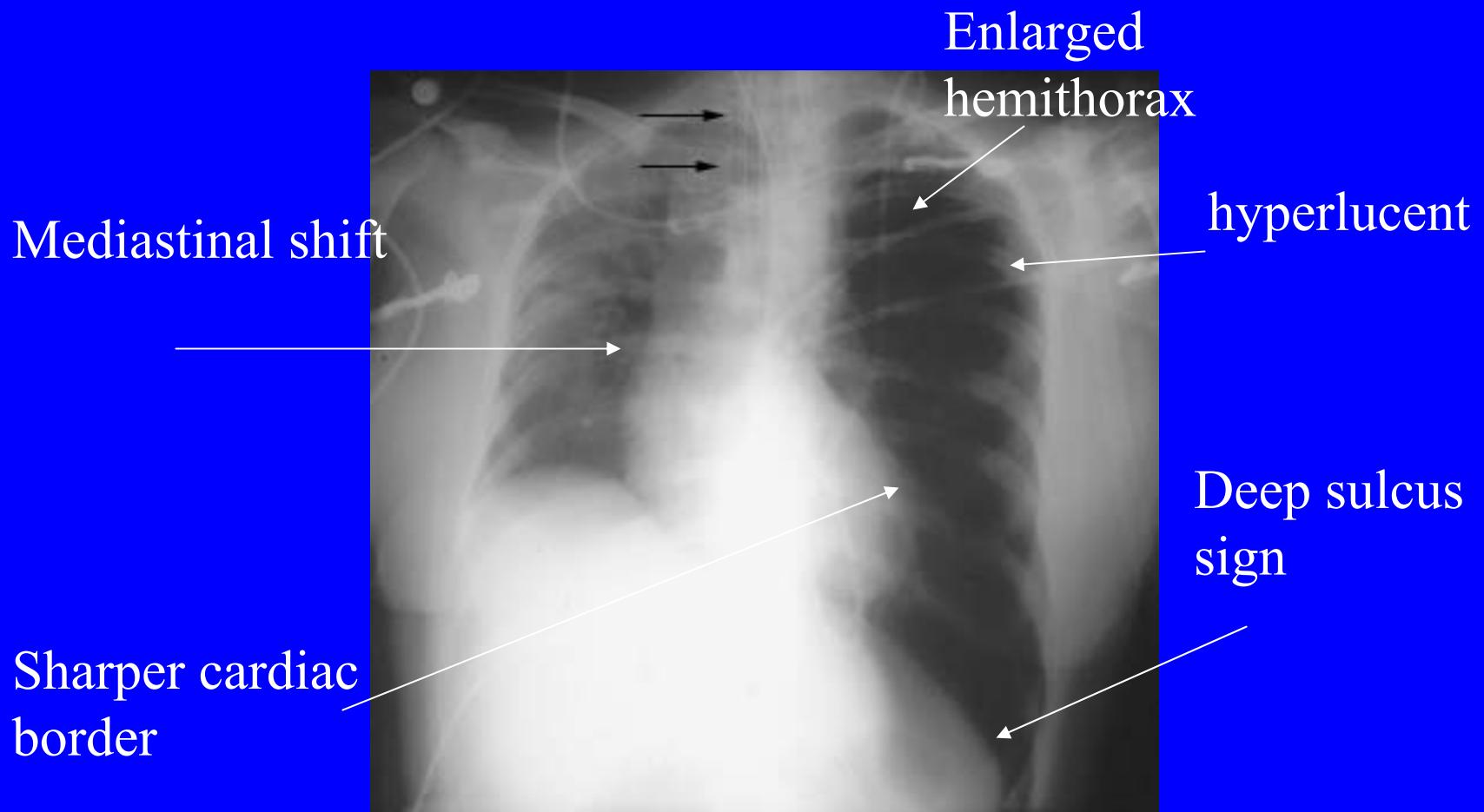


Pneumothorax



Tension
PTX.

Pneumothorax in the Supine Patient

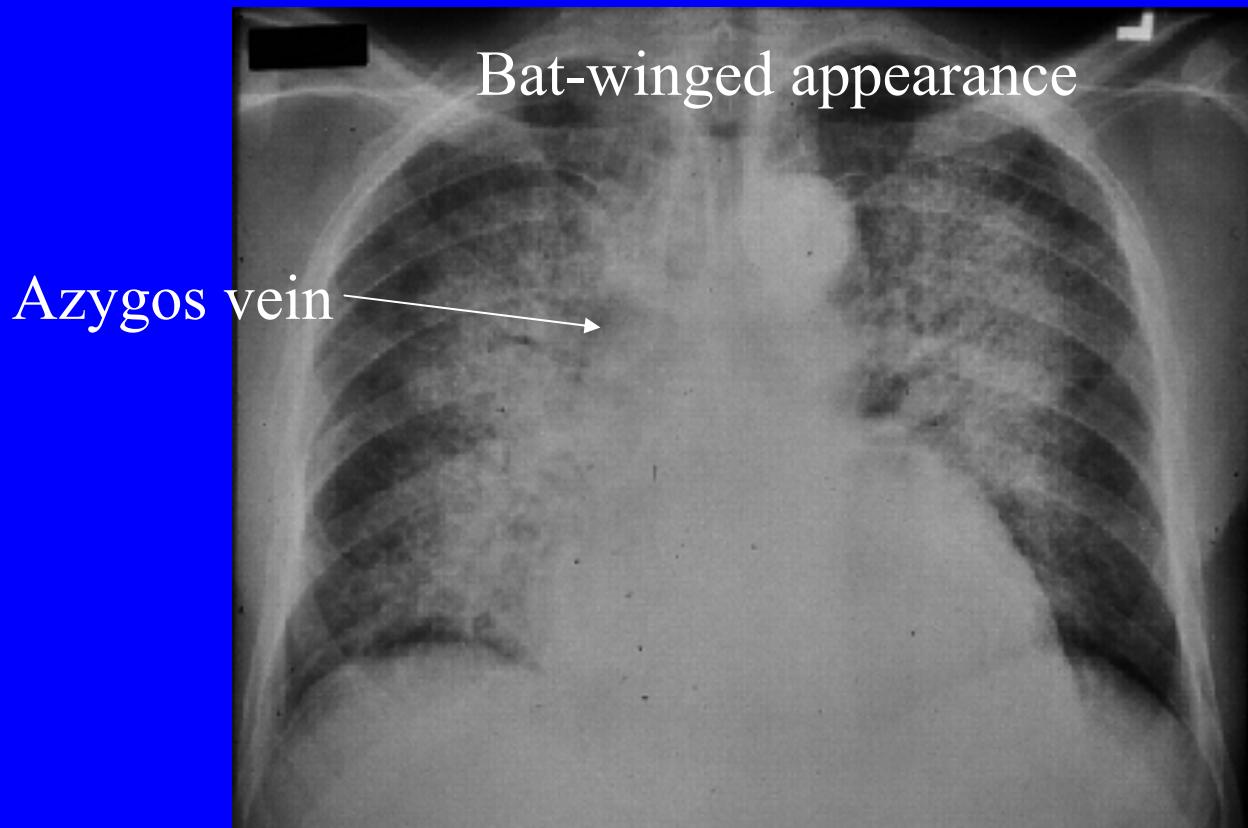


Not a pneumothorax



Don't respond to the cxr. Make
sure the clinical picture fits

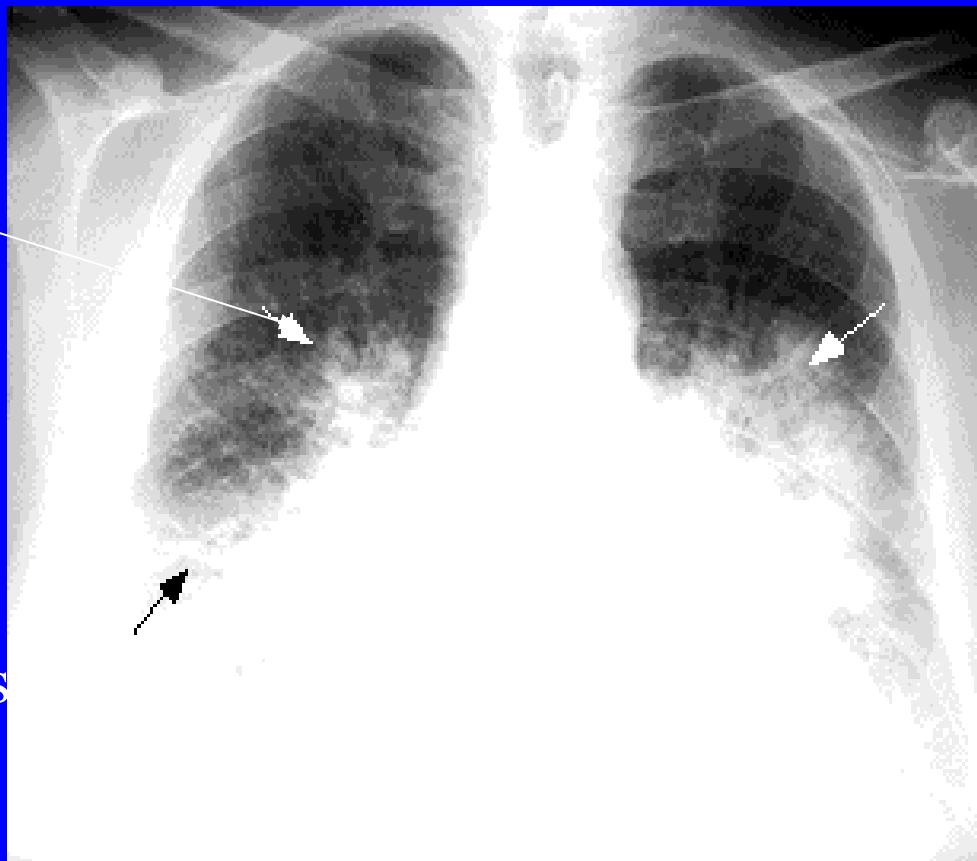
CHF



Enlarge cardiac sill

CHF

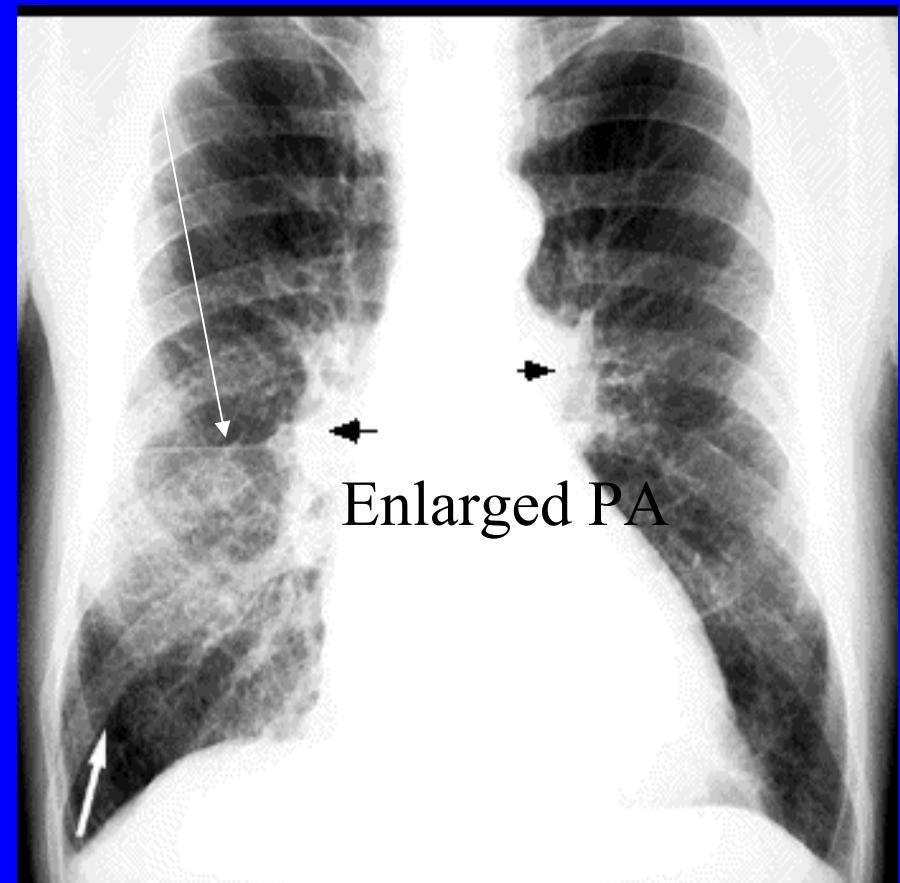
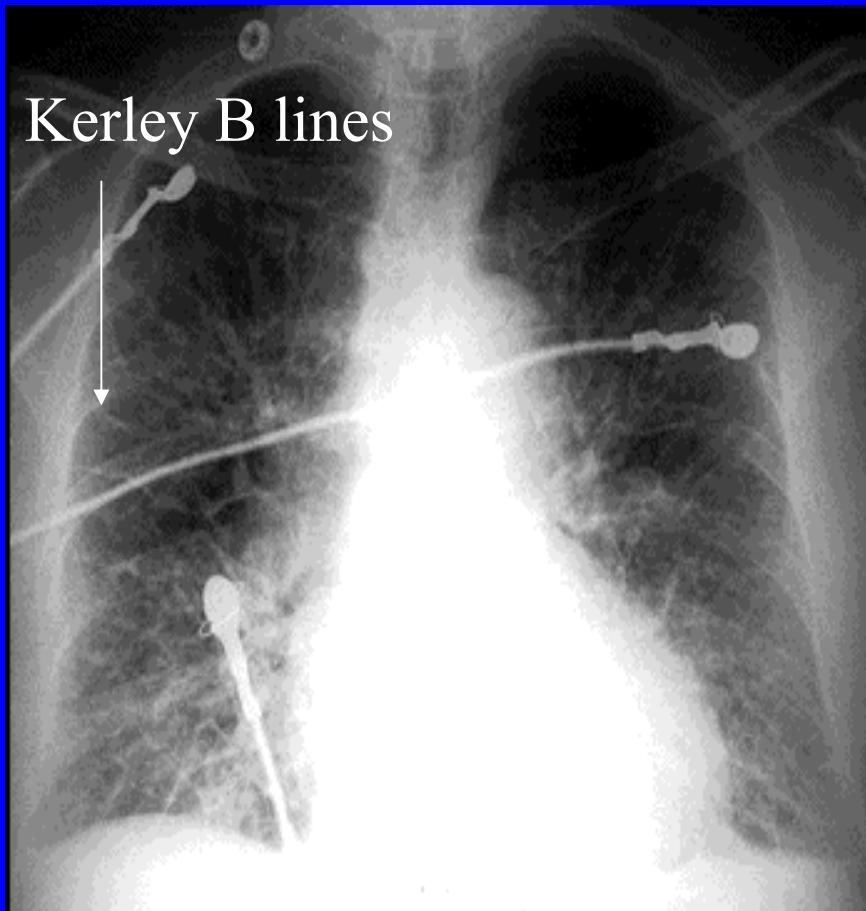
Perihilar
infiltrates/enlarge
PA



Pleural effusions

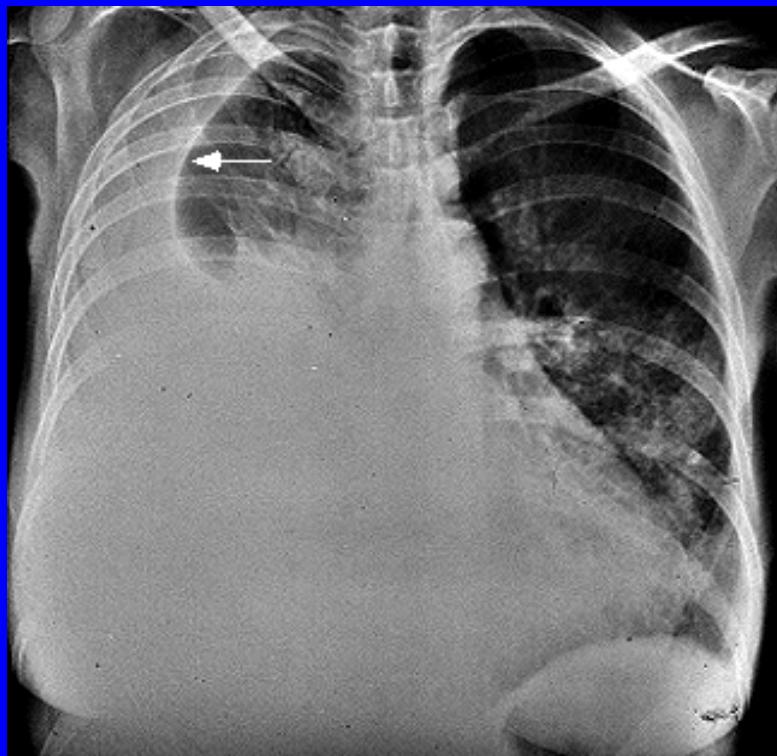
CHF

Fluid in fissure



Kerley B line

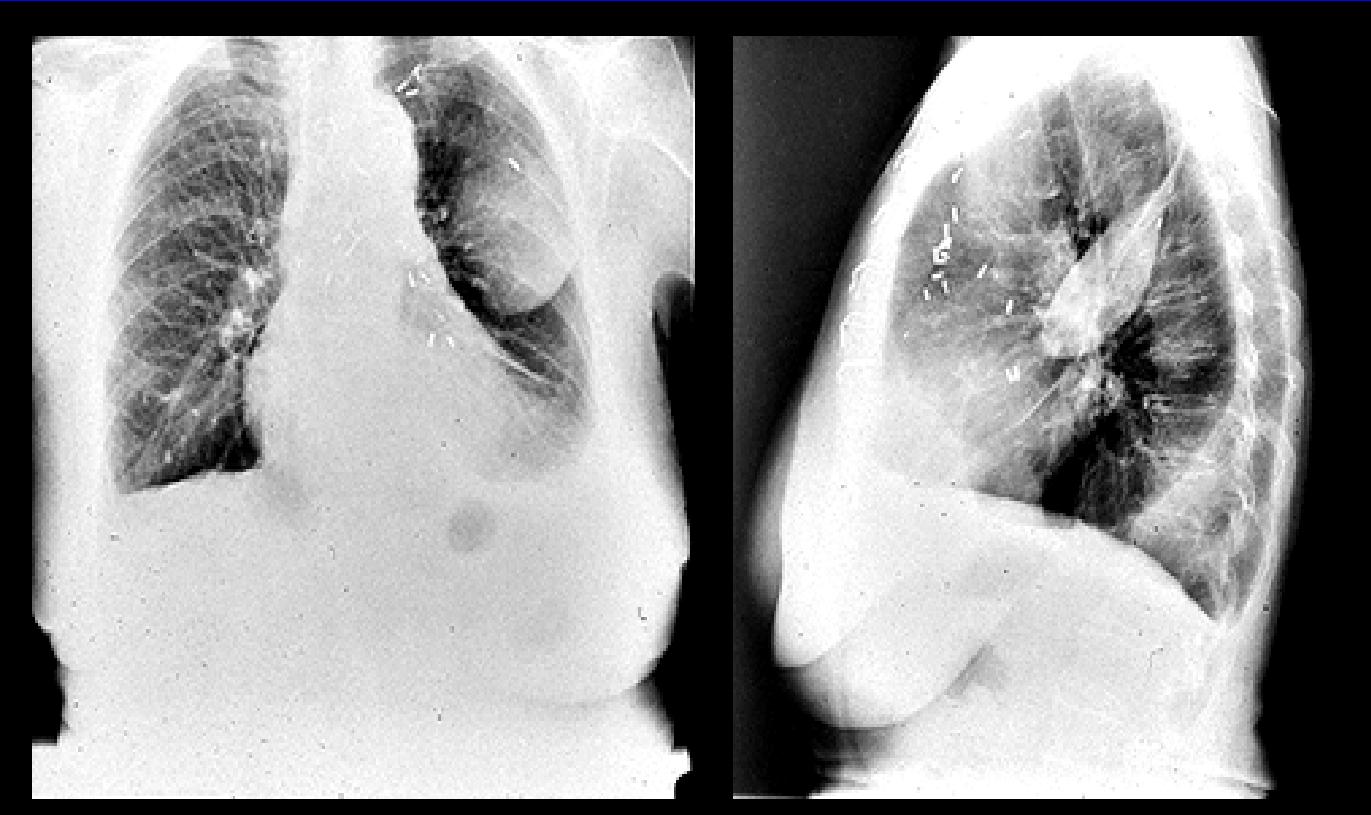
Effusion

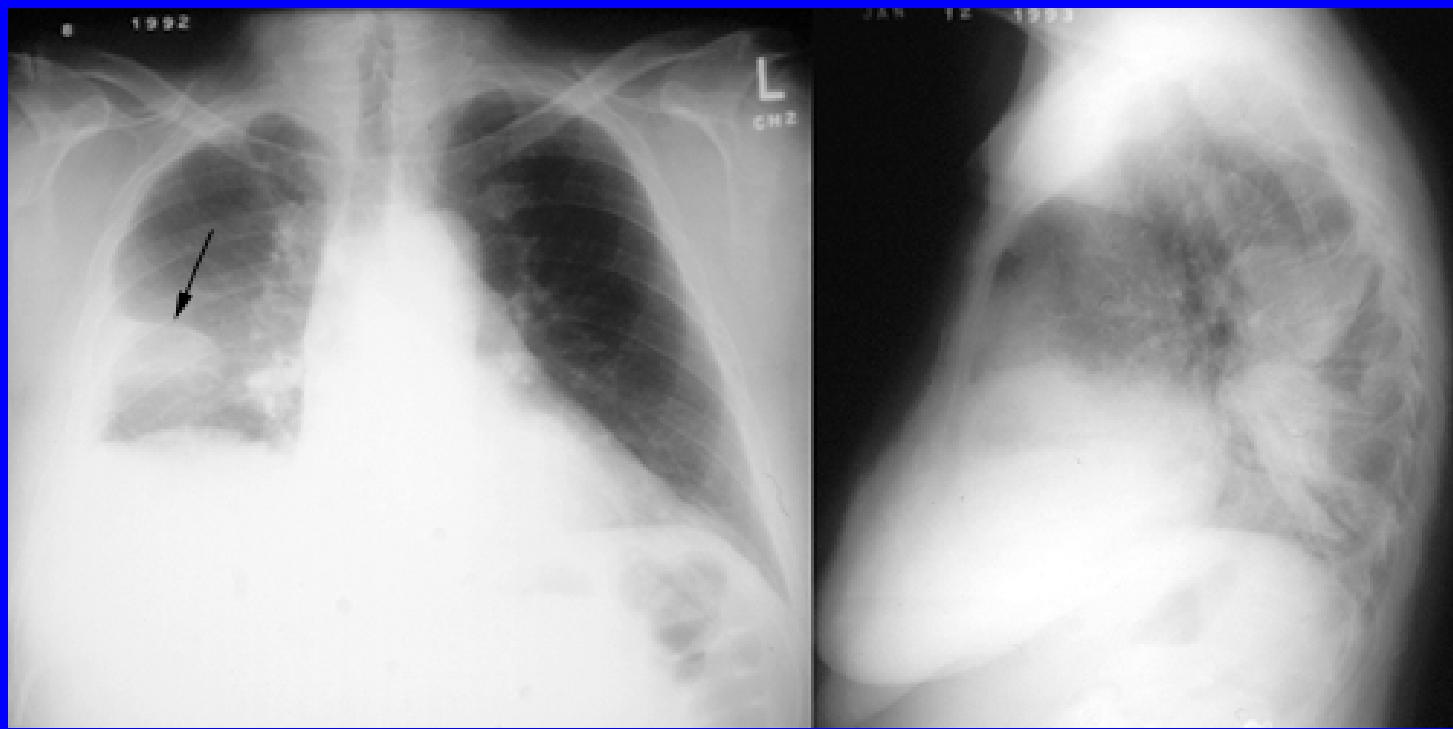


Effusion



Effusion





Total White Out of the Lung!
What do you do?



