New York-Presbyterian Hospital
Weill Cornell Medical College
Medical Intensive Care Unit

MICU Curriculum
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For use by staff and students at the New York Presbyterian Hospital MICU

ICU Curriculum
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Chapter 1 Introduction to Critical Illness

Severe injuries result in organ failure and the systemic inflammatory response syndrome (SIRS) [1]. Examples of injuries include infection, trauma, intracranial hemorrhage, burns, major surgery, cardio-pulmonary bypass, rapidly proliferating malignancies and sterile tissue necrosis. The stereotypical pattern of SIRS and organ failure arising from such diverse injuries suggests that some host responses are maladaptive and contribute to organ dysfunction. The severity of the illness is influenced by host factors, prior health status and comorbidities. When this cascade is severe and generalized it is called the multiple organ dysfunction syndrome (MODS). The most common organ failures are shock, respiratory failure, encephalopathy, acidosis and oliguric renal failure. Coagulopathy is very common and manifests as thrombocytopenia and elevation of prothrombin time and D-dimers.

Figure 1. Simplified model of the pathways leading from injury to MODS

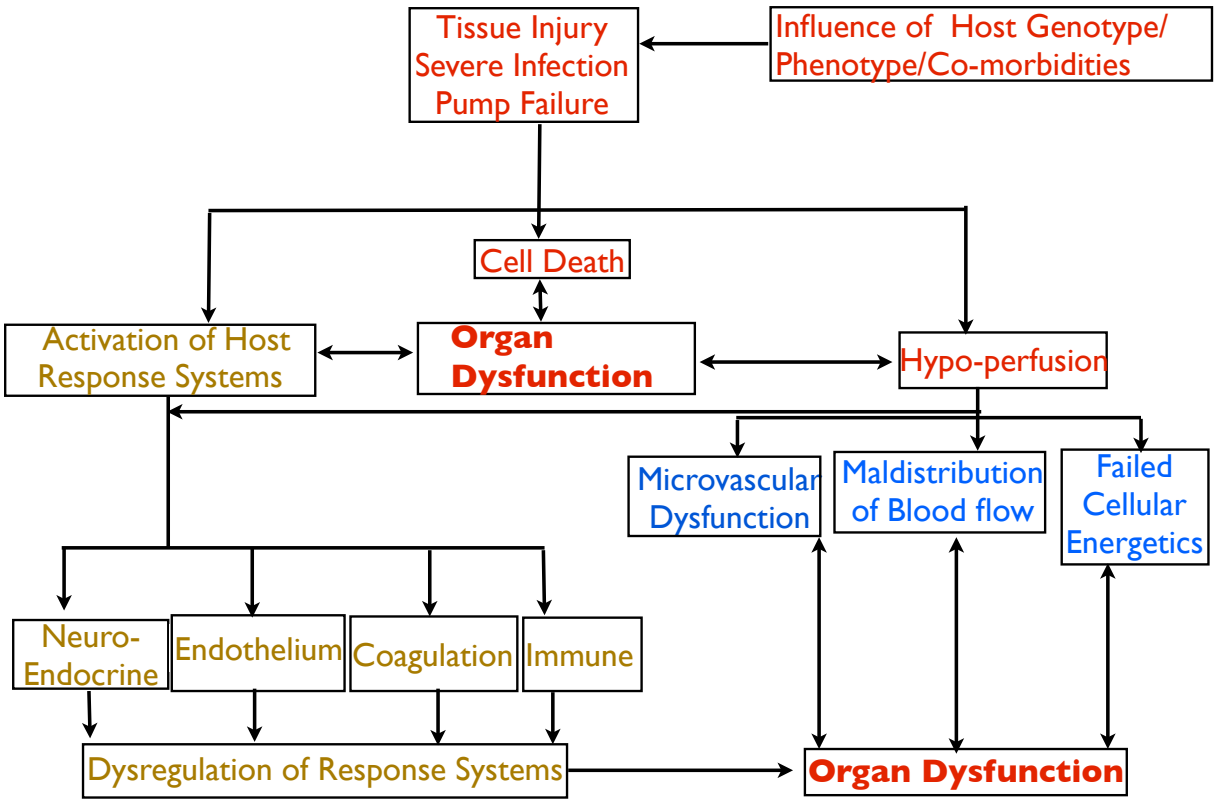


Figure 2. Systemic Inflammatory response Syndrome

- Fever or hypothermia
- Tachycardia
- Tachypnea or respiratory alkalosis
- Leukocytosis or elevated band forms