- Chest PT

H. Acid-Base Disorders: Eight quick steps

Step #1: Gather the necessary data (ABG and serum chemistries).

Step #2: Look at the pH. If it is > 7.4 , then pt has primary *alkalosis*, proceed to Step 3a. If $pH < 7.4$, then pt has primary *acidosis*, proceed to step 3b.

Step #3: Look at the PCO₂.

3a: If PCO₂ is > 40 , then pt's alkalosis is metabolic; if < 40 then respiratory.

3b: If PCO₂ is > 40 , then pt's acidosis is respiratory; if < 40 , then metabolic.

Step #4: Check if patient has a significant anion gap ($> 12-18$). (Formula for this is: $Na - Cl - HCO_3$.)

When calculating AG pay attention to serum albumin values. For every 1 g/dL decline in serum albumin <4.4 g/dL, a 2.5 mEq/L reduction in AG occurs.

Step #5. FOR METABOLIC ACIDOSES- CALCULATE PREDICTED PCO₂

WINTERS FORMULA:

$$pCO_2 \text{ predicted } (+/-2) = (1.5 \times HCO_3) + 8$$

If pCO₂ is different than predicted then there is an additional respiratory problems beyond mere compensation.

Step #6: If there is an anion gap calculate the corrected HCO₃. (Pt's gap – 12 + pt's serum bicarb)

If gap excess > 30 , then pt has an underlying metabolic *alkalosis* in addition to whatever disorders Steps #1 through #5 yielded.

If gap excess < 23 , then pt has an underlying metabolic *acidosis* in addition to whatever disorders Steps #1 through #5 yielded.

Step #7: Figure out what's causing the problem(s), using the differentials below.

Anion Gap Metabolic Acidosis	Non-Gap Metabolic Acidosis	Acute Respiratory Acidosis	Metabolic Alkalosis	Respiratory Alkalosis
“MUDPILERS” <ul style="list-style-type: none"> • Methanol <ul style="list-style-type: none"> • Uremia • DKA/Alcoholic KA • Paraldehyde • Isoniazid • Lactic Acidosis • Etoh/Ethylene Glycol • Rhabdo/Renal Failure • Salicylates 	“DURHAM” <ul style="list-style-type: none"> • Diarrhea • Uretero-Pelvic Shunt • Renal Tubular Acidosis Hyperalimentation • Acetazolamide • Hypocapnia (post) 	Can't breath, won't breath <ul style="list-style-type: none"> • CNS Depression (drugs/CVA) • Airway Obstruction <ul style="list-style-type: none"> • Pneumonia • Pulmonary Edema • Myopathy 	“CLEVER PD” <ul style="list-style-type: none"> Contraction Licorice* Endo: (Conn's/ Cushing's/Bartter's)* Vomiting Excess Alkali* Refeeding Alkalosis* Post-hypercapnia Diuretics* <p>*assoc with high urine CL levels</p>	“CHAMPS” <p><i>anything that causes hyperventilation, i.e.:</i></p> <ul style="list-style-type: none"> • CNS disease <ul style="list-style-type: none"> • Hypoxia • Anxiety • Mech Ventilators • Progesterone • Salicylates/ Sepsis

Step #8: Fix it!

I. & J. Severe Sepsis/Septic Shock

I. Definitions

- a. Systemic Inflammatory Response Syndrome (SIRS), need 2/4
 - i. Leukocytosis ($>12K$), BANDEMIA, OR Leukopenia or ($<4K$)
 - ii. Fever >100.4 OR Hypothermia <96.8
 - iii. Tachypnea >22
 - iv. Tachycardia $>90\text{bpm}$
- b. Sepsis: SIRS + Suspected Infection
- c. Severe Sepsis: Sepsis + Evidence of Organ Dysfunction
 - i. Lactate is useful, >4
- d. Septic Shock: Severe sepsis + hypotension DESPITE adequate resuscitation (20-30cc/kg, 2L-3L NS over 30min) or Pressor requirement.

II. Most Important Things to do in Severe Sepsis/Septic Shock

- a. Give Appropriate, Broad spectrum Antibiotics early
 - i. ICU Mortality 50% vs 12% if inappropriate Abx given
 - ii. ICU Mortality increases by 7% per hour of no antibiotics in hypotensive patients
- b. Give Appropriate Fluid Resuscitation early
 - i. Insert a Central Line
 - ii. Subclavian and IJ are preferential
 - 1. Lower complication rate (infections)
 - 2. Able to monitor CVP
 - iii. Give 2-3 L immediately, goal CVP 8-12 nonintubated, 10-14 intubated
 - iv. Will need on avg 5L in 1st 6hrs (Rivers)
 - v. NS is equal to, and less expensive than colloids, albumin
- c. Start Pressors early if after 2L of fluid MAP<60
 - i. Norepinephrine is 1st Line
 - ii. Consider vasopressin 2nd
 - iii. Patient is in big trouble if you are thinking about a 3rd

III. Controversies in Resuscitation of Severe Sepsis/Septic Shock: O2 delivery

- i. Sepsis is a disease of impaired cellular metabolism, does boosting O2 delivery help?
- ii. Inotropic Support: does increasing cardiac output help septic patients?
 - 1. Pro: Rivers 2001 NEJM: Early, Goal-directed Therapy
 - a. OR=0.67 28 day mortality
 - b. Dobutamine part of protocol if svcsat<70%
 - c. But, Only 13% (18) patients received it
 - 2. Con: Gattinoni 1995 NEJM: Goal-oriented Hemodynamic Therapy
 - a. No difference between groups treated with inotropes and controls
 - 3. Bottom line: It is possible that increasing O2 delivery *to the normal range* in the 1st 6 hours of sepsis is beneficial, but after this it is likely not (as later sepsis is associated with problems of cellular metabolism...the O2 can get there, but might not be used). There is not enough evidence now to support this practice.

- iii. RBC transfusion: does increasing O₂ delivery through transfusion help?
 - 1. Pro: Rivers
 - a. 64% of EGDT group Transfused to 30% HCT in 1st 6hrs, see above Bottom line.
 - 2. Con: Multiple studies show RBC transfusion in critically ill, nonbleeding patients increased mortality, risk of ARDS
 - 3. Bottom line: may be helpful early

V. Controversies in Adjunctive Therapies for Severe Sepsis/Septic Shock

- iv. Steroids: “relative” Adrenal insufficiency is common in sepsis~50% and associated with poor outcomes.
 - 1. Defined by <9mcg/dl response 60min after 250mcg ACTH
 - 2. Annane 2002 JAMA: In patients with Hypotension DESPITE pressors, ACTH nonresponders had lower mortality if given hydrocort 50q6 + fludrocort 50mcg.
 - a. Etomidate issue: etomidate causes adrenal insufficiency and probably poorer prognosis in sepsis (CORTICUS)
 - b. 24% Annane patients got etomidate, but controlling for etomidate, still get mortality benefit!
 - 3. CORTICUS Trial
 - a. No mortality benefit to steroids in relative adrenal insufficiency, increased infectious complications.
 - b. Markedly different patient population (not as sick) as Annane study, no use of fludrocortisone, steroids given in 72 (not 8) hrs
 - 4. Bottom Line: Recommend hydrocort 50/fludrocort to **pressor-refractory (ie, very sick) relative** adrenal insuff patients only.
- v. Activated Protein C (Xigris): Sepsis involves microvascular coagulation dysfunction. Does correcting this help?
 - 1. PROWESS study: 20% Relative risk reduction in mortality only for APACHE II>25, treated within 24hrs
 - 2. Only excess harm if Xigris given and patient is low risk of death (APACHE <25)
 - 3. Excluded many, many patients: pregnant, age<18, Platelets<30K, any condition w/increased risk of bleeding (recent surgery, stroke w/i 3mos, aneurysm/avms, GIB in 6weeks), hypercoag state, known DVT/PE, HIV CD4<50, life expectancy <28d prior to sepsis, s/p transplant, known cirrhosis or portal HTN, acute pancreatitis, treatment with therapeutic dose heparin/coumadin.
 - 4. Bottom line: Very hard to find a patient who will meet criteria to get Xigris: can't be too sick or too well. Probably beneficial in those that meet criteria.
- vi. Insulin: Hyperglycemia is associated with worse outcomes in critical illness. Does lowering glucose help?
 - 1. Van de Berghe NEJM studies:
 - a. in surgical patients, intensive insulin therapy (goal fsbs 80-110) reduced mortality risk by 40%

- b. In medical patients, results not as clear: No mortality benefit if all patients studied, +benefit to quicker weaning, d/c from ICU and hospital.
- c. In subgroup analysis, a mortality benefit appeared if a patient was in the ICU >3days. There was INCREASED mortality w/intensive insulin if patients stayed in the ICU<3d. Other studies show no benefit to intensive insulin in MICU (eg. Barhurst NEJm 2008)
- d. Bottom line: Standard prescription of IV insulin in septic MICU pts is controversial, and aggressive reductions in BS is probably not warranted. Subgroup analysis suggests that use of insulin to lower BS in patients in MICU for greater than 3d is beneficial.

K. Vasopressors

Indications: Hypotension associated with sepsis
Cardiogenic shock
Neurogenic hypotension
Drug-induced hypotension
Anaphylactic shock
ACLS

Site of action: Adrenergic receptors

- α-1
 - Peripheral arteriolar vasoconstriction
- β -1
 - Increased heart rate and force of contraction
 - Bronchial smooth muscle dilation
 - Vasodilation in skeletal muscle
- Dopamine
 - Increased renal, mesenteric, cerebral blood flow via DA receptors
 - Unclear if any clinical meaning to these effects

After insuring adequate volume resuscitation begun, two questions to ask when choosing a vasopressor:

- What is the cardiac function?
- What is the SVR?

Available pressors

Phenylephrine

- Pure α1 receptor agonist
- Increases SVR with a potential reflex bradycardia (maybe benefit in afib)
- Infusion 20-50mcg/min
- Hyperdynamic sepsis, drug-induced hypotension, neurogenic hypotension; not in cardiogenic shock
- Complications: bradycardia, excessive afterload

Norepinephrine

- α 1activity with some β1-activity
- Increases SVR with some chronotropic and inotropic effect
- 1-40mcg/min
- Sepsis, cardiac related hypotension
- Complications: vasoconstriction with hypoperfusion of tissues

Dopamine

- Dose-dependant activity acting on DA , alpha, beta
- Dose – dose response varies between patients.
 - <10mcg/kg/min - acts on B receptors to increase cardiac output
 - >10mcg/kg/min - additionally has effects on α1 receptors to vasoconstrict.
- Sepsis with some cardiac dysfunction, cardiogenic shock,
- Complications: vasoconstriction with tissue hypoperfusion

Dobutamine

- β -1 and β -2
- It increases cardiac output and reduces afterload (β_2 effects on skeletal muscle).
- Cardiogenic shock.
- 2-20mcg/kg/min
- Complications: hypotension, tachycardia, arrhythmias

Epinephrine

- Acts on α_1 , β_1 and β_2
- Anaphylactic shock, status asthmaticus, ACLS
- Anaphylactic shock - 1:10,000 adrenaline given iv in 1 ml doses until effective. If no iv access available then 0.5ml of 1:1,000 im.
- Acute severe asthma attack unresponsive to normal treatment may require infusions of epinephrine, though 0.5ml of 1:1000 s/c may be used

L. Treatment of Massive Thromboembolism

- I. Introduction: Massive pulmonary embolism is a rare but often fatal illness. Most patients die within the first few hours so the immediate institution of effective therapy is critical. In fact, patients suspected of having a massive PE therapy should be initiated prior to performing diagnostic evaluation.
- II. Treatment:
 - a. Resuscitation:
 - i. Airway: Hypoxemia and respiratory failure require immediate intubation.
Caution: Positive pressure can lead to worsening of hemodynamic status.
 - ii. Hemodynamic:
 1. IV fluids: may be necessary, but be cautious because fluids can precipitate RV failure in an already strained right side. This is in contrast to treatment of RV infarct where fluids are required.
 2. Unless clearly volume depletion IV fluids should be limited to 1L.
 3. Begin vasopressors early. Norepinephrine and dopamine. Dobutamine should be used with caution because of the risk of worsening hypotension.
 - b. Anticoagulation: SubQ heparin is first line in hemodynamically stable patient. IV Heparin is recommended in renal failure, morbid obesity and hemodynamically unstable patient (see below).
 - c. Thrombolytics:
 - i. Accelerates lysis of clot, but associated with increased risk of major hemorrhage.
 - ii. No study has been large enough to CONCLUSIVELY demonstrate mortality benefit.
 - iii. Persistent hypotension and severe hypoxemia are accepted as indications for thrombolytic therapy.
 - d. IV filters:
 - i. Indicated in patients with contraindication to anticoagulation.
 - ii. Recurrent PE on anticoagulation
 - iii. Bleeding on anticoagulation
 - iv. Some physicians recommend IVC filters in patients with poor cardiac reserve because a recurrent PE would likely be fatal. Consider in all pts with massive PE and +lower ext dopplers.
 - e. Embolectomy:
 - i. Catheter or surgical: Performed in patient with massive PE and contraindication to therapy or refractory to treatment.

M1. Sedation and Pain Control – Courtesy John Marshall PharmD

I. Introduction

- A. Presentation
 - 1. Hypermetabolic symptoms (increased heart rate, blood pressure, and respiratory rate).
 - 2. Mental status changes (confusion, irritability, restless, insomnia, and combativeness).
 - 3. Agitation can be caused by any one or combination of the following factors:
- B. Pain
 - 1. Unrelieved pain may contribute to inadequate sleep, possibly causing exhaustion and disorientation.
 - 2. Agitation in an ICU patient can often be due to inadequate pain relief and must always be considered first when selecting appropriate therapy.
 - 3. Potential causes of pain include preexisting diseases, invasive procedures, trauma, monitoring and therapeutic devices (i.e. catheters, endotrachial tube), routine nursing care (suctioning, dressing changes, positioning), and prolonged immobility.
- C. Anxiety
 - 1. The causes of anxiety in an ICU patient is likely multifactorial.
 - 2. When a patient exhibits signs of anxiety, first rule out any underlying physiologic disturbances such as hypoxia, hypoglycemia, hypotension, pain, and withdrawal from alcohol or other drugs.
 - 3. Other potential causes of anxiety include an inability to communicate, continuous noise, continuous lighting, excessive stimulation, mechanical ventilation, and sleep deprivation.
- D. Delirium
 - 1. Characterized by an acutely changing or fluctuating mental status, inattention, disorganized thinking, and an altered level of consciousness that may or may not be accompanied by agitation.
 - 2. Potential causes of delirium include altered sleep-wake cycle, sleep deprivation, continuous noise and lighting, excessive stimulation, alcohol withdrawal, and other drugs.
 - 3. See Appendices I and II for further information on evaluating delirium.

II. Non-Pharmacologic Therapy

- A. Therapy should be targeted at treating the underlying process. Treat underlying physiologic disturbances first (i.e. hypotension, hypoxemia, etc.).
- B. Patient orientation can be very effective and should include the following:
 - 1. Orientation to time, date and place.
 - 2. Orientation to and reassurance regarding sound identification, procedures and actions.
 - 3. Maintenance of normal activity cycles.

** This document is not intended to provide complete information on pain control, but rather offers input on the role of pain control in the treatment of agitation and anxiety. For more assistance with pain treatment there is a policy on pain management at BMC.*

III. Pharmacologic Therapy

A. Indications

1. Organic causes ruled out or treatment for organic causes initiated and
2. Orienting/reassurance attempts have failed and
3. Agitation impairing ability to deliver care or
4. Ability to demonstrate signs/symptoms of agitation impaired.

B. Cautions

1. While there is no policy governing the use of benzodiazepines, haloperidol, or opioids based on patient location, caution should always be used when administering these medications.
2. Patients who require aggressive treatment of agitation may be best treated in areas where extensive monitoring is available. Clinical judgment should be used to evaluate each patient.

IV. Monitoring

A. Establish common outcome goals at the initiation of therapy.

1. A goal Riker score (see below) **MUST** be specified prior to initiation of therapy and recorded in Sunrise Clinical Manager (SCM) as part of the ventilator orders for **ALL** mechanically ventilated patients.

B. Evaluating sedative therapy: The Revised Riker Sedation-Agitation Scale should be used to monitor sedative therapy.

1. The Riker score **MUST** be evaluated and recorded in the nursing flowsheet every 4 hours for **ALL** mechanically ventilated patients, even if they are not receiving pharmacologic sedation.
 - i. Exception: Patients requiring neuromuscular blocking agents for paralysis. See the medication guideline “Neuromuscular Blocker Use in the ICU” for more information.
2. If the goal Riker score is changed at any time during therapy, it must also be changed on the ventilator orders in SCM.
3. Use the accompanying flow diagram to help titrate medications according to goal Riker score.
4. If deemed candidates, an order for daily wake-ups can be placed into SCM for patients receiving sedation for > 48 hours. The order can be found by typing “sedation” into SCM.
 - i. The following patients are excluded from this protocol:
 - a. Patients receiving neuromuscular blocking agents
 - b. Patients with an FiO₂ > 80%
 - c. Patients on pressure-control ventilation

Table 1. Revised Riker Sedation-Agitation Scale

Score	Description	Definition
7	Dangerous Agitation	Pulling at ET tube, trying to remove catheters, climbing over bedrail, striking at staff, thrashing side to side
6	Very Agitated	Does not calm despite frequent verbal reminding of limits, requires physical restraints, biting ET tube
5	Agitated	Anxious or mildly agitated, attempting to sit up, calms down to verbal instructions
4	Calm and Cooperative	Calm, awakens easily, follows commands
3	Sedated	Difficult to arouse, awakens to verbal stimuli or gentle shaking but drifts off again, follows simple commands
2	Very Sedated	Arouses to physical stimuli but does not communicate or follow commands, may move spontaneously
1	Unarousable	Minimal or no response to noxious stimuli, does not communicate or follow commands

C. Evaluating pain severity and relief:

1. Visual Analogue Scale or Numeric Pain Intensity Scale utilizing a scale 0-10 (0 = no pain, 10 = worst pain) can be used to evaluate pain severity and relief.
2. B/C Scale can be found on the critical care flowsheet.
 - a. "B+" indicates the patient demonstrated behavior consistent with pain (i.e. grimacing).
 - b. "C+" indicates the patient demonstrated hemodynamic derangements thought to be due to pain (i.e. tachycardia, tachypnea).

D. Evaluating delirium

1. The Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) should be done daily to evaluate delirium in the ICU. The CAM-ICU scale assesses for four factors of delirium in mechanically ventilated patients: (1) fluctuating mental course (2) inattention (3) disorganized thinking (4) altered level of consciousness (See appendix).

E. Patient State Analyzer (PSA) Monitor

1. Used to optimize sedation in a patient receiving neuromuscular blockade.
2. The device acquires EEG signals from an electrode set applied to the head of the patient and converts the signals into a numerical value displayed on the monitor.
 - a. Goal: < 50 for a patient receiving neuromuscular blockade

Analgesia – Opioids

A. General Information

1. This document is not intended to provide complete information on pain control, but rather offers input on the role of pain control in the treatment of agitation

and anxiety in the intensive care unit setting. For more assistance with pain treatment the Anesthesia Pain Team or Dr. James Otis (Neurology) may be consulted.

2. Meperidine is NOT recommended for routine use.
 3. All patients on opioids should be ordered for a bowel regimen that combines a stool softener and mild peristaltic stimulant
 - a. Example: docusate sodium 100 mg po bid PLUS senna 2 tablets po qhs OR bisacodyl 10 mg pr qday
 - b. Bowel regimen should be adequately titrated with increasing opioid dose.
2. Opioids

	Fentanyl	Hydromorphone	Morphine
Onset of action	1-2 min	IV: ~15 min PO: ~30 min	IV: 10-20 min PO: 30-60 min
Duration (after bolus)	30-60 min	4-6 hr	2-3.5 hr
Typical bolus dose*	25-100 mcg IVP	0.25-0.75 mg IVP/PO	2-5 mg IVP/PO
Typical bolus frequency*	<ul style="list-style-type: none"> q5-15 min until pain acutely controlled q15-60 min PRN breakthrough pain 	<ul style="list-style-type: none"> q5-15 min until pain acutely controlled q2-4 hr PRN breakthrough pain 	<ul style="list-style-type: none"> q5-15 min until pain acutely controlled q2-4 hr PRN breakthrough pain
Initial infusion rate	25-100 mcg/hr	Not recommended	1-5 mg/hr
Renal Insufficiency	Preferred agent	Preferred agent	Use with caution, metabolites may accumulate
Hepatic insufficiency	Preferred agent	Consider dose reduction	Consider dose reduction
Use in hemodynamic instability	Preferred agent	Preferred agent	Avoid
Monitoring	Titrate to goal Riker score	Titrate to goal Riker score	Titrate to goal Riker score
Preferred method of administration	Continuous infusion	Intermittent bolus	Intermittent bolus
Patient controlled analgesia (PCA)	<i>For PCA dosing and administration, see "Adult Patient-Controlled Analgesia" on pharmacy website.</i>		
Dose equivalence	100 mcg	1.5 mg	10 mg
Active metabolites	No	No	Yes, cleared renally
Histamine release	No	No	Yes
Common adverse effects	Constipation, delayed gastric emptying	Constipation, delayed gastric emptying	Constipation, delayed gastric emptying, hypotension, itching

* The dosing and frequency recommendations are meant to serve as a guide. Agent selection and dosing must always be tailored to the individual patient and clinical situation.