Time course of critical illness

Critical illnesses tend to follow a typical pattern. During the initial response to injury the patient develops SIRS and there is a tendency towards hypoperfusion and respiratory failure. The hypoperfusion is typically associated with a reduction in oxygen delivery. Patients often require mechanical ventilation and fluid resuscitation and often benefit from normalization of indices of oxygen delivery. For example, continuing trauma resuscitation until there is reversal of hypoperfusion induced acidosis and base deficit results in better outcomes[2]. With sepsis, resuscitation should continue until there is normalization of the central venous oxygen saturation or arterial lactate[3, 4]. During this initial phase of critical illness patients commonly have a high work of breathing even on mechanical ventilation and may benefit from deep sedation and neuromuscular blockade[5, 6]. Central venous access and invasive monitoring are usually necessary.

After the initial phase of resuscitation and stabilization the focus should be on limiting medications and indwelling catheters. Attempts to measure physiologic variables and increase oxygen delivery are less useful and may be harmful[7, 8]. You must continuously attempt to liberate the patient from the interventions that were lifesaving during the resuscitation phase. Remove catheters, attempt negative fluid balance, and institute early physical therapy[9, 10]. Awaken patients on mechanical ventilation daily and attempt an unassisted breathing trial[11]. The patient recovers or enters a phase of more chronic critical illness. This phase is dominated by recurrent nosocomial infections. Strict infection control, provision of adequate nutrition and prophylaxis against thromboembolism is essential at every phase of the illness.

General Approach

The survey approach is applicable to all critically ill patients. During the primary survey you must ensure the airway is patent, and provide adequate ventilation/oxygenation and organ perfusion and cervical spine immobilization. In the next phase perform a complete physical examination and determine which organs systems are failing. Use the history, medical records and

radiologic/laboratory data to create a narrative of what events have led up to and created the critical illness. Information provided from the patient and their family/friends as well as their main physicians is absolutely essential. Determine if the current crisis has occurred in the context of a long-standing illness. Make a careful assessment of the performance and nutritional status and the details of chronic health problems.

Prognostication

In general I find the composite of three factors useful for predicting the outcome of a critical illness:

- Number and severity of organ failures
- Performance and nutritional status prior to onset of critical illness
- Presence of an untreatable chronic illnesses that is contributing to the current crisis

Unfortunately you will often be in the position of having to decide weather or not to provide life sustaining invasive interventions to patients who may be too ill to benefit from them. If the goals of care are unclear, in general it is wise to proceed with stabilization until you are able to set appropriate goals.[12]

Chapter 2 Airway Management

The first priority in managing any critically ill patient is to secure the airway. Foreign bodies can obstruct the airway as occurs during choking on food (treated with the Heimlich maneuver or extraction with Magill forceps). The most common cause of airway obstruction in an unconscious patient, however, is occlusion by the tongue and soft tissues of the pharynx. The following protocol enumerates steps to maintain a patent airway in an unconscious patient. This protocol emphasizes manual ventilation and delays endotracheal intubation until adequate pre-oxygenation and ventilation have been performed. One of the most common errors made by physicians in emergency situations is proceeding directly to endotracheal intubation without first establishing a temporarily secure airway and manual ventilation.

Unconscious Patient with Stable Cervical Spine

I) Determine if airway is patent by physical examination
- Assess for stridor
- Assess if chest wall rises and falls with each breath
- Assess breath sounds

II) If airway is patent
- Provide supplemental oxygen if indicated
- Continue with general assessment of patient

III) If airway is not patent or inadequate spontaneous breathing
- Head tilt and chin lift to open airway
- Set up suction apparatus with rigid suction catheter
- Attach bag-valve mask (BVM) to high flow (>11L/min) oxygen
- Place BVM over patient's face
- Press down gently with your thumbs on cephalad portion of mask against the bridge of the nose
- Press down gently with your index fingers on the portion of the mask covering the chin
- Gently lift the mandible *anteriorly* with your remaining three fingers on each hand