V. Sedation

Table 3. Benzodiazepines

	Midazolam	Lorazepam	Diazepam
Onset of action	IV: 1-5 min	IV: 5-20 min PO: 20-30 min	PO: ~30 min
Duration	1-2 hr	2-6 hr	2-4 hr
Half-life	1-4 hr	13-16 hr	20-50 hr; Active metabolite: 50-100 hr
Initial dose* for acute agitation	1-2 mg IVP prior to procedure; 2-5 mg IVP q5-15 min	1-4 mg IVP q10-20 min	5-10 mg PO q3-4 hr
Intermittent* dosing - Preferred	1-5 mg IVP q1-2 hr; higher doses may be necessary	1-4 mg IVP/PO q2-6 hr; higher doses may be necessary	5-10 mg PO q3-4 hr; will accumulate with repeated dosing
Initial infusion rate	Consult the ICU pharmacist. See below for more information on continuous infusion. Intermittent dosing should be tried before continuous infusion is considered.		
	Start at 2-4 mg/hr	Start at 2-4 mg/hr	N/A
Monitoring	Titrate to goal Riker score	Titrate to goal Riker score	Titrate to goal Riker score
Renal insufficiency	Avoid with severe impairment	Use with caution; half-life can increase to 32 to 70 hours	Avoid with severe impairment
Hepatic impairment	Avoid with severe impairment	Use with caution	Avoid with severe impairment
Metabolism and Elimination	CYP450 3A4, Renal, and biliary excretion	Hepatic metabolism, Renal, and biliary excretion	CYP450 3A4, renal elimination
Active metabolites	Yes	No	Yes
Dose Equivalence	2-3 mg	1 mg	5 mg
	No	Yes	N/A
Propylene glycol	<i>For more information on the effects of propylene glycol, see "adverse effects" of benzodiazepines.</i>		
Short-term sedation	Benzodiazepine of choice; Sedative for specific procedures; Use ≤ 48 hours	May be used but not ideal when rapid awakening is desired (i.e., CVA, TBI)	Very long duration of action; should not be used when rapid awakening is desired
Long-term sedation	Use > 48 hr may produce prolonged sedation after discontinuation for the following reasons: 1. drug accumulation in CNS 2. accumulation of active metabolite 3. inhibition of CYP450 3A4 by other medications 4. hepatic insufficiency	Long duration of action – ideal for prolonged sedation when continuous infusion is required (i.e., ventilator- dependent patients). Monitor for propylene glycol toxicity.	High risk for over-sedation with repeated drug administration; accumulation of parent drug and its active hepatic metabolites may occur.
Alcohol withdrawal	Midazolam is not recommended due to its short duration of action.	Lorazepam is recommended in patients with cirrhosis or severe liver impairment	Diazepam is recommended in absence of liver impairment due to rapid onset and long duration of action.

For more information, see “Alcohol Withdrawal and Treatment in Adults” medication guidelines on our pharmacy website.

* Initial dose for naïve patients not on chronic benzodiazepines and those without significant history of alcohol use. The dosing and frequency recommendations are meant to serve as a guide. Agent selection and dosing must always be tailored to the individual patient and clinical situation.

VI. Sedation

A. General information

1. Drugs of choice in patients with no pain or adequate pain control.
2. Mechanism of benzodiazepines involves binding to stereospecific benzodiazepine receptors on the postsynaptic GABA neuron at several sites within the central nervous system (CNS) and thereby enhancing the inhibitory effect of GABA on neuronal excitability resulting in hyperpolarization (a less excitable state) and stabilization.

B. Dosing and administration

1. Cross tolerance and increased requirements occur with chronic use or history of alcohol abuse.
2. Patients on benzodiazepines long-term should be tapered off of therapy and not abruptly discontinued.
3. Dose all patients receiving paralytic agents with around the clock scheduled benzodiazepines in addition to the narcotics, if being used. Titrate sedation to a Riker score of 1 prior to commencement of paralysis.
4. Consider a combination therapy of low dose benzodiazepine and a neuroleptic in patients with respiratory depression.

C. Continuous infusion-specific dosing recommendations

1. To initiate therapy, review the patient's previous requirements of benzodiazepines in the past 24 hours to help estimate the starting dose of midazolam or lorazepam.
2. At the initiation of therapy and before any changes in the infusion rate, a bolus dose should be administered since it may take 2-4 hr before steady state is reached on the new infusion rate.
3. Additional bolus doses should be administered if the patient becomes acutely agitated rather than increasing the hourly rate. Bolus doses may be given every 5 to 15 minutes as needed. If several bolus doses are given consecutively, the hourly rate may be increased by 1-2 mg/hr.
4. Bolus doses should be at least as much as the hourly infusion rate. For example, if a patient is on an infusion at 3 mg/hr and requires a bolus dose, a 3 mg bolus dose should be administered.
5. Ideally, infusion rates should not be increased more frequently than every 3 hours, since it will take at least 3 hours before new steady state is reached.
6. To wean off a continuous infusion, the hourly rate may be reduced by half every 4-6 hours, as tolerated. Alternatively, the midazolam infusion may be turned off immediately and intermittent doses of lorazepam with increasing intervals and

decreasing doses may be used. Patients on infusions for less than 5 days may not require weaning.

D. Adverse Effects

1. Respiratory depression and apnea may occur with all benzodiazepines especially in patients with underlying respiratory insufficiency.
2. Hypotension may occur with all benzodiazepines; however, propylene glycol in lorazepam infusion may increase the risk and severity of hypotension.
3. Propylene glycol (PG) and toxicity
 - a. Intravenous preparations of lorazepam contain the solvent propylene glycol to enhance drug solubility in plasma. This solvent can cause local irritation to veins, which is minimized by injecting the drug into a large vein.
 - b. A bolus of PG can cause hypotension and bradycardia, and prolonged administration of PG can cause paradoxical agitation, hyperosmolarity, acute renal failure, lactic acidosis, and a clinical syndrome that mimics severe sepsis. When PG toxicity is suspected, lorazepam infusion should be stopped and the following therapeutic approaches should be considered:
 - i. Switch to midazolam or propofol
 - ii. Use intermittent dosing of intravenous lorazepam
 - iii. Administer lorazepam (or diazepam) tablets down a nasogastric tube
 - c. Patients receiving high doses of intravenous lorazepam (≥ 6 mg/hr) should have acid-base status and osmol gap checked daily while on a continuous infusion. May consider monitoring the osmol gap 2-3 times per week in patients receiving infusions < 6 mg/hr.
 - d. Osmol gaps > 10 have been associated with PG toxicity in patients receiving continuous lorazepam infusions. However, the clinical manifestations of PG toxicity (acute renal failure, lactic acidosis) may or may not occur at gaps > 10 . To calculate the osmol gap:
 - i. Osmol Gap = CALCULATED Osm – MEASURED Osm
 - ii. Order a MEASURED serum osmolarity at the same time as a chemistry panel.
 - iii. CALCULATED Osm = $(2 \times \text{Na}^+) + (\text{BUN} / 2.8) + (\text{Glucose} / 18)$

Table 4. Other Sedatives

	Propofol (Diprivan®)	Dexmedetomidine (Precedex®)
Uses and Restrictions	<ul style="list-style-type: none"> Drug of choice for patients expected to be intubated < 48 hr. NOT recommended for routine long-term use due to adverse effects. Only in mechanically ventilated patients or under the guidance of an anesthesiologist. Preferred agent for neuro and neurosurgery patients when frequent neuro exams are required. 	<ul style="list-style-type: none"> Reserved for use in patients in whom sedation/delirium therapy has been titrated appropriately and meets clinical criteria to be extubated [ex: protects airway, cuff leak, Rapid Shallow Breathing Index < 105, tidal volume 3 mL/kg, vital capacity 2-3 x tidal volume, negative inspiratory force ≤ 20] Restricted to use by approval of SICU attendings (Drs. Burke, Agarwal, Emhoff, Dennis, Azocar, Lopes, Glantz) Infusion duration ≤ 24 hours
Mechanism of action	Propofol is a highly lipophilic compound with general anesthetic properties	<ul style="list-style-type: none"> Highly selective alpha-2 adrenergic agonist. Does not produce respiratory depression.
Clinical effects	Sedative hypnotic with amnestic properties; NO analgesic activity	Sedative hypnotic with anxiolytic, mild analgesic and sympatholytic activities
Bolus dose	Not recommended	+/- 1 mcg/kg over 10 minutes
Continuous infusion	<ul style="list-style-type: none"> Initiate at 5-10 mcg/kg/min and titrate by 5-10 mcg/kg/min q5-10 min to goal Riker score. Usual dose ranges 5 to 50 mcg/kg/min. For therapy > 48 hr, consider switching to a benzodiazepine. 	<ul style="list-style-type: none"> Start at 0.2-0.7 mcg/kg/hr for ≤ 24 hours Titrate to Riker score of 3-4
Discontinuation	Decrease dose by 5-10 mcg/kg/min q5-10 min. If patient becomes agitated, go to the least effective dose and wean more slowly.	Agitation and "sympathetic rebound" following drug withdrawal (similar to that observed with clonidine) may occur. To minimize this risk, discontinue therapy within 24 hours.
Onset of action	Within 1 min	Sedation within few minutes; analgesia w/n 30 min; hypertension w/n 60-90 min
Duration of action	20 to 30 minutes with short-term use	Less than 10 minutes
Metabolism and Elimination	Hepatic metabolism and renal elimination	Hepatic (glucuronidation and CYP450 2A6) metabolism and renal elimination
Caution	Use with caution in the elderly and patients with severe renal or hepatic insufficiency.	Lower dose should be used in patients with severe liver dysfunction.
Adverse effects	Infection, hypotension, hypertriglyceridemia, pancreatitis, propofol infusion syndrome at doses > 75 mcg/kg/min for > 48 hr (cardiac arrhythmias, metabolic acidosis, rhabdomyolysis)	Hypertension associated with rapid infusion, hypotension as a result of peripheral alpha-2 stimulation, bradycardia, nausea

Drug interactions	Propofol is a substrate of CYP450 2B6 and 2C9 isoenzymes AND it is a strong inhibitor of 3A4	Dexmedetomidine is a substrate of CYP450 2A6 and strong inhibitor of 2D6.
Nursing care	Tubing should be changed every 6 hr with ampules and every 12 hr with vials; may turn patient's urine brown or pink	May adsorb to certain types of natural rubber; use components made with synthetic or coated natural rubber gaskets whenever possible.

VII. Delirium - Haloperidol

A. General Information

1. There is no standardized treatment for delirium. Promoting non-pharmacological interventions such as: (1) sleep (2) interaction (3) and reducing environmental stimulation should be optimized in all patients. Avoiding the inappropriate use of medications (benzodiazepines, anti-cholinergics, dopaminergics) that affect mental status may also be beneficial.
2. See CAM-ICU assessment tool in Appendix I.

B. Pharmacology

1. Haloperidol is a CNS depressant and dopamine receptor antagonist. Haloperidol produces less respiratory depression and hypotension than other sedatives (i.e., opiates or benzodiazepines).

C. Pharmacokinetics / Pharmacodynamics

1. Metabolized in the liver to predominately inactive metabolites
2. Onset of sedation after an IV dose is 10-20 min and the duration of sedative effects is approximately 4-6 hr.

D. Precautions

1. May lower seizure threshold. Caution is advised when used concomitantly with other drugs that lower the seizure threshold.
2. Use with caution in patients with thyrotoxicosis since neurotoxicity (i.e., rigidity) may occur in these patients.

E. Dosing

1. See "Alcohol Withdrawal Guidelines" for additional information on the use of IV haloperidol.
2. Starting dose:
 - a. Mild agitation/delirium: 2 mg
 - b. Moderate to severe agitation: 5 mg
3. Titration and Maintenance:
 - a. If patient continues to be agitated after 20 minutes, increase the previous dose by 5 mg every 20 minutes until agitation subsides. Maximum single dose is 30 mg.
 - b. If starting with 2 mg and patient uncontrolled at 20 minutes, increase to 5 mg and follow guidelines above. See exception to maximum dose below.
 - c. Once patient responds to haloperidol, 25% of the loading dose required should be given every 6 hours on a scheduled basis.

- d. For breakthrough agitation between regularly scheduled doses, a PRN haloperidol IV order should be written (i.e. 5-10 mg IV q2-3h PRN). Oral haloperidol may be used instead of the IV form for maintenance dose once the patient is stabilized.
- e. If a patient requires frequent PRN doses, then the scheduled should be readjusted. Maximum daily dose 30mg q4h.
- f. If patient is still not effectively sedated with maximum daily doses of haloperidol, consider using a different drug for sedation or the addition of a second drug with haloperidol (e.g., benzodiazepine or narcotic).

F. Adverse Effects

- 1. Neurologic
 - a. Extrapyramidal symptoms, parkinsonian symptoms, akathisias, dystonic reactions, and tardive dyskinesia (long-term use)
 - b. Neuroleptic malignant syndrome is uncommon; not dose related.
 - i. Increased temperature, WBC, and CPK, autonomic instability, altered consciousness, acute renal failure.
 - ii. Treatment: Discontinue haloperidol, supportive therapy, dantrolene or bromocriptine
- 2. Cardiovascular
 - a. Prolonged QT interval, potentially leading to torsades de pointes.

G. Monitoring

- 1. Observe for neurologic adverse effects.
- 2. Electrolytes: K⁺, Mg²⁺
- 3. EKG: Check QT interval before haloperidol is started and intermittently throughout therapy.

VIII. Reversal Agents – Flumazenil and Naloxone

A. Flumazenil

- 1. Flumazenil is NOT intended for routine reversal of benzodiazepine-related sedation or to diagnose benzodiazepine-induced sedation.
- 2. Indications and Dosage: Suspected benzodiazepine overdose
 - a. Initial dose: 0.2 mg IV over 30 sec
 - b. If desired level of consciousness not obtained after 30 sec: 0.3 mg IV over 30 sec
 - c. Wait another 30 sec to determine level of consciousness
 - d. Further doses (if necessary): 0.5 mg IV over 30 sec at 1 min intervals
 - e. Maximum cumulative dose: 3 mg

B. Naloxone

- 1. To be used for complete or partial reversal of narcotics in suspected overdose or for diagnostic/therapeutic purposes.
- 2. Dosing:
 - a. Initial dose: 0.1-0.2 mg IV
 - b. Repeat doses of 0.4-2 mg every 2-3 min to a total dose of 10 mg.
 - c. Naloxone may be given IM or SC if IV route is not possible.

M2. Neuromuscular Blocking Agents

Courtesy John Marshall, PharmD

BMC NMB Formulary

Short -Acting:

Succinylcholine

- the only depolarizing NMB (acts like Ach and depolarizes membrane)
- resistant to acetylcholinesterase, not metabolized at junction
- leads to initial fasciculations followed by flaccid paralysis
- depolarization causes cells to lose K⁺ ions, typically increasing K by 0.5-1.0 mEq/L
 - life-threatening hyperkalemia has occurred in patients with denervated muscle caused by upper and lower motor neuron disease (spinal cord injury, stroke, demyelinating disease) and in burn and trauma patients (thought to be safe to give within 24 hours of trauma or burn)

Intermediate-Acting

Vecuronium

- structural analogue of pancuronium
- not vagolytic (minimal effect on BP and HR)
- metabolism: 35% renally excreted; 50% excreted in bile
- metabolite: 3-desacetylvecuronium (50% activity)
- more commonly associated with prolonged blockade once discontinued compared to other agents

Cisatracurium

- benzylisoquinolinium structure
- minimal (if any) cardiovascular effects
- should be administered as a continuous infusion (short half-life)
- metabolism: Hoffman degradation pH and temperature dependant break down -- acidosis/hypothermia will affect metabolism

Long-Acting

Pancuronium

- aminosteroid structure
- vagolytic (add about 10 BPM on average to HR)
- avoid in patients with cardiovascular disease (risk of myocardial ischemia)
- metabolism: 60-80% renal, 15-40% hepatic

- metabolite: 3-hydroxypancuronium (50% activity)
- Principals of Neuromuscular Blocking Agent Use**

Indications:

- facilitate short procedures (endotracheal intubation)
- facilitate mechanical ventilation (decreased oxygen consumption)
- prevent uncontrolled muscle contractions w/ certain conditions
- prevent patient interference with surgical repairs and devices (caution on this one)
- decrease ICP

Administration strategies:

- Intermittent bolus dosing
 - controls tachyphylaxis (occurs after 72 hours of infusion)
 - monitoring for accumulation (limits complications related to prolonged or excessive blockade)
 - monitoring for analgesia
- Continuous infusion -- MONITOR CLOSELY
- Monitoring - Train of four

Factors altering the effects of NMB

- there are many drugs that can affect the action of neuromuscular blockers (potentiating or antagonizing)
- aminoglycosides and clindamycin -- both decrease Ach release by blocking calcium influx
- increased magnesium levels
- phenytoin, theophylline, hypercalcemia all can antagonize the effects of NMB

Prolonged Paralysis / Muscle Weakness

Prolonged recovery from NMBs

- increase (after cessation of NMB therapy) in the time of recovery 50-100% longer than predicted by pharmacologic parameters
 - due to elevated levels of parent drug or metabolites
 - excessive drug administration
 - renal or hepatic impairment
 - acidosis/hypothermia with cisatracurium
 - drug interactions (potentiation)

Acute quadriplegic myopathy syndrome

- diffuse weakness persists long after drug and active metabolites are eliminated
- global motor deficit affecting muscles in both upper and lower extremities and decreased motor reflexes
- presents as clinical triad of acute paresis, myonecrosis with increased CPK concentration, abnormal EMG
- no clear evidence of what places patients at risk
- ? concurrent drugs (aminoglycosides, cyclosporine), hyperglycemia, renal/hepatic dysfunction
- concurrent administration of corticosteroids and NMB:
 - NMB administration beyond one or two days increases risk

Estimates approach 30% with greater than 3 days concurrent use
Shown to occur with all NMB's when used with corticosteroids

NMB selection

1. Indication
 - rapid sequence intubation - 1. Succinylcholine 2. rocuronium
 - non-rapid intubations 1. Vecuronium 2. Cisatracurium
 - ICU paralysis 1. Pancuronium 2. Vecuronium 3. Cisatracurium
2. Drug characteristics (pharmacokinetics)
3. Patient characteristics
4. Adverse effects
5. Cost effectiveness

ALWAYS PROVIDE ADEQUATE SEDATION AND PAIN RELIEF TO PATIENTS ON NMB

N. Diagnosis and Management of Delirium Tremens and Alcohol Withdrawal

I. Pathogenesis

- a. Hyperarousal secondary to ETOH induced downregulation of GABA receptors.
- b. Elevated levels of norepinephrine. Likely secondary to decreased alpha2 receptor inhibition.

II. ETOH withdrawal conditions

- a. Minor withdrawal symptoms – tremor, anxiety, headache, GI upset.
 - i. Onset 6 hours after last drink.
 - ii. Resolves within 48 hours
- b. Withdrawal seizures – Generalized tonic-clonic seizures. 3% of all alcoholics.
 - i. Onset within 48 hours last drink.
 - ii. Risk factors – chronic alcoholism.
 - iii. Prolonged or recurrent seizures demands further workup
 - iv. Treatment with anticonvulsants is controversial. No clear benefit from treatment (Pollycarpou et al Anticonvulsants for alcohol withdrawal Cochrane Rev 2005).
- c. Alcoholic hallucinosis – Hallucinations that develop within 12-24 hours and resolve within 24-48 hours. Usually visual, but auditory can occur. *In contrast to DTs, AH are not associated with global clouding of sensorium.*
- d. DTs –
 - i. 5% of all alcoholics
 - ii. Hallucinations, disorientation, tachycardia, hypertension, fever, agitation, diaphoresis.
 - iii. Onset 40-96 hours after last drink.
 - iv. Duration 1-5 days.

III. Risk factors for DTs:

- a. Duration of consumption
 - i. Sustained ETOH intake is biggest risk factor.
 - 1. Approximate 90% of individuals who drink etoh for >40+ consecutive days develop major withdrawal symptoms. In contrast, in individuals with sustained intake <30 days most develop only minor symptoms upon cessation of alcohol (Isbell et al Q J Stud Alcohol 1955).
- b. History of previous DTs
- c. Age greater than 30
- d. Concurrent illness

IV. Mortality

- a. Risk factors for death include old age, pulmonary disease, body temp >104 F and co-existing liver dz. Mortality 5%.

V. Treatment DTs:

- a. Give thiamine 100mg prior to glucose-containing fluids to avoid precipitating Wernicke's.
- b. Exclude other causes. R/o infection
- c. Replace volume and electrolytes.

- d. Aspiration precautions.
- e. Benzos- see BMC protocol. Reduces duration of symptoms and mortality.
(Mayo-Smith et al Meta-analysis and EBM of AWS JAMA 1997, Lejoyeux et al Benzos treatment of ETOH dependent pt Alcohol 1998).
- f. MVI and folate
- g. Anti-psychotics- may help control hallucinations for pts on high dose benzos.
Controversy over use of anti-psychotics relates to the potential for these agents to lower seizure threshold. Should only use in pts on high dose benzos.

VI. Other

- a. Watch for signs of infection
- b. Watch for signs of GI bleed
- c. Follow electrolytes closely- Mg and Phos
- d. Look for evidence of rhabdomyolysis.

O. Pneumonia

Adapted From ATS/IDSA Guidelines 2005 and 2007

- I. For all definitions below, pneumonia equals a new infiltrate, signs/symptoms of infection (fever, leukocytosis), purulent sputum, and/or worsening oxygenation.
- II. Who NEEDS ICU admission? Need 3 minor or one major criteria below:

Table 4. Criteria for severe community-acquired pneumonia.

Minor criteria ^a
Respiratory rate ^b ≥ 30 breaths/min
$\text{PaO}_2/\text{FiO}_2$ ratio ^b ≤ 250
Multilobar infiltrates
Confusion/disorientation
Uremia (BUN level, ≥ 20 mg/dL)
Leukopenia ^c (WBC count, <4000 cells/mm ³)
Thrombocytopenia (platelet count, $<100,000$ cells/mm ³)
Hypothermia (core temperature, $<36^\circ\text{C}$)
Hypotension requiring aggressive fluid resuscitation
Major criteria
Invasive mechanical ventilation
Septic shock with the need for vasopressors

NOTE. BUN, blood urea nitrogen; $\text{PaO}_2/\text{FiO}_2$, arterial oxygen pressure/fraction of inspired oxygen; WBC, white blood cell.

^a Other criteria to consider include hypoglycemia (in nondiabetic patients), acute alcoholism/alcoholic withdrawal, hyponatremia, unexplained metabolic acidosis or elevated lactate level, cirrhosis, and asplenia.

^b A need for noninvasive ventilation can substitute for a respiratory rate >30 breaths/min or a $\text{PaO}_2/\text{FiO}_2$ ratio <250 .

^c As a result of infection alone.

III. Community-Acquired Pneumonia (CAP)

a. Diagnostic studies ICU patients should have had:

- i. CXR
 - ii. Blood cultures
 - iii. Urine legionella antigen: most common atypical bug in the ICU
 - iv. Sputum cultures
 - v. Influenza testing in appropriate clinical setting
 - vi. Thoracentesis if effusion $>5\text{cm}$ on lateral
- b. Recommended Antibiotic regimens for ICU CAP:
 - i. B-lactam (ceftriaxone, ampicillin-sulbactam) PLUS a macrolide (azithromycin or clarithromycin) or PLUS a fluoroquinolone (levofloxacin 750mg).
 - ii. If penicillin allergic, recommend aztreonam PLUS fluoroquinolone
 - iii. If pseudomonas is suspected (chronic steroid use, severe underlying bronchial disease, ETOH abuse, frequent Abx use), use anti-pseudomonal penicillin (piperacillin-sulbactam, cefepime, meropenen, imipenem) PLUS fluoroquinolone, or plus aminoglycoside AND macrolide

- iv. Add Vanciomycin if MRSA is suspected
- v. Osteltamivir if suspect influenza
- vi. Anaerobes are rarely pathogens alone; only need to treat in chronic aspiration with pleuropulmonary involvement.

IV. Hospital Acquired Pneumonia (HAP)

- a. Characterized by multi-drug resistant pathogens: MRSA, pseudomonas, acinetobacter, Extended Spectrum Beta-Lactamase (ESBL) gram neg rods (serratia, klebsiella, enterobacter), Legionella, and those pathogens selected by local antibiotic practice.

TABLE 2. RISK FACTORS FOR MULTIDRUG-RESISTANT PATHOGENS CAUSING HOSPITAL-ACQUIRED PNEUMONIA, HEALTHCARE-ASSOCIATED PNEUMONIA, AND VENTILATOR-ASSOCIATED PNEUMONIA

-
- Antimicrobial therapy in preceding 90 d
 - Current hospitalization of 5 d or more
 - High frequency of antibiotic resistance in the community or in the specific hospital unit
 - Presence of risk factors for HCAP:
 - Hospitalization for 2 d or more in the preceding 90 d
 - Residence in a nursing home or extended care facility
 - Home infusion therapy (including antibiotics)
 - Chronic dialysis within 30 d
 - Home wound care
 - Family member with multidrug-resistant pathogen
 - Immunosuppressive disease and/or therapy
-

- b. Early sputum cultures are key
- c. When clinical improvement is seen with appropriate antibiotics course can be short: 7-8 days

V. Ventilator-Associated Pneumonia

- a. This is HAP occurring in those on a ventilator. It is more difficult to diagnose given limited utility of portable CXR and questionable specificity of culture data. In general, it is more diffuse, involving lower, dependent lung.
- b. A negative gram stain on endotracheal aspirate has a 94% negative predictive value for VAP (Blot F et al AJRCC 200) and should warrant serious consideration of alternative diagnoses and discontinuation of VAP antibiotics.
- c. What is the best way to diagnose VAP?
 - i. Clinical criteria (sign/Sx of infection) are very sensitive but not at all specific
 - ii. Clinical prediction scores (CPIS) are probably not helpful
 - iii. Bacteriologic strategies using quantitative culture thresholds result in less antibiotic use; however suffer from methodologic difficulty (lab expertise, bronchoscopy).
 - iv. There is conflicting data on outcomes using quantitiative/BAL diagnostic approach vs semi-quantitative endotracheal aspirate (Fagon et al Annals

2000: reduced 14d mortality w/ invasive approach vs Canadian Group
NEJM 2006: no difference between bronch or no bronch).

v. IDSA/ATS Algorithm for diagnosis of VAP

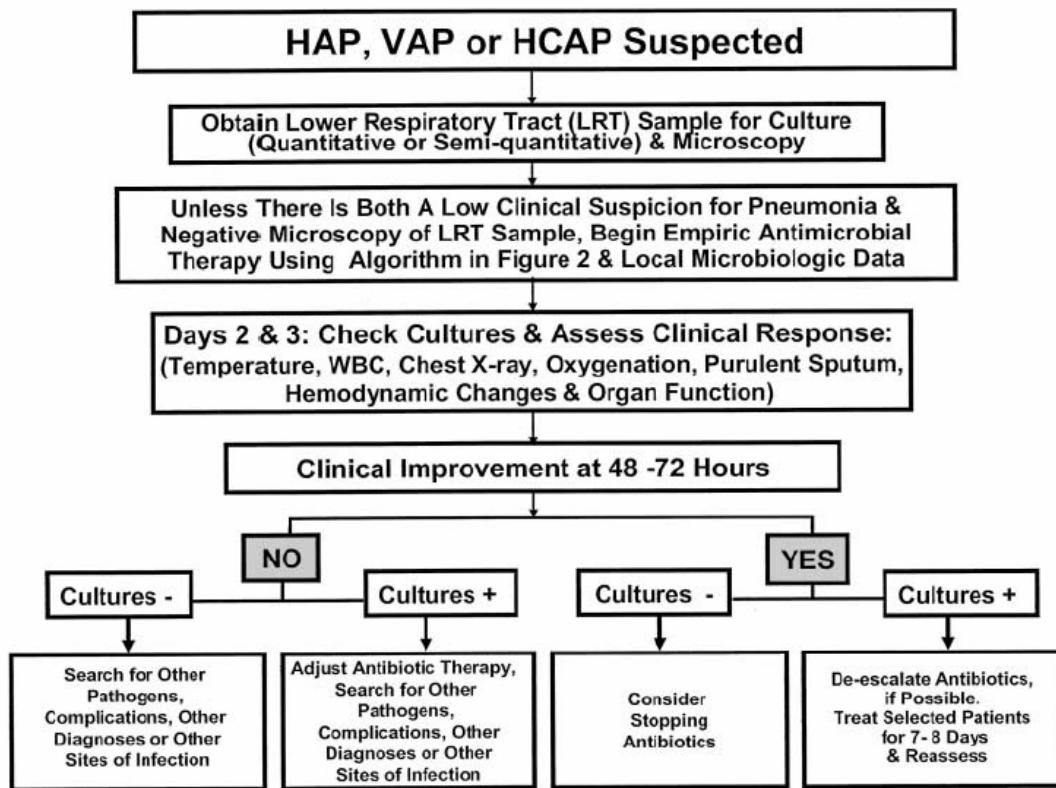


Table 7. Recommended empirical antibiotics for community-acquired pneumonia.

Outpatient treatment
1. Previously healthy and no use of antimicrobials within the previous 3 months A macrolide (strong recommendation; level I evidence) Doxycycline (weak recommendation; level III evidence)
2. Presence of comorbidities such as chronic heart, lung, liver or renal disease; diabetes mellitus; alcoholism; malignancies; asplenia; immunosuppressing conditions or use of immunosuppressing drugs; or use of antimicrobials within the previous 3 months (in which case an alternative from a different class should be selected) A respiratory fluoroquinolone (moxifloxacin, gemifloxacin, or levofloxacin [750 mg]) (strong recommendation; level I evidence) A β -lactam plus a macrolide (strong recommendation; level I evidence)
3. In regions with a high rate (>25%) of infection with high-level ($MIC \geq 16 \mu\text{g/mL}$) macrolide-resistant <i>Streptococcus pneumoniae</i> , consider use of alternative agents listed above in (2) for patients without comorbidities (moderate recommendation; level III evidence)
Inpatients, non-ICU treatment
A respiratory fluoroquinolone (strong recommendation; level I evidence) A β -lactam plus a macrolide (strong recommendation; level I evidence)
Inpatients, ICU treatment
A β -lactam (cefotaxime, ceftriaxone, or ampicillin-sulbactam) plus either azithromycin (level II evidence) or a respiratory fluoroquinolone (level I evidence) (strong recommendation) (for penicillin-allergic patients, a respiratory fluoroquinolone and aztreonam are recommended)
Special concerns
If <i>Pseudomonas</i> is a consideration An antipseudomonal β -lactam (piperacillin-tazobactam, cefepime, imipenem, or meropenem) plus either ciprofloxacin or levofloxacin (750 mg) or The above β -lactam plus an aminoglycoside and azithromycin or The above β -lactam plus an aminoglycoside and an antipseudomonal fluoroquinolone (for penicillin-allergic patients, substitute aztreonam for above β -lactam) (moderate recommendation; level III evidence)
If CA-MRSA is a consideration, add vancomycin or linezolid (moderate recommendation; level III evidence)

NOTE. CA-MRSA, community-acquired methicillin-resistant *Staphylococcus aureus*; ICU, intensive care unit.

P. Severe Obstructive Lung Disease : Asthma

Acute severe asthma with impending respiratory failure

Issue in Presentation and Severity

1. Prior Intubation
2. Duration of symptoms – use of prednisone
3. Identifiable triggers – including illicit drug use.
4. Recent symptoms – use of albuterol / nocturnal symptoms
5. Severity
 - a. HR >120 / Fatigue/ Full sentences / Upright Posture
 - b. PEFR <30% previous best (or less than 100)
 - c. Pulsus Paradoxus
 - d. PCO₂. >36 (ABG required in severe asthma only)

Two broad clinical scenarios:

a. Acute Severe Asthma	b. Acute Asphyxia Asthma
Slowly progressive over days or weeks	Rapid Onset
Inflammation / Eos and Mucus	Little inflammation / mucus- probably smooth muscle contraction
Unlikely to improve rapidly – ++++ Initial Risk of high Barotrauma / autopeep	May rapidly improve with bronchodilators +++++
+++ Atelectasis	+

Management:

1. Assess Severity
2. Initiate Therapy
 - a. Bronchodilators
 - i. Beta-agonists: Continuous / Back to back nebs x 3 over 1 hour- reassess
 - ii. Ipratropium bromide: Add to first neb – no clear proven efficacy
 - iii. Theophylline – not used
 - iv. Magnesium 2g IV over 1 hours- no harm no evidence for efficacy.
 - b. Corticosteroids:
Dose: Study: Solumedrol at 125 or 40mg better than 15mg
Usual 60-125mg every 6-8 hrs overnight
Type: No specifics
 - c. Antibiotics Not routinely

3. Mechanical Ventilation

- a. Oxygenation: Usually not a major problem – if hypoxic likely to represent mucus plugging + lobar collapse.
 - b. Ventilation: Major issue. Hypoventilation reflects an inability to get sufficient air to the alveoli for gas exchange due to severe air-trapping. In addition there is complex V/Q mismatching with high airway pressures (peep) creating areas of lung without effective perfusion (essentially dead space). Fatigue also contributes.
 - c. Synchrony: Tachypnea, air-trapping, and severe acidosis make it impossible for patient to synchronize – requires heavy sedation + paralysis
 - d. Barotrauma: High air pressure generally reflects dynamic (airway resistance = peak – plateau pressure) but static (plateau pressure) is also increased due to air-trapping. Keep PIP <45 / Plateau < 35. High risk for pneumothorax and pneumomediastinum especially if plateau >35.
 - e. Autopeep: Severe air-trapping is the major risk and cause of death in SA. If initial ventilation strategy results in significant stacking of breaths and thus autopeep or dynamic hyperinflation - eventually this will cause decreased venous return with hypotension, shock, cardiac arrest etc. The aim is to limit minute ventilation and maximize expiratory time, and thus reduce the risk of air-trapping. This will result in elevation of PCO₂ (permissive hypercapnia) which is not fatal unlike critical dynamic hyperinflation.
 - f. Initial Vent Settings: IMV or PRVC / FIO₂ 100% / RR 8-10 / TV 400 / No peep / Inspir Flow 60-100L/sec
[low RR and high inspiratory flow results in longer expiratory times]
4. Sedate + Paralyze (synchrony and decrease WOB / CO₂ production)
 5. Monitor pressures: Assess PIP <40-45 Keep plateau <35 AutoPeep < 15. Monitor BP / HR – signs of autopeep

If Autopeep >15 consider decreasing RR as low as 4 / Increasing flow time 100-120

If Hemodynamically unstable –

- a. ask RT to disconnect from vent and bag- if due to air-trapping will allow release of trapped air. If air-trapping will need even lower respiratory rates.
- b. Assess for pneumothorax (examine and CXR)
- c. Permissive hypercapnia: hypoventilate to decrease airway pressures. In response PCO₂ will increase. As long as pH is above 7.0 and patient is hemodynamically stable very high pCO₂ is tolerated. – IV bicarbonate is sometimes utilized to maintain pH greater than 7. Caution with HCO₃ because it can worsen pH after it is metabolized.

Last Resort:

- Systemic β-agonists: Either terbutaline, epinephrine or isoproterenol, Terbutaline 0.25mg SQ lasts about 2 hours. Can be repeated at 0.25mg in 30 min

- Heliox – helium has lower density than N₂ = less turbulent flow = improved gas delivery
- Propofol is a bronchodilator but can increase RQ and therefore CO₂ production.
- Anesthesia: Inhalational anaesthesia (isoflurane 1%) will cause dramatic bronchodilation which will reverse immediately on discontinuation of anaesthesia. Aim is to get bronchodilation and then aggressively deliver inhaled medications to the distal airways. Usually requires 2-12 hours of anaesthesia. Can result in serious hemodynamic instability.

Severe COPD Exacerbation

In many ways, presentation and ventilator management of acute COPD and asthma are similar (see above). Presented below are major differences in management.

Definition: Patient with history of COPD presenting with increased cough, sputum production and/or dyspnea, generally without infiltrate on CXR.

Etiology: most frequent etiology is viral or bacterial URI (~50%). Other causes are environmental irritants, or idiopathic. One study showed that 25% of idiopathic COPD exacerbations were due to PE (Tillie-Leblond Ann int Med 2006)

Treatment:

- Inhaled Beta agonist/Anticholinergic
- Systemic corticosteroid: If in the ICU: IV methylprednisolone 125mg QID x 72h weaned to prednisone 60mg day 4-7 was used in Niewohner NEJM 1999 which showed benefit to steroids. Duration of wean recommended 7-14days.
- Antibiotic: this is major area where COPD and asthma treatment differ. Exacerbations are associated with the acquisition of different strains of the same bugs (H. flu, Moraxella, s. pneumo) that usually colonize COPD patients. Thus, sputum culture is generally not helpful, as it cannot identify these strains. Antibiotics have been shown to improve outcomes in COPD (Antonisen Ann Int Med 1987).
- NIPPV: Early non-invasive ventilation improves morbidity and mortality in Hypercapnic COPD exacerbation (Ram FS, Cochrane Database 2004).
- Theophylline: In randomized, placebo-controlled trial, theophylline had *no difference* vs placebo in objective or subjective outcomes in acute exacerbations of COPD treated with nebulizers, antibiotics and steroids (Rice KL, Ann Int med 1987).

Q. Nutrition in Critical Illness

I. Overview:

- Although malnutrition in the ICU is associated with poor outcomes, the details of feeding critically ill patients--when, what, where-is a much debated topic, with little evidence. Presented below are brief discussions of the major issues in critical care nutrition.
- Expert opinion recommends starting nutrition in patients expected to be NPO for >7days (probably most ICU patients).

II. Enteral or Parenteral?:

- With the exception to contraindications to enteral feeding (bowel obstruction, severe ileus, intractable vomiting, severe GI bleeding, bowel ischemia, abdominal compartment syndrome, significant hemodynamic instability), enteral feeding is first line because it is associated with fewer infectious complications (Gramlich et al. Nutrition 2004). This may be due to maintenance of the integrity of bowel mucosa, or increased infections associated with hyperglycemia or central line of TPN.

III. Gastric or post-pyloric?:

- There is no evidence that post-pyloric feeding reduces risk of pneumonia or enhances tolerance of feeds in unselected patients (Ho et al Intensive Care Med 2006). Therefore, gastric feeds are suitable in most patients.
- Post-pyloric feeds (nasojejunal) are recommended in severe acute pancreatitis over TPN due to reduction in infectious complications and length of stay (ACG, AGA Guidelines). That being said one 50pt study has shown no significant difference between NG and NJ feeds in pancreatitis (Eatoock FC et al Am J Gastro 2005)

IV. Early or Late Initiation of Feeding?

- Guidelines recommend initiation of feeds early, within 24hrs (National guidelines Clearinghouse). This is due related in part to results of the ACCEPT trial, which implemented early nutrition as part of multiple nutrition guidelines in a multicenter trial and found reduced mortality and hospital stay. Other retrospective studies show similar benefits to early feeds. Note that one 150pt randomized trial (Ibrahim JPEN 2002) found worse outcomes in early feeds.]

V. High Residuals/Intolerance?

- Evidence suggests Erythromycin is a superior prokinetic to Reglan in setting of critical care tube feed intolerance, but combination is even better (Nguyen Crit care med 2007). Tachyphylaxis develops to both. Use side effect profile of each when choosing (ie avoid raglan in patients w/seizure, emycin in long QT, etc). Post pyloric feeding is another option for intolerance.

VI. Special Formulations?

- There is new evidence that omega 3 acids and anti-oxidants added to feeds early improve outcomes in sepsis and ARDS (Berger Crit Care Med 2007 and Pontes-Arruda Crit Care Med 2007). An earlier meta-analysis found arginine reduces infectious complications (Heylan JAMA 2001). ARDSNet is currently running a large trial to further look at this exciting issue.

R. Ischemic Stroke

Background

- 1) The most common neurologic cause for hospital admission in the US, (2000)
- 2) Incidence declining (?better treatment of hypertension)
- 3) 80% are ischemic; remainder are intracerebral bleeding or SAH

Risk Factors

- 1) General: Hypertension, age, diabetes mellitus, Race, lipid disorders, ETOH, elevated Hct or fibrinogen, smoking (most powerful risk for SAH)
- 2) Previous cerebral vascular disease (stroke or TIA)
 - a) 30% of TIA patients will have CVA within 2 yrs
 - b) Surgery for significant stenosis
 - c) Medical treatment: ticlopidine 250 mg bid (m/f)
- 3) Asymptomatic bruits: 2 %CVA risk/yr
 - a) No data on whom to work up
 - b) Asymptomatic males with > 70% stenosis may benefit from endarterectomy
 - c) Medical treatment: ASA
- 4) Differential diagnosis of patients <55 yr
 - a) Antithrombin III, protein S/C, or antiphospholipid antibody
 - b) Marfanoid appearing; heterozygous homocysteineuria (medical treatment-vit B6)

Common Presentations

- 1) Carotid/cerebrovascular artery disease (MCA>ACA>VBA)
- 2) Cardiac disease (emboli; 10-30%)
- 3) Aortic arch (emboli?)

Medical treatment of primary event

- 1) Embolic/ischemic
 - a) Thrombolysis
 - 1) Must be given within 3 h of onset of symptoms for embolic/ischemic stroke
 - 2) rt-PA 0.9 mg/kg, with 10% as a bolus and the remainder over 1 h
 - 3) Inclusion Criteria
 - a) age > 18 yr
 - b) clinical diagnosis of ischemic stroke causing measurable neurologic deficit
 - c) Time of symptoms onset well established as <180 min before rx would begin
 - iv. Exclusion Criteria
 - 1) blood on CT
 - 2) only minor or rapidly improving symptoms
 - 3) high clinical suspicion of SAH, even with normal CT
 - 4) active internal bleeding (e.g. GI, GU) within 21 days
 - 5) known bleeding diathesis, including platelet < 100,000, heparin within 48 h resulting in increased PTT, recent anticoagulant use with increased INR/PT
 - 6) intracranial surgery, serious head trauma, or stroke within 3 months
 - 7) major surgery or serious trauma within 14 days
 - 8) recent arterial puncture at non-compressible sites

- 9) LP within 7 days
- 10) history of ICH, AV malformation or aneurysm
- 11) witnessed seizure at stroke onset
- 12) recent acute MI
- 13) SBP > 185 mm Hg, or DBP > 110 mm Hg on repeated measurements, requiring aggressive treatment to bring BP to this range
- b) Heparin
 - 1) No indication for heparin in the treatment of stroke (either complicated or in evolution)
 - 2) Ischemic If > 6 hr into ischemic stroke, no treatment has proved useful
 - 3) Embolic (cardiac source)
 - b) Coumadin (INR 3.0 (2-5) if nonvalvular AF): no increase in major bleeding vs control
 - c) ASA may reduce risk; use in patients who cannot take coumadin

Treatment of Complications

- 1) Improve flow through stenotic vessels
 - a) Prevent hypotension
 - b) Keep SBP>140-160 mm Hg
- 2) Treat extreme hypertension SBP>220 or DBP > 120
 - a) nitroprusside and/or labetalol
 - b) aim for 10-20 % reduction
- 3) Keep blood sugar normal (BS>300=worse outcome, but no control studies exist)
- 4) Control of Intracranial Pressure (ICP)
 - a) in first 3-4 days increases risk for herniation and death (
 - b) symptoms; reduced level of consciousness, followed by ipsilateral CN III palsy);
 - c) treatment; hyperventilation, mannitol, craniotomy but not steroids unless vasculitis.

S. Subarachnoid Hemorrhage

I. I. Background:

- SAH accounts for 10% of all strokes, mortality is 50%.
- Risk factors are smoking, HTN, ETOH, family history
- worst HA of life is SAH 20% of the time (Morgenstern, Ann Emerg Med 1998)
- Most are caused by ruptured aneurysm.
- Rare causes are cocaine, AVM, vasculitis, amyloid angiopathy, trauma, bleeding diathesis and dissection.

II. Diagnosis:

- Noncontrast CT head
- LP is mandatory (after 2 hrs is when xanthochromia would appear) if strong suspicion + negative CT
- Once SAH is confirmed, need cerebral angiography

II. Clinical grading: the Hunt and Hess score predicts long term outcome:

- Grade 1: mild HA and nuchal rigidity
- Grade 2: Moderate-severe HA, nuchal rigidity, cranial nerve palsy
- Grade 3: Drowsy or confused, mild focal neurologic deficit
- Grade 4: stupor, moderate-severe hemiparesis
- Grade 5: Coma, decerebrate posturing

II. Radiographic grading: Fisher scale-predicts vasospasm risk.

- Group I: no blood seen
- Group II: diffuse deposition of blood max 1mm thick
- Group III: localized clot or layering >1mm
- Group IV: intracerebral or intraventricular clots

III. Determinants of outcome

1. Rebleeding: occurs within 24hrs in 5%. Need early angiography to detect any amenable aneurysms to therapy. If rebleeding happens → 12x risk of poor outcome.
 - a. Prevent by treating underlying aneurysm (coils via IR or clip via Neurosurgery within 24-72hrs).
2. Vasospasm: results from breakdown of blood products causing vasospasm. The major cause of morbidity and mortality in SAH. Occurs days 3-8.
 - a. Detect by change in neuro status. Daily Transcranial Doppler exams may detect impending spasm before clinical symptoms (stroke) develop.
 - b. Prophylactic PO nimodipine 60mg q4hr given in 1st 4 days significantly improves outcomes in SAH OR 0.46 (Barker, J neurosurg 1996)
 - c. There is poor evidence for "Triple H" therapy (hemodilution, hypertension, hypervolemia in SAH (Cochrane 2004) as prophylaxis, but it may be helpful as treatment for vasospasm.
 - d. Other treatments of vasospasm include angiography w/angioplasty, and/or intra-arterial milrinone or papaverine (case reports).
3. Hydrocephalus: SAH patients need early consult by neurosurgery for ? ventricular drain, especially with any blood in the ventricles. A ventricular drain also allows measurement of intracranial pressures.

4. Seizures: there is no evidence that prophylactic dilantin changes outcomes in a positive manner. Certainly anyone with seizures should get anti-seizure med.

IV. Other ICU measures

1. BP control: no evidence for any specific range; standard of care is keeping SBP 120-140 in awake patients. In SAH, DBP >100 increases risk of re-bleed whereas diastolic pressure <100 increases risk of stroke. If pressures need to be treated, may use labetalol; nitroprusside and nitroglycerin increase ICP. If questions arise as to treating blood pressure, intracranial pressure monitoring may be beneficial to guide therapy to CPP >60.
2. DVT prophylaxis: boots until aneurysm is treated, then can use SQ heparin
3. reverse coumadin
4. keep on bedrest
5. ulcer prophylaxis
6. HOB >30 degrees
7. frequent neurologic checks

T. Seizures and Status Epilepticus

Seizure – sudden change in baseline electrical activity resulting in physiologic change in patient

Types

- Simple (no loss of consciousness) versus complex (LOC)
- Partial versus generalized

Causes of status epilepticus

Number one cause is medication non-compliance.

- Withdrawal syndrome
- Ischemia
- Remote structural changes
- Electrolytes –na, ca, mg
- Endocrine – hypoglycemia, hyperthyroid
- Hypercarbia
- Hypoxia
- Uremia
- Fulminate Hepatic failure
- Complication of medication- theo/bupropian/lithium

What tests are needed? EEG/CT/MRI- Imaging is not needed for ETOH withdrawal unless clinical picture suggests another cause (e.g not waking up, head laceration)

LP is only useful when malignancy, subarachnoid bleed and infection is suspected

Status epilepticus - The term status epilepticus refers to the occurrence of a single unremitting seizure with duration longer than 5 to 10 minutes or frequent clinical seizures without an interictal return to baseline.

Refractory status epilepticus- continual seizures after 1-2 meds have been tried
20% of these patients go on to have persistent neurological defects- behavior, memory, emotional

Incidence of status epilepticus- Less than 1 % of all seizures

Management –

1. Protect airway
2. Move to icu
3. Suppress fever
4. Aspiration precautions
5. Control seizures with medications
 - a. benzos

- i. ativan- brain quickly and stays around for 4-6 hours,
 - ii. dose – 2mg , followed by 2mg
 - iii. valium- lipid soluble, gets to brain quickly, but goes to fat stores quickly
20 min needs re-dosing. Stable in vial for long time so usually in code
cart 7mg followed by 7mg
 - iv. versed
- b. barbs
 - c. dilantin 20mg/kg – hypotension and skin irritation
 - d. fosphenytoin – parent compound, hydrolyzed to phenytoin, same dose, for
pts who are hypotensive no skin irritation
 - e. propofol
 - f. etomidate
 - g. halothane

U. Hypertensive Crises

Definitions:

1. Hypertensive emergency- increase in systolic and diastolic blood pressure leading to end-organ damage
 - A. Hypertensive encephalopathy
 - B. Acute aortic dissection
 - C. Acute pulmonary edema with respiratory failure
 - D. Acute myocardial infarction/unstable angina
 - E. Stroke
 - F. Blindness
 - G. Acute renal failure
 - H. Microscopic hemolytic anemia
2. Hypertensive urgency- patients with elevated blood pressure without evidence of end-organ damage.

The clinical differentiation between these two entities is the presence or absence of end organ damage not the level of blood pressure elevation.

Epidemiology:

Hypertensive crises will occur in < 5% of all hypertensive patients. The majority have pre-existing diagnosis of HTN and have been prescribed medication, but have inadequate follow-up.

L

Evaluation:

- 1) History (Prior hypertensive episodes, medication compliance, baseline BP, substance abuse-ETOH, cocaine).
- 2)PE – BP all limbs, don't forget eye exam
- 3)Labs: CBC, electrolytes, BUN, Cr, U/A, CK and isoenzymes, urine tox screen (check for use of cocaine, amphetamines, phencyclidine) peripheral smear to detect microangiopathic hemolytic anemia
- 4)Other studies CXR, EKG, Consider Head CT for any neuro changes

Treatment:

- Hypertensive emergency requires immediate control of BP to stop end-organ damage. Control does not mean immediate normalization of BP. Usually intravenous medications are used to lower the diastolic BP by 10-15%, or to a diastolic BP 110 mm Hg. For aortic dissection this goal should be reached within 5-10 minutes. In other pts with hypertensive emergency, the goal should be reached within 30-60 minutes. Once the end-point is reached, maintenance therapy with an oral agent can be instituted.
- Hypertensive urgency- BP is gradually reduced over 24-48 hrs usually with an oral medication

Recommended Antihypertensive Agents for Hypertensive Crises

- Uncomplicated patient: Labetolol, nicardipine, esmolol, nitroprusside.
- Pulmonary edema: nitroprusside with nitroglycerin and loop diuretic
- Acute myocardial ischemia: labetolol or esmolol with nitroglycerin
- Encephalopathy: labetalol, or nicardipine
- Acute aortic dissection: labetolol or combination of nitroprusside with esmolol. The aim is to lessen pulsatile load and force of left ventricular contraction to slow the propagation of the dissection. Surgical consultation for possible repair.
- Eclampsia: labetalol, nicardipine, or hydralazine. Immediate delivery.
- Acute renal failure/microangiopathic hemolytic anemia: fenoldopam or nicardipine
- Sympathetic crisis: Re-administer the discontinued drug. Or nicardipine, verapamil, or fenoldopam

Medications that should be avoided in HTN crisis:

- Nitroglycerin – Classically, pt's with hypertensive crisis are volume depleted. Nitroglycerin can cause a precipitous drop in BP by decreasing preload.
- Diuretics- Long acting, variable response.
- Nifedipine- Cause precipitous drop in BP
- Hydralazine: Direct vasodilator. Begins to work in 5-15 minutes. Can cause a precipitous drop in BP. $\frac{1}{2}$ life 3 hours but for some unknown reason pharmacologic effects can last for 10 hours in some individuals. Because of prolonged and unpredictable effects hydralazine should be avoided.

V. BRAIN DEATH*

Clinical diagnosis: complete and irreversible cessation of all brain function (including Brainstem); confirmatory laboratory testing not needed.

Who: Adults and children > 5 yr of age (if < 5, consult pedi neurologist or neurosurgeon)

Notify: N.E. Organ Bank (Fed Law) when anticipated (1-800-446-6362)

Prerequisites:

- T>32.2° (90°F)
- Barbiturate level < 1 mg%
- Tox screen when indicated (negative drug screen required)
- Absence of severe hypotension (shock), significant cardiopulmonary or neurological disease

Criteria: Neurologist, Neurosurgeon or critical care MD familiar with criteria and exam:

- Unresponsive Coma, cerebral unresponsiveness; No movement, withdrawal, seizures, posturing (spont or induced). May have spinal cord reflexes.
- Apnea; No spontaneous respiration in presence of adequate CO₂ drive
 - Apnea testing: done at bedside; tests medullary/brainstem response to p CO₂ drive (in absence of significant cardiopulmonary disease or neuromuscular paralysis/disease).
 - Procedure: requires passive oxygenation of trachea with 100% O₂ (4 lpm; no MV) to allow CO₂ to rise without hypoxia. ABG is drawn at 0, 5, 10 min and pt observed; placed back on MV at 10 min. Baseline paCO₂ = 35-45 torr, and PaO₂ > 80 torr (or SaO₂ > 95 %)
 - Pt is observed for duration of test: if there is no spontaneous respiratory efforts and paCO₂ has risen to > 60 torr, apnea is present
 - STOP the test if SaO₂ falls to < 90%, if loss of V.S., or if respiratory efforts noted.
 - DOCUMENT test results in Progress Note and ICU Flow Sheet; include times, V.S., ABG, SaO₂, observations and personnel present.
- Absent brainstem reflexes; Perform oculocephalic and oculovestibular reflex testing, standard testing on CN function
- Duration of Observation; Persistence for > 24 h. Observation < 24 hr is permissible if structural brain damage and dx is certain.

Confirmatory Testing: (not required for clinical dx of brain death)

- Radionuclide blood flow study (not adequate alone in some situations)
- 4 vessel cerebral angiogram demonstrating absence of blood flow to cerebrum and brainstem
- electrocerebral silence on EEG, may supplement clinical testing.

Details: BMC Policies/Procedures, Policy #3.31, Sect 3.0

W. Severe Electrolyte Abnormalities

Hyponatremia

I. Definition: Hyponatremia is generally defined as a plasma sodium level of less than 135 mEq per L (135 mmol per L). Symptomatic hyponatremia (usually < 120 mEq per L) leads to significant morbidity and mortality. Morbidity can also result from rapid correction of hyponatremia. This handout provides a logical and efficient approach to evaluate and manage hyponatremia.

II. Evaluation:

Step 1: Begin with the history and physical exam. Many conditions are causes are apparent just from the history and physical exam (e.g. medications, cardiac dz, renal failure, etc)

Step 2: Calculate serum osmolality $2 \times [\text{sodium}] + [\text{urea}] + [\text{glucose}]$. Normal plasma osmolality is 280 to 300 mOsm per kg.

A. If serum osmolality is normal consider:

a. Pseudohyponatremia: This condition results from increased percentage of large molecular particles in the serum relative to sodium. These large molecules do not contribute to plasma osmolality resulting in a state in which the relative sodium concentration is decreased, but the overall osmolality remains unchanged. Severe hypertriglyceridemia and hyperproteinemia are two causes of this condition.

B. If serum osmolality is high (> 300 mOsm per kg of water) consider:

a. Severe hyperglycemia. Glucose molecules exert an osmotic force and draw water from the intracellular compartment into the plasma, thereby causing a diluting effect.

C. If serum osmolality is low go to Step 3:

Step 3: Assess volume status:

a. Hypervolemic hyponatremic conditions: congestive heart failure, liver cirrhosis, and renal diseases such as nephrotic syndrome.

b. Hypovolemic hyponatremic conditions: drugs (e.g. thiazide diuretics)

c. Euvolemic hyponatremic conditions: SIADH, Beer potomania, psychogenic polydipsia, adrenal insufficiency, hypothyroidism

III. Treatment:

Step 1: Based on Na levels and severity of symptoms decide whether immediate treatment is required.

Step 2: Determine whether hyponatremia occurred acutely or developed over a longer period of time (>48 hours). Timing is often difficult to determine.

In patients with chronic hyponatremia, overzealous and rapid correction should be avoided because it can lead to central pontine myelinolysis. In central pontine myelinolysis, neurologic symptoms usually occur one to six days after correction and are often irreversible.

Step 3: Determine the most appropriate method of correcting the hyponatremia. In some conditions Na can be corrected by simple fluid restriction; however, in many situations NA supplementation is required.

Hypernatremia

I. Definition: Hypernatremia is defined as plasma Na concentration > 145 mEq/L and is caused by a deficit of water relative to solute

II. Causes:

A. Hypernatremia with hypovolemia Extrarenal losses – GI (Vomiting, diarrhea), Skin (fever, burns, excessive sweating). Renal losses: Intrinsic renal disease, Loop diuretics osmotic diuresis (glucose, urea, mannitol)

B. Hypernatremia with euvoolemia Extrarenal losses Skin (fever, excessive sweating). Renal losses - central diabetes insipidus, nephrogenic diabetes insipidus. Decreased intake- inability to access water, primary hypodipsia

C. Hypernatremia with hypervolemia Hypertonic fluid administration (hypertonic saline, NaHCO_3 , total parenteral nutrition), mineralocorticoid excess, adrenal tumors

III. Treatment

A. Replace free water - Oral hydration is effective in conscious patients without significant GI dysfunction. In severe hypernatremia or in patients unable to IV hydration is required. Hypernatremia < 24 h can be corrected within 24 h; however, chronic hypernatremia should be corrected over 48 h, and the plasma osmolality should be lowered at a rate of no more than 2 mOsm/L/h to avoid cerebral edema. The amount of water necessary to replace existing deficits may be estimated by the following formula:

$$\text{Free water deficit} = \text{TBW} \times [(\text{plasma Na}/140) - 1]$$

This formula assumes constant total body Na content. In patients with hypernatremia and depletion of total body Na content (ie, who have volume depletion), the free water deficit is greater than that estimated by the formula.

- A. In patients with hypernatremia and ECF volume overload - free water deficit can should be replaced with 5% D/W followed by a loop diuretic to remove excess NA.
- B. In patients with hypernatremia and euvoolemia, free water should be replaced with 0.45% saline.
- C. In patients with hypernatremia and hypovolemia 0.9% normal saline is required.

X. Renal replacement therapy

I. **Indications for renal replacement therapy:**

- a. Fluid overload
- b. Severe hypertension
- c. Hyperkalemia
- d. Metabolic Acidosis
- e. Uremia

II. **Terminology:**

- a. Dialysis (diffusion): The movement of solutes from a high concentration compartment to a low concentration compartment. Movement occurs along an electrochemical gradient. An electrolyte solution (dialysate) runs countercurrent to blood across a semi-permeable (small pore) filter. Small molecules in blood such as urea move along the concentration gradient into the dialysate fluid. Larger molecules are poorly removed by this process. Solute removal is directly proportional to the dialysate flow rate.
 - i. Conventional hemodialysis blood flow is 350-450 ml/min and dialysate flow is 500-800 ml/min. In continuous hemodialysis (CVVHD) blood flow is usually set at 100-200 ml/min, and dialysate flows at 1000-2000 ml/hr.
- b. Ultra-filtration (convection) – Solute is carried (in solution) across a semipermeable membrane in response to a transmembrane pressure gradient (a process known as solvent drag). This mimics what actually happens in the normal human kidney. The rate of ultrafiltration depends upon the porosity of the membrane and the hydrostatic pressure of the blood. This is very effective in removal of fluid and middle-sized molecules.

III. **Types of renal replacement therapy:**

- a. Intermittent hemodialysis is the most efficient – Large amounts of fluid can be removed and electrolyte abnormalities can be rapidly corrected. However, this is not suitable in unstable patients. Even in hemodynamically *stable* patients with ARF 20-30% become hypotensive during dialysis. Many ICU patients are too hemodynamically unstable for this therapy.
- b. Peritoneal dialysis has the advantage of being simple and cost effective. The major disadvantages of PD are poor uremia control, risk of peritoneal infection and mechanical obstruction of pulmonary and cardiovascular performance.
- c. Continuous Renal Replacement Therapy: The concept behind continuous renal replacement techniques is to dialyse patients in a more physiologic way, slowly, over 24 hours, just like the kidney. Intensive care patients are particularly suited to these techniques. In general, these therapies require that pts are on anticoagulation.
 - i. CVVH – continuous venovenous hemofiltration. The ultrafiltration rate is high, and replacement electrolyte solution is required to maintain hemodynamic stability. This mode is also very effective for clearing mid

- sized molecules. It is hypothesized that removal of mid sized inflammatory cytokines may play a role in improving outcome in sepsis.
- ii. CVVHD -continuous venous venous hemodialysis- the dialysate is driven in a direction countercurrent to the blood. This provides reasonably effective solute clearance, although mostly small molecules are removed.
 - iii. CVVHDF - continuous venous venous hemodiafiltration is the most popular method of dialysis in ICU. It combines convective and diffusive dialysis. Both small and middle molecules are cleared, and both dialysate and replacement fluids are required. CVVHDF is similar to IHD in slow motion: the blood flow is 100 – 200ml/min, the dialysate flow is 1000ml/hour, the filtration rate is 10-20ml/hour (very efficient), the urea clearance is 10-20ml/hour.

Y. Acute Pancreatitis

I. Diagnosis:

- a. abdominal pain and increased pancreatic enzymes >3X upper limit of normal, and/or CT showing pancreatitis.
- b. Pancreatitis should be considered in SIRS of unknown etiology.

II. Pathophysiology: premature activation of trypsin in pancreatic acinar cells sets off inflammatory cascade. Extent of inflammation determines severity, extra-pancreatic inflammation (eg., ARDS) occurs in severe pancreatitis.

III. Severity/Prognosis:

- a. **Apache II>8** available immediately and consistent with 'severe pancreatitis' and high risk for necrotizing pancreatitis (usually occurs 7-10d), which is associated with 20% mortality. These patients should be cared for in ICU.
- b. **Ranson Criteria:** Score of 4 or more is LR 2.5 for major complications/mortality, but takes 48hrs. One point each for admission factors of age >55, wbc>16K, glucose>200, LDH>350, AST>250; 48 hrs HCT decrease >10%, BUN increase >5, Ca++<8, acidosis, >6L IVF, paO₂ <60.
- c. 1/3 of patients with 'severe pancreatitis' will develop infected necrosis.
- d. Patients with severe disease generally need ICU care and a CT after 72hrs to look for amount of pancreatic necrosis.
- e. **Other risk factors** for severe pancreatitis are: **serum CRP >150 at 48-72h** (predicts necrosis), **age >55, BMI>30, organ failure or pulmonary involvement** (effusion, infiltrate) on admission, signs of **hemoconcentration** on admission or lack of a decrease in hematocrit after 48hrs.

IV. Etiology: Generally need US on admit to look for evidence of gallstone, check LFTs, serum calcium, triglycerides, ETOH history.

- a. Those patients with suspected gallstone pancreatitis should have urgent GI evaluation for ? ERCP/sphincterotomy.

V. Management: Mostly supportive. Aggressive IVF, pain control, if predicted NPO >7 days, consider naso-jejunal tube feeding.

- a. Early aggressive IVF decreases pancreatic necrosis
- b. If NJ feeds are not tolerated, then consider TPN.
- c. Prophylactic antibiotics are not currently recommended in all patients
- d. Confirmed infected necrosis can be treated with imipenem, fluoroquinolone+flagyl, or cephalosporin + flagyl, all +/- vanco.
- e. CT-guided aspiration is recommended to determine if necrosis is suspected (this is only way to confirm infection other than insensitive retroperitoneal gas)
- f. Consider surgery evaluation in infected necrosis for debridement.

From American College of Gastroenterology Practice Guidelines on Acute Pancreatitis

Z. GI Bleeding in the ICU

Indications for ICU admission

- Any significant Upper or Lower GI bleed without hemodynamic compromise
- Any GI bleed with hemodynamic compromise (including postural symptoms/signs)

Differential Diagnosis

<u>Upper</u>	<u>Lower</u>
Peptic/NSAID ulcer	Diverticulosis
Esophageal varices	Ischemic Colitis
Mallory Weiss tear	AV malformation
Gastritis	
Dieulafoy's lesion	

Initial Assessment

- Assess Volume status and blood loss
 - Orthostasis (10% of intravascular volume loss-i.e., 2-3 liters of blood)
 - Hb/Hct will take hours to reflect acute blood loss (1 gm Hb=1 U blood)
- Determine upper versus lower origin
 - NG aspirate has good positive predictive value but poor negative predictive value
 - Melena takes hours to develop
 - At least 10 % of hematochezia is from an upper source
- Determine clotting ability
 - Coagulopathy (coumadin, heparin, vitamin K/fibrinogen deficiency, hemophilia, DIC)
 - Platelet dysfunction/deficiency (ASA, NSAID, uremia, MIA)

Management

- Establish IV access with 2 large bore peripheral lines (size 18 or bigger) or central line
- Consults to GI and General Surgery (especially for lower bleeding)
- Resuscitate intravascular volume
 - Saline or Ringers initially with goal of stabilizing hemodynamics
 - PRBCs to maintain oxygen-carrying capacity of blood (at least 8 gm/dl; 10 gm/dl for patients with coronary artery disease)
 - Administer 1 amp calcium chloride for every 3 units of PRBC
- Correct bleeding diatheses
 - INR to less than 1.5 with FFP, vitamin K (1 mg IV/10 mg SQ)
 - Platelets to greater than 50,000 functional with DDAVP, platelets and calcium
 - Fibrinogen to greater than 100 with cryoprecipitate

Interventions

- Upper Bleed
 - Endoscopy
 - Sclerosis, banding, laser coagulation
 - Determination risk for re-bleeding (adherent clot, visible vessel, red spot)
 - Proton pump inhibitors
 - Vasoactive agents (if large bleed or hemodynamically unstable)
 - Octreotide (synthetic somatostatin with longer ½ life (50 ug/h x 5 days). Likely to decrease bleeding from esophageal varices but does not change mortality
 - Pitressin (Vasopressin)
 - For gastric ulcers, stress ulcers and gastritis initiate at 0.15-0.2 U/min
 - For varices initiate at 0.03 U/min and titrate by 0.3 U/min q 30 min to control of bleeding or max of 0.9 U/min
 - Use with IV NTG to prevent coronary artery vasoconstriction
 - Tamponade with Sengstaken-Blakemore tube
 - Surgery +/- Interventional Radiology evaluation
- Lower bleed
 - Endoscopy (diagnostic only)
 - Radionuclide bleeding scan (poor sensitivity and specificity)
 - Angiography/Contrast CT (Excellent specificity but insensitive if no active bleeding)
 - Surgery +/- Interventional radiology evaluation for severe bleeding (>4-6 Units pRBCs required)

Monitoring

- Orthostatic vital signs, especially tachycardia, or hematemesis are earliest signs of acute bleeding
- Serial Hb/Hct every 6 h and following transfusions
- Risk modification
 - B blockers
 - H pylori treatment
 - Stopping causes (NSAIDS, ASA, etc.)

A.A Compartment Syndromes

- I. **Definition:** A group of syndromes characterized by increased pressure within a closed anatomical space resulting in local ischemia (limb compartment syndrome) or local and systemic complications (abdominal compartment syndrome). The definitive treatment of both syndromes is surgical.
- II. **Limb Compartment Syndrome (LCS)**
 - a. Injury (trauma, hemorrhage, ischemia-reperfusion, venous obstruction) leads to swelling and increased pressure within a compartment. The increased pressure collapses venules, and as hydrostatic pressure increases, eventually collapses arterioles causing limb ischemia.
 - b. Most common cause is fracture of tibia or distal radius/ulna, in which compartment syndrome has been described in 2-30% of fractures
 - c. Crush injury is another important cause
 - d. Aortic balloon pumps can cause LCS ~5% time through inducing LE ischemia
 - e. Large DVTs → phlegmasia cerulea dolens can cause LCS
 - f. **Symptoms:** (5 P's) pain out of proportion to exam, pallor, paresthesia, pulselessness, paralysis
 - g. **Signs:** tense limb, pain with flexion/extension, loss of 2 point discrimination. Pulselessness implies late disease, limb injury has already begun.
 - h. **Measuring Compartment pressure:** Must be done if LCS is suspected in unresponsive patient. Multiple different techniques available. Most popular is a simple needle manometer-18G needle connected to CVP monitor. The ideal pressure for performing fasciotomy is unknown. Different cutoffs used are- compartment pressure >30, diastolic BP-compartment pressure<30, MAP-compartment pressure<40.
 - i. **Treatment:** Fasciotomy. In Phlegmasia cerulea dolens, treatment is leg elevation and anticoagulation.
- III. **Abdominal Compartment Syndrome**
 - a. Increased intra-abdominal pressure (IAP) results in gut and renal ischemia, decreased venous return, hypotension, decreased lung compliance and impaired ventilation from increased pleural pressures.
 - b. Most common causes are abdominal trauma, intra-abdominal bleeding, AAA repair. Can occur with dilated loops of bowel in absence of trauma, rarely with ascites, peritonitis, pancreatitis.
 - c. **Symptoms:** distended abdomen, hypotension, renal failure, increased peak airway pressures (PIP)
 - d. **Measuring IAP:** Most convenient/least invasive way is through Foley catheter port connected to CVP monitor. IAP > 20 with above symptoms is generally considered abdominal compartment

syndrome. Abdominal perfusion pressure (MAP-IAP) > 60 is desirable.

- e. **Treatment:** surgical decompression leaving open abdomen
- f. **Outcome:** ~70% mortality

B.B. Massive Hemoptysis

Definition: Definition varies depending on source. In general, massive hemoptysis is defined as a volume exceeding 100 to 600 cc over a 24 hour period

Pathophysiology

- Most cases are arterial and originate from the bronchial arterial circulation off the aorta
 - Hypertrophy of vessels
 - Inflammation
- Pulmonary Arterial bleeding
 - AV malformations
 - Iatrogenic
 - Distal tumors

Differential Diagnoses

- 1) Bronchiectasis
- 2) Bronchitis
- 3) Neoplastic (malignant lung primary, endobronchial metastatic, adenoma (carcinoid), Kaposi's)
- 4) Foreign body
- 5) Airway trauma
- 6) Coagulopathy
- 7) Arterial-tracheal or bronchial fistula
- 8) Active infection (Mycobacterium, aspergillus, bacteria)
- 9) Acute congestive heart failure/Mitral Valvular disease
- 10) Autoimmune (Goodpasture's, Wegener's, Lupus, pulmonary hemosiderosis)
- 11) Pulmonary Vascular Disease (AV malformation, pulmonary infarction, Pulmonary Hypertension, Pulmonary Veno-Occlusive disease)
- 12) Cocaine
- 13) Endobronchial endometriosis
- 14) Procedure (Transbronchial, Transthoracic, Endobronchial, Wang needle, Swan-Ganz)
- 15) Cryptogenic (30%)

Management Goals

- 1) Establishment of patent airway
- 2) Control of bleeding
- 3) Determination of site and etiology
- 4) Determination of surgical candidacy

Data Collection

- 1) History
 - Prior history of lung, cardiac or renal disease
 - Smoking
 - Prior hemoptysis

- Evidence for infection with cough, fever, sputum production
- Family history of hemoptysis or cerebral aneurysms (hereditary hemorrhagic telangiectasia)
- Skin rash
- Travel
- Bleeding disorders
- Medications (NSAIDS, ASA, anticoagulants)
- Epistaxis or GI complaints (r/o pseudohemoptysis)

14) Physical Examination

- Telangiectasias
- Skin rash (vasculitis, SLE, fat embolism, endocarditis, DIC)
- Clubbing (bronchiectasis, neoplasm, CF, IPF or other chronic lung diseases)
- Loud P2, RV lift, TR, JVD (pulmonary hypertension)
- Heart murmur (vascular heart disease especially mitral)
- Leg swelling (DVT)

15) Initial Investigation-

- CBC
- Chemistry with renal function
- Coagulation studies including fibrinogen
- LFTs
- U/A especially for hematuria and casts
- ABG
- Sputum specimens: Gram stain, culture, AFB stain and culture, fungal stain and culture
- Cytology including inclusion bodies for DNA viruses
- Chest x-ray

16) Specialized Studies

- CT scan (consider CT-PA)
- Anti-glomerular basement membrane antibodies (anti-GBM)
Goodpasture's syndrome
- ANA- Systemic Lupus Erythematosus
- Anti neutrophil cytoplasmic antibodies (c-ANCA and p-ANCA)
Wegener's and other vasculitides

5) Management

- Monitor in an ICU setting
- **Emergent consultation to pulmonary, interventional radiology and cardiothoracic services**
- If bleeding site identified place with bleeding side down in lateral decubitus position which decreases spillage into uninvolved lung
- Ensure adequate oxygenation
- Supplemental O₂ by cannula or mask
- Intubation with #8.0 ET tube or larger if unable to oxygenate or bleeding continues and patient cannot clear airway
- Broad spectrum antibiotics
- Cough suppression with codeine

- Emergent bronchoscopy within 12-18 h of presentation
 - FOB can be done at bedside if rate of bleeding is slow enough to allow visualization. Note: FOB is high risk if patient bleeds.
 - Rigid bronchoscopy under general anesthesia for rapid bleeding
 - Localization of segment
 - Definition of etiology
 - Placement of fogarty balloon to tamponade bleeding
- b) **Arteriography** – Gold standard procedure in bleeding patient.
- Localize bleeding site by visualization of tortuous and hypervascularized vessels
 - Embolization with coils
 - Complication is paraplegia (rare) due to embolization of the anterior spinal cord artery which arises from a bronchial artery in 5 % of the population
 - Safer than bronchoscopy.
- c) **High resolution chest CT**
- Better define etiology
 - Performed after patient is stabilized
- d) **Surgical resection**
- Second option if conservative measures fail or if re-bleeding develops
 - Prior knowledge of prior lung capacity through FEV1 essential

C.C. 1 SHOCK

Shock Definition: acute circulatory failure causing inadequate tissue perfusion and organ dysfunction

You'll see low MAP (SBP + (2*DBP)/3), evidence of organ dysfunction (brain, kidney, etc)

Circulatory system has three major parts that can fail to produce an adequate perfusion pressure:

pump, fluid, or tubes. Pressure=Force (fluid volume, cardiac output)/ area (vasodilation)

When one part fails, others try to compensate (hopefully).

Types of Shock

1. Cardiogenic-failure of pump, cardiac output. CO=SVxHR, SV=EDV-ESV, seen more in CCU

- LV failure: MI, AS, AI, cardiac contusion, septal rupture
- RV failure: MI, pulm HTN
- Obstruction: PE, taponade, tension PTX, abd compartment syndrome, high PEEP, stenotic valves
- Tachy or bradyarrhythmias

2. Hypovolemic: failure of fluid

- Hemorrhagic
- Dehydration: I<<<Os from urinary, GI, skin, lungs
- "3rd spacing": pancreatitis, portal HTN, burns

3. Distributive-same amt of fluid in larger area, low SVR≈(MAP-CVP)/CO

- Septic-MOST COMMON IN ICU. Failure of tubes and tissues.

• Anaphylactic

- Neurogenic-spinal shock-sudden sympathetic collapse/vasodilation
- Adrenal insufficiency
- ? severe hypothyroidism

End pathway of all types is distributive physiology, and overlap between each type.

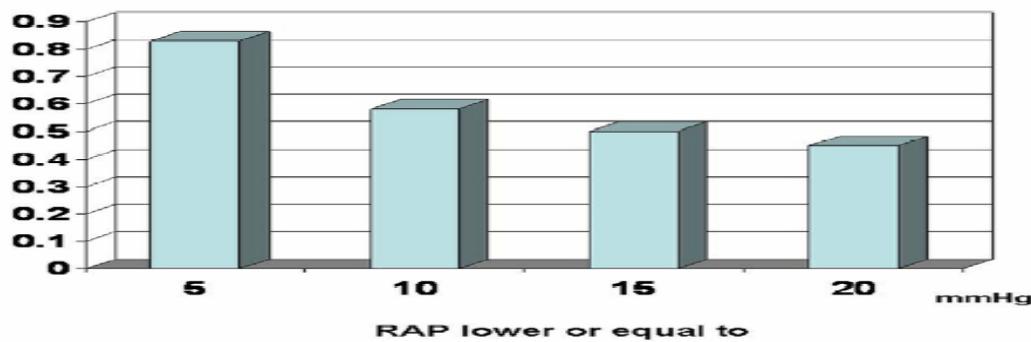
	Preload	Pump	Afterload	Tissue O2 extraction
	JVD PCWP CVP	Cap refill CO (fick, thermod)	Cool,clammy LV: SVR RV: PVR	(inverse of MvO2sat) nl~65%
Cardiogenic	↑	↓↓	↑	↑
Hypovolemic	↓↓	↑	↑	↑
Distributive	↓	↑	↓↓	↓

C.C.2 Evidence-Based Hemodynamic Monitoring

- I. Definition: use of invasive device for continuous, detailed assessment of hemodynamics in order to guide treatment decisions.
- II. Static vs dynamic measurements: In general, static hemodynamic measurements (pressure: CVP, PCWP, or volume: RVEDV, LVEDA) do not predict hemodynamic improvement to volume loading. Trends over time may be helpful, but single values do not predict response to volume load.
- III. Static measurements:
 1. Exam: generally poor at predicting volume responsiveness and estimating cvp, except maybe the abdomino-jugular reflux Which is a fair estimate of cvp/pcwp .(see Ewy GA. The abdominojugular test: technique and hemodynamic correlates. Ann Intern Med. 1988;109:456-460; Eisenberg PR, et al Crit Care Med. 1984)
 2. Central venous line and CVP: A central line is generally present and necessary in unstable patients in order to deliver vasoactive medications; therefore, CVP transduction offers a convenient and low-risk static estimate of preload.
 - It seems to be equivalent measured either by SVC or femoral approach (Desmond, Emerg Med J 2003).
 - It does not predict volume responsiveness in most studies.
 - But, a CVP below 5 will predict fluid responsiveness in spontaneously breathing patients~80% of the time. Above 5, it's 50/50 whether bolus will be effective (see graph below from Heenan et al Crit Care 2006).

Figure 6

Proportion of patients responding to fluid challenge



Relationship between right atrial pressure (RAP) and the likelihood of responding to fluid challenge.

3. Pulmonary Artery Occlusion Pressure (PCWP): Needs to be measured via PA catheter.
 - Does not predict volume responsiveness.
 -
- IV. Dynamic measurements: Assess change in hemodynamic variables over time/after physiologic maneuver. Studies are limited to specific patient

populations (eg., change in pulse pressure is limited to paralysed/ventilated >8cc/kg) or special equipment (echo, ultrasound).

1. Change in Right Atrial Pressure: A spontaneously breathing patient without a decrease in RAP >2 mmHg during inspiration will NOT respond to volume (Magder et al J Crit care 1992).
2. Change in Pulse Pressure: Mechanically ventilated patients who are not initiating breaths and have variations in pulse pressure during their respiratory cycle have been shown to respond to volume challenges.
 - To assess changes in pulse pressure an a-line is needed. Notably, recent evidence suggests that changes in O₂ sat waveform may also be a useful to guide treatment (Natalini et al. Anesth & Analges 2006).
 - The criteria for volume responsiveness is: maximum pulse pressure minus minimum pulse pressure over one respiratory cycle/average of these two values >13%. PPV 94% NPV 96%. The cutoff is >15% if using the pulse oximeter.
 - There has recently been the first clinical outcomes study using purely pulse pressure changes to guide volume resuscitation (Lopes et al Crit Care Med 2007); it was in intra-op patients and showed reduction in complications, mechanical vent time, and LOS using pulse pressure variation only to guide volume expansion.
3. Change in Aortic blood velocity with passive leg raise: Leg raise results in ~300cc bolus, therefore, it should predict response to IVF bolus.
 - An increase in aortic blood flow via Doppler predicts volume responsiveness with PPV 85% NPV 91% and this is better than change in pulse pressure, probably due to lower tidal volumes used in this study (Lafanchere et al Crit care 2006).
 - Brennan et al Chest 2007 showed that brachial artery velocity changes with mechanical ventilation (measured with a Sonosite) correlated well with change in Pulse Pressure, but did not measure outcomes. Could a combination of brachial artery velocity and SLR be the best, noninvasive/bedside test of volume responsiveness?

V. Why not just give an empiric fluid bolus? One expects that increasing preload will result in increased stroke volume/cardiac output, but:

- In the critically ill, fluid bolus leads to an increase in SV/CO in only 40-70% of patients (Michard F&Tebul J, Chest 2002).
- Fluid administration in some states (cardiogenic shock, massive PE, pulm HTN) may be detrimental and awaiting the results of an ineffective empiric bolus delays correct treatment (eg., pressors, inotropes).

Conclusion: Little evidence exists for utilizing static measurements to predict beneficial response to volume expansion. Dynamic changes in right atrial pressure in spontaneously breathing patients, or changes in pulse pressure over the respiratory cycle, are more accurate means of predicting response to IVF.

D.D.Hypothermia

Definition: Core temp < 95 C.

- Response to stress and cold environment is controlled by hypothalamus.
- Three basic mechanisms – Shivering; Vasoconstriction, and endocrine response (thyroid, cortisol, catechol).
- Cold induces a diuresis which results in susceptibility to severe hypovolemia.

Grades of Severity:

Mild 90-95F (32-35C): Increased HR, RR, shivering – MS changes

Mod 82-90F (28-32C): Decreased HR, RR, CO, BP, No shivering, MS changes

Severe <82F (<28C): Obtundation, pulmonary edema, arrhythmias.

Causes:

Accidental: Environmental Exposure

Non Accidental:

Severe stress (sepsis, pancreatitis, uremia, trauma,burns)

Drugs (Etoh, benzo, b-blockers)

Endocrine- thyroid, adrenal, HPA, hypoglycemia

Neurological event – CVA, seizure

Clinical Features: confusion and obtundation

EKG: classic Osbourne (or J) waves, bradycardia, PR and QRS prolongation.

Labs: Acidosis, coagulopathy, hypoglycemia

Management:

1. ABC – consider intubation
2. FSBS
3. Place large bore IV – consider femoral CVL to avoid placing a wire in the heart which may ppt V fib.
4. Thiamine, folate, dextrose
5. IVF (warm) (if not in pulmonary edema – aggressive 150-200/hr).
6. Re-warm:
 - a. Passive External – Mild hypothermia- Blankets (bear hugger) –.
 - b. Active External - Moderate hypothermia. Forced warm air over patient via bear hugger.
 - c. Active Internal – Severe hypothermia. Warm IVF, humidify and warm O₂ for MV, Consider gastric or balder lavage. Chest tube and peritoneal lavage is rarely used. If severe hypothermia or failure to respond to initial measures would call anesthesia to consider cardiopulmonary bypass (or renal for warm HD)
7. Draw blood cultures, TSH and cortisol level
8. Consider empiric antibiotics +/- cortisol replacement (hydrocortisone 50-100mg every 8 hrs)

Major complications:

1. Core temperature afterdrop: warming the peripheries may result in vasodilation with a rapid shunt of acidotic and cold blood to the central regions while at the same time there is an abrupt drop in SVR (due to peripheral vasodilation). As hypothermia also causes hypovolemia and decreased CO there can be a profound fall in BP. Have IVF fluid running aggressively and dopamine at hand. Consider steroids if persistent.
2. Arrhythmia: Afib and V tach/fib is common. Can be resistant to treatment. Usual management with cardioversion x 3. If no response continue resuscitation until core body temp exceeds 95C and then repeat cardioversion. There is some unconvincing evidence that bretyllium is the best anti-arrhythmic in this setting.
3. Pulmonary edema.

E.E Ingestions and Toxins

Standard approach to all ingestions:

- 1) Assume there is more than one toxin; however, statistics show that greater than 90% of all accidental and intentional ingestions are only one substance.
- 2) Vital signs, pupil assessment (see below), pulse oximetry, finger stick for blood glucose, EKG and mental status should be assessed immediately.
- 3) If airway is a concern early intubation is recommended.
- 4) Obtain IV access. Give thiamine (100mg) to all patients and before glucose in patients with low blood glucose levels.
- 5) Determine time of ingestion and if recent (less than 1 hr) consider gastric lavage. Gastric lavage should only be performed in patients that present early after ingestion
- 6) It is still recommended that everyone receive charcoal (1 g/kg). Especially if patient presented within the first hour of ingestion. Controversy exists because recommendation is not supported by randomized clinical trial and some opponents say charcoal increases patients risk of aspiration pneumonia. Charcoal may be repeated Q 4-6 hrs, especially for toxins with enterohepatic circulation. It is reasonable to withhold charcoal in patients who present late after ingestion
- 7) Do a more thorough physical exam to look for classic signs of toxic syndromes.
- 8) Send labs- ABG, CBC, chem. 20, serum osmolarity, calculate anion and osmolar gap, urine and serum tox screen
- 9) Call Poison Control.

Pupils - Pupillary size (normal 3-4 mm in diameter) and reactivity is dependent on sympathetic parasympathetic innervation. Brain stem reflexes, such as the pupillary reaction to light offer clues to the location of the lesion responsible for the coma.

- 1) Bilateral dilated pupils - Are greater than 7 mm in diameter and do not react to light. Seen in:
 - a) Transtentorial herniation of both medial temporal lobes
 - b) Anticholinergic
 - c) Sympathomimetic drug intoxication
 - d) Hallucinogens
 - e) Drug withdrawal states
 - f) Miscellaneous –MAO I, Serotonin syndrome, alcohols
- 2) Bilateral pinpoint pupils - Have 1-1.5 mm in diameter and are seen in:
 - a) Opiod poisoning
 - b) Pontine hemorrhage
 - c) Sedative/hypnotics
 - d) Neurosyphilis
 - e) Organophosphates poisoning
 - f) Miotic eyes drops
 - g) PCP overdose

- 3) Asymmetric pupils(anisocoria) - With a difference of 1 mm or less in diameter and a normal constriction response to light is a normal finding in 20% of the population. If the dilated pupil does not react to light or reacts slowly, it usually indicates a rapidly expanding lesion on the ipsilateral side as in subdural or middle meningeal hemorrhage or brain tumor, that is compressing the midbrain or oculomotor nerve directly or by mass effect.
- 4) Fixed midsized pupils - Are about 5 mm in diameter. These do not react to light and are the result of midbrain lesion.

F.F. Smoke Inhalation, CO, CN Poisoning

- 70% of patients with combined cutaneous and inhalation injuries.
- Smoke is defined as the mixture of gases and aerosolized matter generated by the burning of fuel.
- Smoke is the byproduct of two processes: oxidation and pyrolysis.
 - Oxidation: Oxygen combines with fuel that is burning (nylon, wood, person) and byproducts are made (benign: H₂O, CO₂ and noxious SO₂, NO₂.) Byproducts of this process are heat, light and incompletely oxidized carbon or carbon monoxide.
 - Pyrolysis: Direct liberation of constituents from burning substance.

4 ways for Injury to Occur:

- Thermal Injury: Strictly from the high temperature. Upper airway has great heat exchanging properties so when thermal injuries occur it is rare from them to damage anything but the upper respiratory tract. Distal lung injuries can occur from steam (humidified hot air.)
 - Resulting injuries are rarely acute although acute laryngospasm has been reported. Typical problems result from persistent edema causing stridor and superinfection from airway ulceration. These tend to be later probems 24 hours to 72 hours.
- Hypoxic Injury: This tends to not be the major problem. Most fires will burn out when FIO₂ drop below 15% enough oxygen for most humans. However, the low O₂ concentration may potentiate the toxicities of carbon monoxide and hydrogen cyanide which compete with the oxygen for the heme molecule.
- Direct Bronchopulmonary Toxins: These are lower molecular weight stuff. The toxicity is mostly due to the substances pH or ability to form free radicals. Examples are formaldehyde, chlorine, SO₂, NO, NO₂. Important: SOOT can cover airway and absorb these toxic chemicals and help deliver them to distal airway.
 - These chemicals contribute to the neutrophilic infiltrate, distal lung injury, hypoxia and ARDS which can develop 12-36 hours after exposure
- Systemic Toxins: Two big ones are hydrogen cyanide and carbon monoxide. CO is leading cause of smoke-related fatalities, accounting for up to 80 % of deaths. HCN is less commonly recognized and is probably freq missed.

CO poisoning:

- Results from incomplete combustion of organic matter (wood, coal, gasoline, tobacco.)
- Odorless, colorless, tasteless

- It has a high affinity from heme molecule. 240 times greater than oxygen from heme
- Once bound it shifts the oxygen-dissociation curve to the left making it harder for bound O₂ to disassociate.
- Normal CO levels are less than 5% in nonsmokers and around 5% in smokers.
- Toxicity develops around 15% with headache, nausea, vomiting, tinnitus. 20-40% weakness and depressed mental status.
- Greater than 40% obtundation and arrhythmias.
- Late sequelae are gait disturbances, incontinence, neuropathies, blindness, mutism, mental deterioration.
- 10-30% of mild to mod toxicity will have late sequelae.
- Diagnosis must be considered in all pts exposed to smoke: Normal sats, normal PaO₂ with acidosis, hyperventilation occasionally cherry red skin and lips.
- Treatment 100% O₂ is first line cuts ½ life of CO to 30min to 1 hour (half-life is 5 hours at room air.) Hyperbaric oxygen may work better by decreasing half-life to 20-30 minutes but no study has proven that hyperbaric oxygen decreases late sequelae.
- Isocapnic hyperpnea. In dog studies seems to be as good or better than hyperbaric oxygen.

HCN poisoning:

- HCN results from burning natural and synthetic household goods, paper, nylon, polyurethane, wool, silk, synthetic polymers.
- Bitter almond odor but 20-40% of population is unable to smell it.
- Rapidly fatal. No sense in sending off values because by the time it comes back pt will be dead.
- Major finding is **lactic acidosis**. Cyanide binds to iron chelating enzymes such as heme but more importantly cytochrome a-a3. Inhibits oxidative phosphorylation and anaerobic metabolism ensues.
- Treatment involves inhalation of amyl nitrate followed by intravenous sodium nitrite followed by iv sodium thiosulfate.
- The nitrates work by oxidizing hemoglobin to methemoglobin (changing the iron to the ferric form) CN has an affinity for the ferric form and dissociates from the cytochrome a-a3 molecule. Sodium thiosulfate through an enzyme rhodenase converts CN to thiocyanide which is then excreted in the urine. Thiosulfate must be available otherwise you trade CN toxicity for methemoglobinemia.

Later complications of smoke related injuries: late ARDS, and bacterial pneumonia.

Much later complications: bronchiectasis, tracheal stenosis, bronchiolitis obliterans and pulmonary fibrosis.

G.G. 1 Diabetic Ketoacidosis

A life threatening condition, mortality ranges from 2-10% in developed countries. Mortality was 100% before discovery of insulin

Pathophysiology:

1. Deficiency of insulin
 - Induces increased hepatic production of glucose
 - Decreased peripheral utilization of glucose
 - Induces lipolysis which generates ketoacids (acetoacetate, B-hydroxybutyrate, and acetone) which causes acidemia
2. Increased counter regulatory hormones
 - Glucagon and catecholamine levels increase inducing glycogen phosphorylase to break down hepatic glycogen stores
 - Growth hormone levels increase which worsen hyperglycemia
 - Cortisol level is increased which stimulates protein catabolism which provides amino acids for gluconeogenesis

As a result of the insulin deficiency and increased counter regulatory hormones, there is hyperglycemia. Glucosuria develops because the blood glucose levels exceed the glomerular reabsorptive capacity. Glucosuria induces an osmotic diuresis in which the patient loses 5-7 liters of free water, and electrolytes. This process causes the hyperosmolarity seen in serum. Lipolysis as a consequence of insulin deficiency causes the formation of the ketoacids which accumulate and create the anion gap metabolic acidosis.

Clinical symptoms:

Thirsty, weak, fatigued, abdominal pain (resolves when ketosis clears), vomiting, polydipsia, polyuria, air hunger, weight loss

Findings:

Volume depleted, hyperglycemic, hyperosmolar, acidotic, ketonemia, ketonuria

Precipitants for DKA:

Noncompliance with insulin	Steroids
Infection	GI bleeding
New-onset DM	Trauma
Myocardial infarction	CVA
Pancreatitis	Thromboembolic disease
Sympathomimetic drugs	

Evaluation:

1. Volume status
2. Acid-base status
3. Electrolytes, osm, glucose
4. Precipitants

Management:

1. Replace fluid losses over 24-48 hrs. Check orthostatics, calculate free water deficit NS IV to expand extracellular fluid volume without abrupt fall in plasma osmolality, then switch to hypotonic 1/2 NS once volume repleted (resolved orthostasis) NS 500cc/hr for 4 hrs, then 250cc/hr
2. Insulin is a must. It lowers glucagon level and counteracts glucagon effects on the liver. It stops lipolysis and the hepatic production of ketoacids. Loading dose 0.1-0.2units/kg IV then continuous infusion of 5-10 units/hr IV. Target the blood glucose level to decline by 75-90 mg/dl per hour.
3. Give glucose (IV D5 1/2NS) when the serum glucose level falls to 250-300 if ketosis persists as evident by acidic pH, persistent anion gap, or serum ketones.
4. Titrate the insulin drip down a unit per hour as needed to prevent hypoglycemia, but continue it until ketosis is resolved.
5. Replace electrolytes lost (potassium, magnesium, phosphate).
6. Bicarbonate use is controversial, no documented benefit. Would not give unless pH is less than 6.9 or there is another indication for use.
7. Treat underlying precipitating cause for the DKA.

Complications of DKA:

Hypokalemia

Hypoglycemia

Cerebral edema-brain adapts to intracellular dehydration by developing idiogenic osmols (myoinositol, taurine, betaine). If the extracellular tonicity is corrected too quickly, there is not sufficient time for the idiogenic osmols to dissipate thus inducing brain swelling.

See review in literature section

G.G.2 Hyperosmolar Nonketotic Syndrome (HONK)

Definition: A life-threatening acute metabolic complication of diabetes mellitus characterized by severe hyperglycemia, dehydration, organ failure, and electrolyte disturbance.

- Typically seen in type 2 diabetics, but 40% in prior series had no previous diagnosis of diabetes.
- Metabolic derangements secondary to a relative insulin deficiency and elevated levels of stress-responding, counterregulatory hormones such as glucagon, catecholamines, growth hormone, and cortisol.

Epidemiology:

- HONK occurs at a frequency of 17.5 cases per 100,000 person years.
Mean age of presentation 57-69 yrs
- Mortality rate 12-46%. Risk factors for mortality include increasing age and higher levels of serum osmolality.
 - Mortality rate of 7% if serum osm < 350 mOsm/L, 14% when 350-374 mOsm/L, 32% when 375-399 mOsm/L, and 37% when > 400 mOsm/L.

Pathophysiology:

- Relative insulin deficiency leads to increased liver glucose production and a decrease in peripheral use of glucose.
- Hyperglycemia exceeds the glomerular reabsorption capacity that results in a volume and electrolyte diuresis.
- Generally no significant ketosis or acidosis, but have a higher degree of volume depletion that causes prerenal azotemia, with further impairment of the glucose disposal with worsening hyperglycemia and hyperosmolality.
- Basal insulin secretion is maintained in HONK, and the insulin levels are adequate to prevent peripheral lipolysis in adipose tissue, but the insulin levels are not adequate to allow peripheral uptake of glucose or to prevent liver overproduction of glucose.
- Counterregulatory hormones (cortisol) are elevated which stimulate protein catabolism to increase circulating amino acids to provide gluconeogenic precursors for the liver. Glucagon and catecholamines induce glycogenolysis in the liver further worsening the hyperglycemia. In HONK, glucagons levels correlate with the degree of hyperglycemia.
- Hyperglycemia causes a significant osmotic diuresis which is associated with major urinary losses of electrolytes.
- Hyperglycemia raises the extracellular osmolality and causes water to shift from the intracellular to extracellular compartment.

- The total-body water deficit in HONK is generally in the range of 8-10 L.
- An intact thirst mechanism and access to free water should lead to increased fluid intake in patients with an osmotic diuresis.
- Mental status changes occur when the hyperglycemia worsens and hyperosmolality develops.
- A depressed level of consciousness will lead to a decrease fluid intake and worsening of hyperglycemia/osmolality.
- In HONK, the degree of mental status change correlates with the degree of hyperosmolality and dehydration.

Clinical Presentation:

- polyuria and polydipsia
- increasing lethargy
- mild confusion
- stupor
- seizures, aphasia, CVA
- hypotension, tachycardia, tachypnea, fever, dehydration, shock

Diagnostic criteria:

- Blood sugar > 600 mg/dl
- Osmolality > 330 mOsm/L
- Prerenal azotemia
- pH > 7.3
- Serum bicarbonate > 20 mEq/L

Precipitants:

- Acute illness such as UTI or respiratory infection
- Noncompliance
- Stopping oral hypoglycemics or insulin, or inadequate dose of these meds
- Substance abuse may contribute to noncompliance

Evaluation:

- Assess volume and hydration status,
- Check baseline labs including lytes, BUN, Cr, ABG, serum osmolality
- Calculate anion gap, free water deficit
- Look for precipitating cause such as infection, myocardial infarction

Management:

- Replace fluid losses: Vigorous fluid replacement is vital. Generally in HONK, free water losses exceed sodium losses which causes a hypertonic dehydration.
 - Hypotensive patients should receive isotonic IV fluids until stable hemodynamics, then switched to hypotonic fluid. When serum osm > 330, give $\frac{1}{2}$ NS at a rate of 1-2 L/hr for 1-2 hours, then 1 L/hr for 3-4 hrs monitoring response of blood pressure, and urine output. Once these parameters have improved, $\frac{1}{2}$ NS is given at a rate to replace half of the free water deficit over the first 12 hrs, and the remainder in the next 24 hrs
- Correct hyperglycemia: With volume and water repletion, the glucose level will fall

by 80-200 mg/dl/hr.

- Insulin regimen of a 10-units regular IV bolus, then continuous infusion of 0.1-0.15 units of insulin/kg/hr will decrease serum glucose from 80-100 mg/dl/hr.
- Once blood sugar reaches 250-300 mg/dl, 5% dextrose can be added to the intravenous fluids and the insulin infusion rate reduced.
- Replete electrolyte losses: pts will have whole body potassium deficits secondary to the osmotic diuresis. Potassium levels will fall during treatment of HONK, so it must be monitored closely to maintain a serum level 4-5 meq/L. Don't give K⁺ on presentation unless K⁺ is less than 4meq/L . Once urine output is adequate, 20-40 meq/L K⁺ can be added to the IV fluids given.
- Detect and treat precipitating cause

Complications:

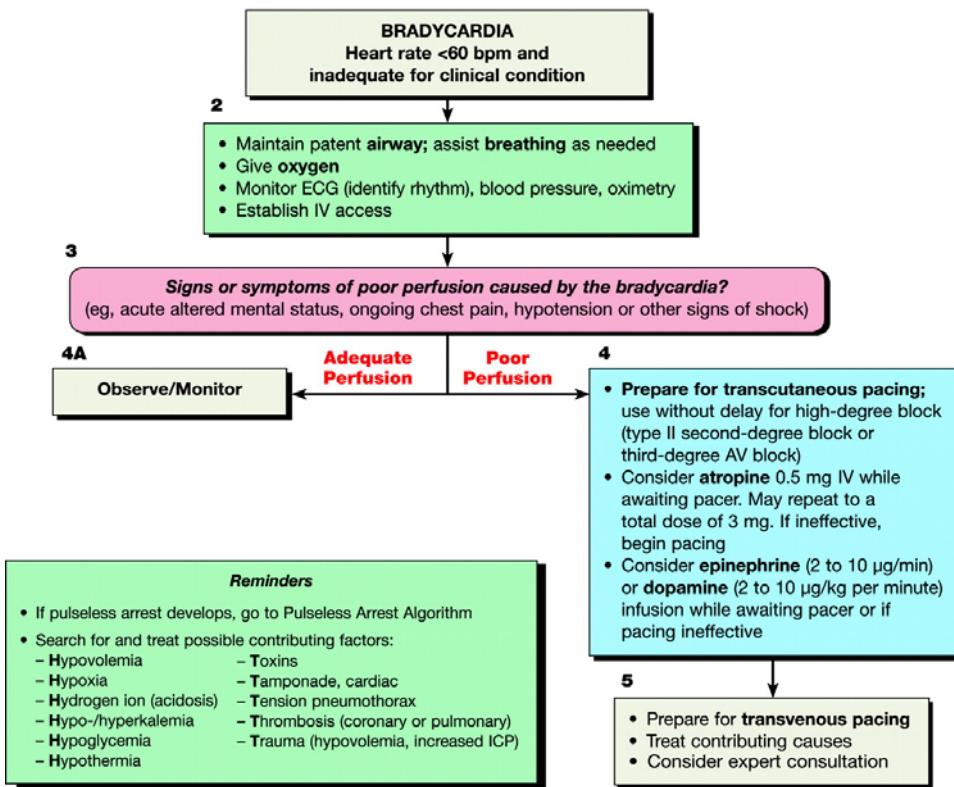
- Hypoglycemia, hypokalemia, cerebral edema
- Cerebral edema resulting from rapid correction of BS is a rare complication, presents with headache, progressive drowsiness, and lethargy in a patient with otherwise adequate resolution of hyperglycemia. Proposed mechanism is the development of an osmotic disequilibrium during correction of the hyperosmolar state. The CNS generates idiogenic osmols to adapt for intracellular dehydration. If correction of the extracellular hyperosmolality occurs faster than the dissipation of the idiogenic osmols, there is an osmotic gradient favoring brain cell swelling.

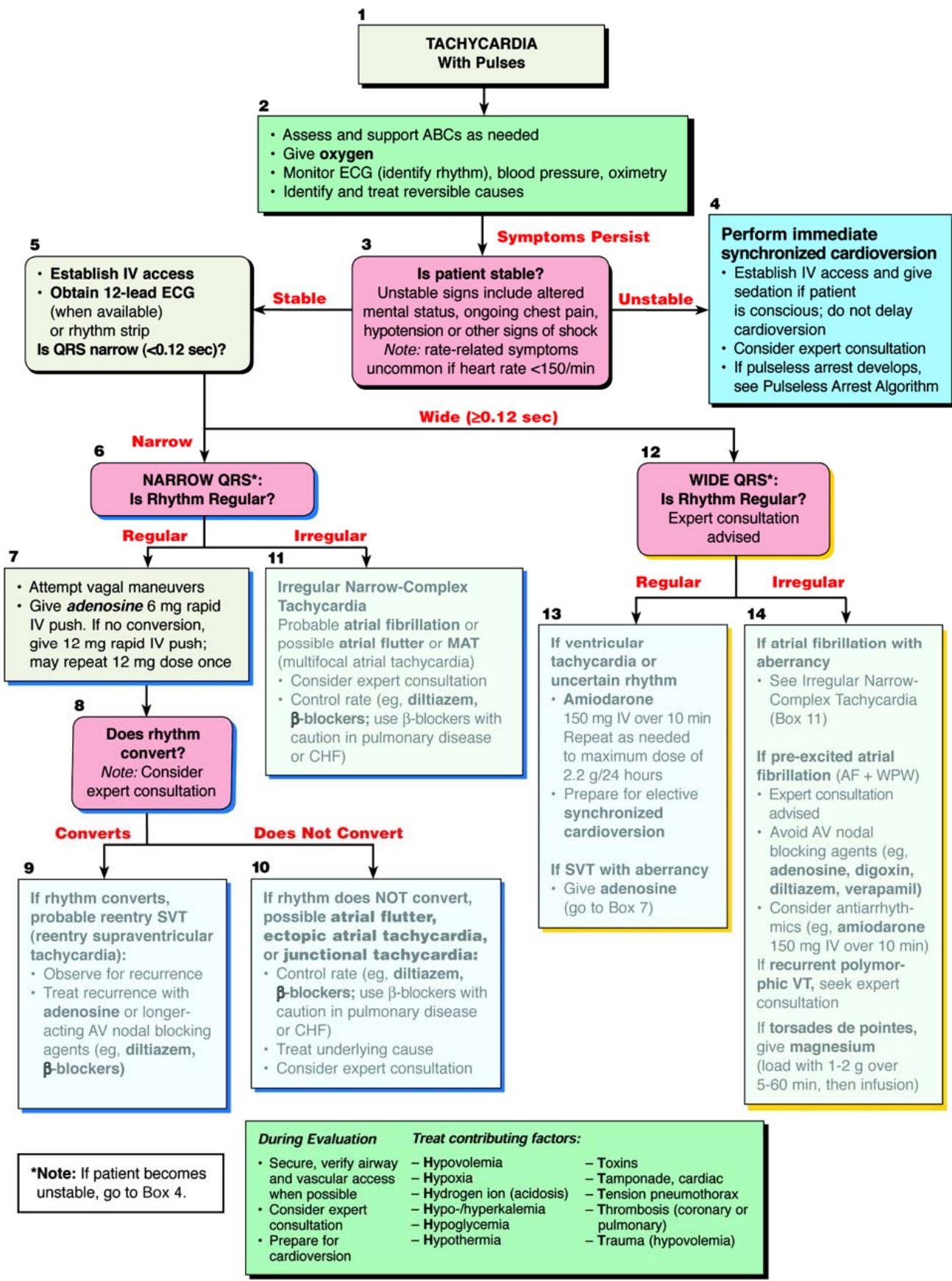
H.H End of Life Care

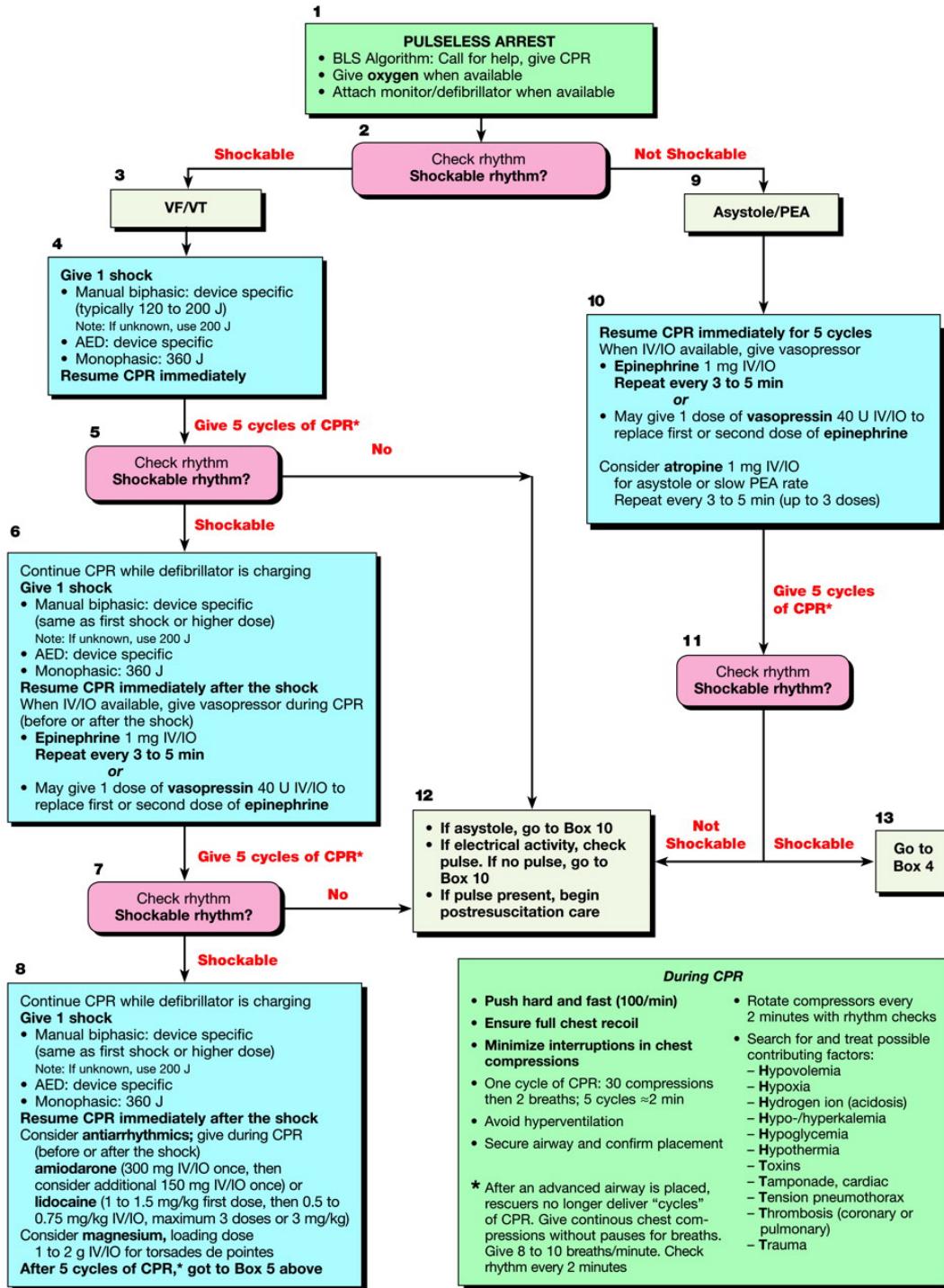
- I. **Introduction:** 20% of all deaths in the US occur in the ICU. The majority of these deaths occur in the setting of life-support withdrawal. ICU care enlists the input of patients' family more than any other setting. Much of the care of our ICU patients includes building trust, as well as bereavement/emotional support of the family. The most important/yet least achieved factor associated with family satisfaction with their loved-ones' care is *communication*. (Levy et al Crit Care Med 2006)
- II. **Communication:**
 - a. Arrange formal family meeting for dying patients, in addition to informal updates (Latrette et al Crit care Med 2006)
 - i. Comfortable room away from ICU
 - ii. Plan ahead: who will be there, family can write down ?'s
 - iii. Offer opportunity for family to tell you about the patient's life- this will help you and them understand pt and their values
 - iv. Find out what family understands about diagnosis, treatmemnts, prognosis
 - v. Provide information about diagnosis treatments, prognosis in straightforward manner. It is Ok to use words like 'dying'.
 - vi. Align family's goals to medical team's, different families want different levels of decision-making
 - vii. Don't use terms like 'withdraw care', instead, can talk about changing direction of care from cure to palliative/comfort care.
 - viii. Don't offer list of treatments for family to use as all equally reasonable. Offer recommendations.
 - ix. Acknowledge emotional burden on families, offer spiritual assistance
 - x. Summarize-diagnosis, prognosis, plan decided on at end of meeting, next meeting schedule.
 - xi. Family satisfaction is higher when the family does most of the talking.
- III. **Palliation:** pain control and patient comfort are paramount at end-of-life. Prolonging inevitable death is NOT palliative. (Brody et al NEJM 1997)
 - a. Stop all interventions will not result in increased comfort (labs, radiographs, frequent vitals, aggressive pulmonary toilet, frequent turning, ? antibiotics, pressors)
 - b. Mechanically ventilated patients may be terminally extubated to humidified air or O₂, or terminally weaned to T piece. The method is often attending preference-though terminal extubation is probably preferable allowing for greater interaction between the patient and family. Terminal weaning may be used if a patient has copious secretions.

- c. Dying patients experience no increased discomfort after discontinuing artificial hydration or nutrition
- d. Morphine is 1st line treatment of pain and dyspnea and should not be withheld for fear of hastening death. Benzos for anxiety.
Antiemetics.

I.I ACLS Algorithms







J.J Anaphylaxis

Definition: Life-threatening syndrome of sudden onset with one or more of the following manifestations (generally #1+any other is considered anaphylaxis) :

1. Skin: sudden Urticaria, angioedema (88%)
2. Respiratory: bronchospasm, laryngeal edema/stridor (50%)
3. GI: nausea, vomiting, diarrhea (30%)
4. CV: hypotension, dysrhythmia (30%)
5. Constitutional: diaphoresis, pruritis, anxiety

Etiology: Anaphylaxis: IgE-mediated immediate hypersensitivity reaction to antigen

Anaphylactoid: non-IgE-mediated, but present and are treated the same.

- 60% have idiopathic anaphylaxis
- Drugs: penicillins most common,
 - ASA/NSAIDs, exercise, opiates, radiocontrast produce anaphylactoid reactions
- Food: nuts, fish most common, generally in teenagers
- Venoms: insect stings
- Blood products
- Latex

Treatment: 2% mortality w/ anaphylaxis

- ABC's: intubate for stridor, severe dyspnea; get IV access, give IVF, lie flat
 - AND
- Epinephrine: drug of choice: 0.3 to 0.5 mL of 1:1000 (1 mg/mL) epinephrine intramuscularly into the anterior or lateral thigh
- Antihistamines: Use Both H1 and H2 blockade
- Inhaled B agonists
- Corticosteroids: useful to prevent biphasic anaphylaxis (10hrs out)

For refractory hypotension: epinephrine gtt 5-15mcg/min, glucagon if on BBlocker

Patients need to be discharged with an epi-pen and instruction how to use it. Should have allergy outpatient appointment to test for triggers.

K.K Blood Products in ICU

The Products:

- a. Packed Red Blood Cells: Each unit contains 200ml of red cells, 300ml of volume. One unit will raise the hct by 3 percent. Hct is 55% in pRBC. Stored for up to 45 days. Half-life of RBC variable. Needs to be ABO compatible, crossmatched and Rh typing.
 - b. Whole Blood: Only indicated in massive bleed (usually in trauma setting.)
 - c. Fresh Frozen Plasma: Plasma centrifuged away from blood cells. Once thawed must be used in 24 hours. Factors most sensitive during storage are V and VIII. Needs to be ABO compatible.
 - d. Cryoprecipitate: Thaw FFP at 4 degrees and collect white precipitate. Rich in von Willebrand factor, factor VIII, factor XIII and fibrinogen.
- What drug can increase factor VIII and Von Willebrand factor levels?
- e. Factor VIII and IX precipitate.
 - f. Platelets: Obtained from whole blood as a pooled product. Each bag increases platelets by 5-10 thousand in 70kg person. The presence of alloantibodies may decrease the response to transfusion. Single donor platelets and HLA-matched may be more effective. Small amounts of RBC, WBC and plasma are transfused with platelets. This may sensitize the recipient and make future RBC transfusions more difficult. ABO matching is not mandatory but ABO incompatible platelets is believed to have shortened survival. Women of childbearing age should have Rh typing.
 - g. Leukocyte reduced products: Leukocytes are the cause of many adverse consequences of blood transfusions. Immunologically mediated effects such as GVHD, and FNHTR. Infectious transmissions and reperfusion injury. Indicated for chronically transfused, transplant recipients, individuals with previous transfusion reactions, CMV negative individuals that are immunocompromised.

Red Blood Cell Transfusions:

- a. What is the appropriate hct to begin RBC transfusion therapy in ICU?
- b. Hebert in Canadian Critical Care Trials Group prospective randomized trial. 838 pts randomized to liberal transfusion 10-12 hgb (420) or restrictive 7-9 hgb(418.) Well designed, well matched. Pts in restrictive group received on average three fewer units of blood. Overall restrictive group received 50% less transfusions. No difference in mortality overall but inhospital mortality higher in liberal group. Subgroup analysis showed less severely ill and age <55 assigned to restrictive group were half as likely to die at 30 days. People with cardiac disease did the same in each group. Authors believe this strategy should be used in all populations, cerebrovascular disease included.
- c. Effect of massive transfusions is dilution of clotting factors. Clotting factors will fall by 10% for every 500 ml of blood loss. In normal host bleeding will only occur when clotting factors fall below 25% of normal. Most rec to correct clotting factors but probably correcting reason for bleed (artery under ulcer base) would suffice. Platelets will fall by 25% with 6 units PRBC's.

Platelets:

- a. Thrombocytopenia and bleeding the goal should be to get plts btw 70-100 thousand. Surgery is ok at this point.
- b. Transfusion usually not recommended in HIT, ITP, DIC, uremia, hyper-splenism unless significant bleeding occurs.
- c. When should you perform prophylactic transfusions?
- d. Two studies provide some insight: Beutler et al. 78 pts undergoing induction for acute leukemia. Randomized to transfusion at 10 vs 20 thousand. No difference in bleeding episodes, RBC transfusions, length of stay in two groups. Rebulla et al. 255 adolescents and adults (16-70) with AML randomized to receive prophylactic plt transfusion at 10 vs 20 thousand. Pts in 10 thousand group received 21.5 % less plt transfusions. No difference in major bleeding, number of RBC's transfused, survival or length of stay.

Fresh Frozen Plasma:

- a. Each unit will increase the clotting protein levels by 10%. If ptt or pt is 1.5 x control (normal .8-1.2) then 2 units should suffice.

Complications:

- a. Acute Hemolytic reactions. Estimated to occur 0.016% of transfusions. Always ABO incompatibility. Less than half are fatal. Pain at infusion site, dyspnea, hypotension, mental status changes. In critically ill pt consider this if pt becomes suddenly hypotensive. Stop transfusion. Send blood for free hemoglobin, haptoglobin and Coombs' testing.
- b. Delayed reactions. 0.025% of transfusions. May go undetected. Pts with prior alloimmunization or pregnancy. 35% asymptomatic. Minor antigens.
- c. Febrile nonhemolytic reactions. 7% of transfusions. Antileukocyte antibodies.
- d. Allergic reactions. From mild to anaphylaxis. No hemolysis. Secondary to serum antigens. In IgA deficient patients may develop IgE antibodies to infused IgA.
- e. Hypothermia. Make sure blood is warmed to at least 80 degrees.
- f. Coagulopathy. Occurs in massive transfusions. 8-10 units pRBC's.
- g. Citrate Toxicity. Blood is anticoagulated with citric acid and sodium citrate (citrate binds to calcium). Once transfused citrate can cause hypocalcemia. In addition, citrate metabolism results in production of HCO₃. As a result, metabolic acidosis can develop. Typically this does not occur because transfused blood is acidotic to serum (pH 7.10).
- h. Hyperkalemia. Hyperkalemia leaks out of RBCs at rate of 1meq/d. Concentration is about 90meq/L in 1 unit of PRBC's. Not usually a problem because of small volume of fluid transfused. Hypokalemia is usually transient and is a consequence of transfusion related alkalosis.

Acute lung injury. Transfusion of alloreactive antibodies contained with red cell products or FFP can lead to agglutination and activation of leukocytes and resultant ARDS. More common with FFP.

L.L Miscellaneous

Acute Chest Syndrome

- I. **Definition:** Is a syndrome defined by new lung infiltrate, and/or chest pain, fever, wheeze, cough, leukocytosis in patient with sickle cell (generally Hb SS or Hb SC)
- II. **Prognosis:** 10% mortality (National Acute Chest Study Group, NEJM 2000)
 - a. Predictors of respiratory failure are platelets <199K, increasing # of lobes involved, prior history of cardiac disease
- III. **Etiology**
 - a. Most frequent cause of ACS is thought to be *fat embolism* in the setting of recent sickle cell pain crisis (50% of ACS in clinical studies, 15-75% in post mortem studies)
 - i. Fat embolism is suggested by diffuse ground glass infiltrate on CT (sensitive, nonspecific)
 - ii. BAL or induced sputum containing lipid-laden macrophages can be helpful in establishing the diagnosis of fat embolism.
 - b. Next most common etiology is Atypical pneumonia (Chlamydia, mycoplasma, Legionella and viral)
- IV. **Treatment:**
 - a. Supportive care: ICU level care+ pain control, IVF, O₂, incentive spirometry
 - b. Exchange transfusion: out with the sickled blood, in with normal blood. Standard of care, but no clinical trials. Be sure to measure %HbSS prior to and after exchange. Need dialysis catheter for rapid exchange.
 - c. Antibiotics: As above: need atypical coverage (levaquin, macrolide) and as always in sickle cell, pneumococcal coverage (though rare cause of ACS).
 - d. In children only, Dexamethasone has been shown effective in reducing duration of ACS (impairs generation of toxic free fatty acids from fat emboli), but also associated with hospital readmission: NOT standard of care in adults (never been studied).

Fulminant Hepatic Failure

- I. **Definition:** acute onset of hepatic encephalopathy and worsening hepatic synthetic function (eg., severe coagulopathy).
 - a. Most common causes are: Tylenol (40%), other drug reaction (13%), hepatitis (12%), other: herpetic, Aminita, Wilson's, HELLP, autoimmune hepatitis, Budd-Chiari (17%).
 - b. Survival is terrible: 90% mortality without transplant
- II. **Grading of Encephalopathy:** generally an intracranial pressure monitor and management of cerebral edema is recommended in grades III, IV who are listed for transplant. No survival benefit has been shown with ICP monitors.
 - a. Grade I: euphoria or depression, mild confusion +asterixis
 - b. Grade II: Lethargy moderate confusion +asterixis
 - c. Grade III: 25-35% with elevated ICP. Marked confusion, incoherent speech, arousable, +asterixis
 - d. Grade IV 75% with high ICP: Coma, unarousable, no asterixis
- III. **Management of cerebral edema:** Goal is to maintain cerebral perfusion pressure >60 (MAP-ICP) and/or ICP <20mmHg.
 - a. Head of bed elevation
 - b. Quiet environment
 - c. Mannitol 0.5-1g/kg, monitoring serum osm goal 310-325. Contraindicated in renal failure.
 - d. Other methods include hypothermia, hypertonic saline, pentobarbital coma
 - e. Steroids are not indicated.
 - f. Ammonia level >200 strongly associated with herniation, use Lactulose or consider rifamixin
 - g. Treat seizures with phenytoin, no role for prophylactic phenytoin
- IV. **Coagulopathy management**
 - a. FFP for active bleeding or pre-procedure only
 - b. Recombinant factor VIIa (40mcg/kg) may be used to reduce massive FFP infusion in setting of gross volume overload
- V. **Common issues in FHF**
 - a. Pulmonary: 30% w/ pulmonary edema. Intubate grade III/IV encephalopathy
 - b. Infection: FHF patients are immunocomproized (decreased opsonization, NK cell function, leucopenia). Low threshold for antibiotics if any suspicion for infection.
 - i. Surveillance cultures for fungus/bacteria are indicated
 - ii. Fungal infections are underrecognized, 32% of patients in one study (Rolando et al J Hepatology 1991)
 - c. Renal failure: hepatorenal syndrome is common. Avoid renal toxins. Consider continuous dialysis in those needing bridge to transplant.
 - d. Metabolic:

- i. frequent monitoring of glucose for hypoglycemia, continuous dextrose infusion may be necessary.
 - ii. Replete K, Mgm, phos-but carefully if renal failure
 - iii. Nutrition
- VI. **Specific FHF syndromes:** treatment (transplant consideration for all, see below)
- a. Acetomenophen OD: activated charcoal, NAC
 - b. Aminita mushroom: penicillin/milk thistle are antidotes
 - c. Herpes: acyclovir
 - d. Wilson's: plasmapheresis, dialysis
 - e. HELLP: deliver the baby
- VII. **King's College Transplant criteria**
- a. Acetomenophen: pH<7.3; OR Grade III/IV+Cr >3.4+INR>6.5
 - b. Non-Acetaminophen: INR>6.5; OR 3 of following: age 10-40, jaundice→coma<7d, INR>3.5, bili>17.5, indeterminate cause of liver failure

Stress Ulcer Prophylaxis

- I. **Definition:** Stress ulceration is a gastrointestinal mucosal injury related to critical illness.
- II. **History:** Association between critical illness and development of gastrointestinal bleed has been recognized for > 100 years.
 - a. Cushings ulcer (1832)- Stress ulcer associated with head injury.
 - b. Curlings ulcer (1842) – Stress ulcer associated with burn injury.
- III. **Pathogenesis** – Multi-hit hypothesis: Fennerty MB. Pathophysiology of the upper gastrointestinal tract in the critically ill patient: rationale for the therapeutic benefits of acid suppression. (*Crit Care Med.* 2002;30:S351-S355).
 - a. Decreased mucosal blood flow.
 - b. Decreased synthesis of protective barrier (e.g. prostaglandin) by GI mucosa.
 - c. Decreased proliferation of mucosal epithelial cells (baseline and in response to injury).
 - d. Decreased food intake (buffering effect).
- IV. **Incidence:** Incidence of bleeding is 4.4% and clinically significant bleeding is 1.2%. (Cook DJ, et al, for the Canadian Critical Care Trials Group. Risk factors for gastrointestinal bleeding in critically ill patients. *N Engl J Med.* 1994). Incidence varies depending on severity of illness and type of patient population studied.
- V. **Risk Factors**
 - a. Mechanical ventilation: Cook DJ, et al, for the Canadian Critical Care Trials Group. Risk factors for gastrointestinal bleeding in critically ill patients. *N Engl J Med.* 1994
 - b. Coagulopathy: Cook DJ et al.
 - c. Stroke/Head trauma: Kamada T et al. Gastrointestinal bleeding following head injury: a clinical study of 433 cases. *J Trauma.* 1977;17: 44–47. Davenport RJ et al. Gastrointestinal hemorrhage after acute stroke. *Stroke.* 1996;27:421-424.
 - d. Burns: Pruitt et al Annals Surgery 1970.
 - e. Hypotension
 - Overall there is a strong relationship between severity of illness, length of time in ICU, duration of mechanical ventilation and the development of stress ulceration.
- VI. **Prevention**
 - a. Avoid local irritants (NSAIDS, aspirin)
 - b. Wean vasopressors ASAP.

- c. Initiate enteral feed: (Raff et al Burns 1997)
- d. Pharmacologic therapy.
 - i. H₂ blockers – Appears to be more effective than sucralfate (incidence 1.7% H-2 vs 3.8% sucralfate). Cook DJ, et al, *N Engl J Med*. 1994
 - 1. Some evidence suggests that continuous infusion may be better. Heiselman DE et al Randomized comparison of gastric pH control with intermittent and continuous intravenous infusion of famotidine in ICU patients. *Am J Gastroenterol* 1995. Of note, in Cook et al study H₂blocker was given as a bolus q 8 hour
 - ii. Sucralfate – Meta-analysis suggest may be equal in efficacy to H₂ blockers. Messori et al *BMJ* 2000.
 - iii. PPI – appears to be as effective as H-2 blockers (Levy et al. *Dig Dis Sci* 1997)

VII. **Controversy** – It is established that the use of anti-acid therapy promotes gastric colonization with pathogenic bacteria, and that aspiration of these bacteria may lead to high incidence of nosocomial pneumonia.

In the NEJM paper (Cook et al), the incidence of nosocomial pneumonia in the ranitidine group 19.1% compared with the sucralfate group 16.2% was not statistically significant. In the Messori meta analysis (BMJ 2000), ranitidine was associated with a significantly increased rate of nosocomial pneumonia over sucralfate.

Current practice is to use either H₂-blocker or sucralfate.

Finally, the study by Cook et al (Crit Car Med 1999) also found that the risk of clinically important GI bleeding was reduced in patients receiving enteral feedings. However, patients were not randomized to receive or not receive enteral feedings, so *the practice of stopping GI prophylaxis in patients receiving tube feeds is not recommended.*

VIII. Table summarizing results from controlled studies:

Table 2 Results of controlled trials of stress ulcer prophylaxis in high-risk patients

Study/treatments	No. of patients	% with bleeding	P
Martin et al ³⁷			
H ₂ RA (cimetidine)	65	14	
Placebo	66	33	<.05
Zinner et al ³⁸			
H ₂ RA	100	14	NS vs no treatment
Antacid	100	5	<.005 vs no treatment .005 vs cimetidine
No treatment	100	20	
Weigelt et al ³⁹			
H ₂ RA (cimetidine)	61	5	NA
Antacid	16	0	NA
Kingsley ⁴⁰			
H ₂ RA (cimetidine)	124	4.8	NA
Antacid	125	8.8	NA
Ben-Menachem et al ⁹			
H ₂ RA (cimetidine)	100	5	NS vs placebo
Sucralfate	100	5	NS vs placebo
Placebo	100	6	
Cook et al ³³			
H ₂ RA (ranitidine)	596	1.7	
Sucralfate	604	3.8	.02 vs H ₂ RA
Levy et al ³¹			
H ₂ RA (ranitidine)	35	31	
PPI (omeprazole)	32	6	<.005 vs H ₂ RA
Azevedo et al ⁴¹			
H ₂ RA (ranitidine)	38	10.5	
Sucralfate	32	9.3	
PPI (omeprazole)	38	0	NS vs H ₂ RA and sucralfate
Hastings et al ⁴²			
Antacid	51	4	<.005
Placebo	49	25	

Abbreviations: H₂RA, histamine₂ receptor antagonist; NA, not available; NS, not significant; PPI, proton pump inhibitor.

M.M. PA Catheter and Pulmonary Hypertension

There is only evidence for increased complications, no benefit for routine use of PA catheter in sepsis, ARDS, and cardiogenic shock.

I. Indications (NEED to measure PA pressure, PCWP, CO):

- 1) Diagnose Pulmonary Hypertension
- 2) Rule out Tamponade (equalization of pressures)
- 3) Unable to determine cause of shock after evaluation/CVP
- 4) Complicated hemodynamic management (eg., sepsis plus CHF, plus ESRD)
- 5) Need to calculate Cardiac output/mixed venous O₂ sampling for some reason

II. Contraindications (absolute and relative):

- 1) Prosthetic TV or PV
- 2) Known R cardiac tumor or clot
- 3) R sided endocarditis
- 4) LBBB (everyone needs EKG prior to PA Cath)
- 5) Significant coagulopathy

Complications: mortality rate 0.02%-1.5% (JAMA 2001 review).

Complications are same as CVL, plus arrhythmia, PA rupture, valvular damage.

PA Catheter Insertion Basics

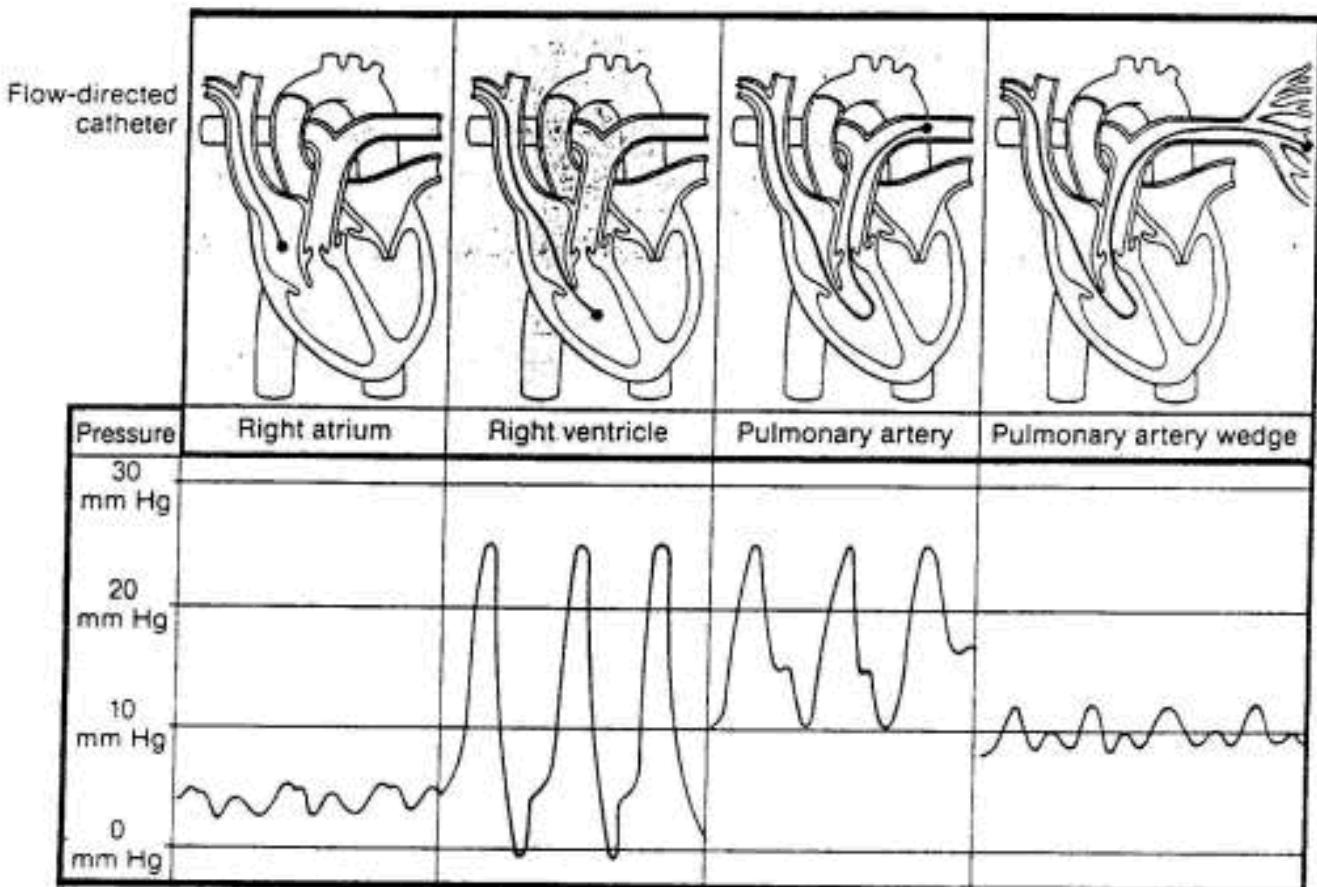
Insertion: after consent, 7French "Cordis" is inserted in same manner as a triple lumen catheter. Best sites to float a PA catheter through the Cordis are:

1. Right IJ
2. Left Subclavian
3. Femoral (usually need fluoroscopy for femoral and any other site)

After flushing the ports, testing the balloon, and testing the catheter for proper waveforms ('fling' catheter look for waves and 'square root sign' after catheter is flushed), you can float the catheter through the Cordis.

REMEMBER: when moving forward, Balloon must be ALWAYS UP. When moving backwards balloon must be ALWAYS DOWN.

PA catheter waveforms:



Normal values:

RA/CVP: 0-5mmHg

RV: 15-30/0-8,

elevated RV diastolic pressure signals RV failure

PA: 15-30/4-14; mean PA pressure >25=pulmonary hypertension

PAOP: mean 9, 5-12

CO: 4-8 L/min

CI: 2.5-4.5 L/min/m sq

Central venous O₂ sat: 65-85%

Mixed venous O₂ sat: 60-80%

SVR: (MAP-RA)80/CO, 800-1200 dynes.sec/cm

PVR: (mean PAP-PAOP)80 /CO, <200 dynes.sec/cm

O₂ content: (0.0138 x Hgb x SaO₂) + 0.0031*PO₂

Typical Hemodynamic Patterns:

Scenario	RA	RV	PAS	PAD	PAOP	CO/CI	SVR
Normal	0-5	15-30/0-8	15-30	5-15	5-12	4-8/2.5-4.5	1200
Hypovolemic	0	12/3	12	7	4	3.5/1.7	1600
Septic	3	12/3	12	7	5	10/5	400
LCardiogenic	13	40/9	40	24	24	3.5/1.7	2000
RVMI	20	40/18	25	12	12	4/2.0	1800
PA HTN	16	70/12	70	35	12	4/2.0	1600
Diastolic dys	16	60/12	60	24	24	4/2.1	1600
Tamponade	18	30/18	30	20	18	4/2	1800

Pulmonary Hypertension

I. **Defined** by mean PA pressure >25 at rest or >30 with exercise, with normal PCWP (<15)

II. **Classified as:**

Group I. Pulmonary arterial hypertension

- Idiopathic (IPAH)
- Familial (BMPR2 mutation)
- Related to other conditions
 - Stimulants/anorectics
 - Portal HTN
 - HIV
 - Sickle cell
 - HHT
 - Splenectomy
 - Thyroid disease
 - Collagen vascular disease
- Pulmonary veno-occlusive disease

Group II. Pulmonary venous hypertension

- Left-sided heart disease (PCWP >15, no PA diastolic-to-PCWP gradient)

Group III. Pulmonary hypertension associated with hypoxemia (or parenchymal lung disease)

- COPD
- ILD
- OSA
- Chronic high altitude
- Developmental disease

Group IV. Pulmonary hypertension due to chronic thromboembolic disease

Group V. Other: Sarcoid, LCH, LAM, extrinsic PA compression

III. **Diagnosis**

a. Right heart catheterization is gold standard

- b. Echo is inaccurate (Arcasoy SM AJRCC 2002): Echo PAP falls within 10mmHg of PA cath 50% of the time, and 10% time the difference is 30mmHg! Also 48% with estimated sPAP >45 on echo do not have pulmonary hypertension by RHC.
 - c. Clinical scenario, RHC data, CTPA, PFTs, serology data, and functional status define Classification Group and treatment.

IV. Treatment

- a. Depends on Group. In general, For all classes besides Group I, treatment focuses on the underlying disease.
 - i. For group I patients, need to assess NYHA functional Class.
- b. Prosteneoids (epoprostenol, treprostienil) are 1st choice for severe disease NYHA III, IV: They are potent, short-acting vasodilators, that have anti-proliferative, and anti-platelet agents activity.
 - i. Reduce mean PAP, PVR, increase CO and 6minute walk, and probably improve survival (Barst RJ et al NEJM 1996).
 - ii. Downside is need for continuous infusion, although newer inhaled Iloprost is an option (though probably should be used in less severe disease)
- c. Endothelin antagonists (eg., bosentan)and Phosphodiesterase inhibitors (eg., Viagra)
 - i. Used for less severe disease
 - ii. Improve symptoms and 6 minute walk time
 - iii. No known survival benefit
- d. Additional treatments:
 - i. O2 supplemtation for hypoxemic patients
 - ii. Anti-coagulation
 - iii. No clear benefit to inotropes (e.g. Digoxin)
 - iv. Pulmonary rehab
 - v. Transplant
 - vi. Atrial septosotomy