- A second operator compresses the bag to deliver tidal volume
- Adequate ventilation occurs when the chest wall rises with each breath delivered and condensation forms in the mask upon exhalation. Excessive amounts of air should not leak out from the sides of the mask.
- Coordinate manual ventilation with patient effort if s/he is breathing spontaneously
- Ventilate at appropriate rate: e.g. 15/min if patient has severe metabolic acidosis or at slower rate (e.g. 10/min) if patient has chronic CO_2 retention. Prevent auto-PEEP by allowing complete exhalation prior to delivery of next breath

IV) If chest wall does not rise with manual ventilation

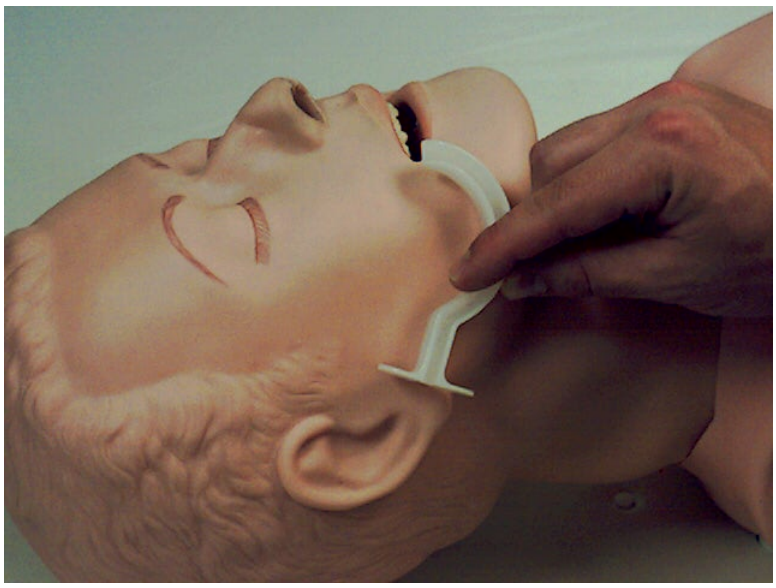
- Repeat head tilt and chin lift
- Reposition seal with mask and re-attempt manual ventilation

IV) If chest wall still does not rise with manual ventilation

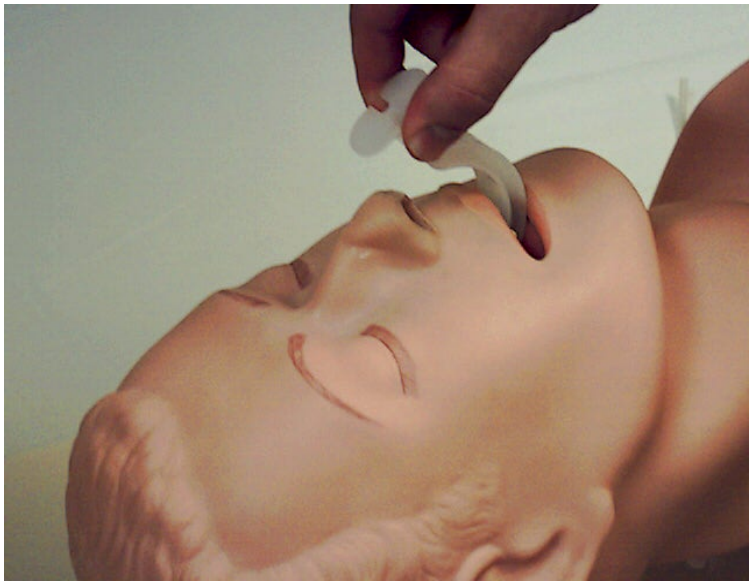
- Temporarily remove BVM and inspect airway for secretions or foreign bodies
- If patient unconscious, place an appropriate sized oral pharyngeal airway (should reach from tragus to ipsilateral angle of the mouth when held against the side of the face). The oral airway's curved tip should face the palate during insertion. Advance the oral airway between the palate and tongue until approximately 2/3 of it lies within the mouth. Next, rotate the oral airway 180^0 around its long axis so that the curved tip points caudad. Advance the oral airway until the proximal end lies anterior to the teeth and the distal end lies posterior to the tongue. A properly placed oral airway prevents the tongue from occluding the airway.
- Repeat head tilt/jaw lift and replace BVM with a good seal

II) The above steps should secure the airway and provide adequate ventilation in the overwhelming majority of patients

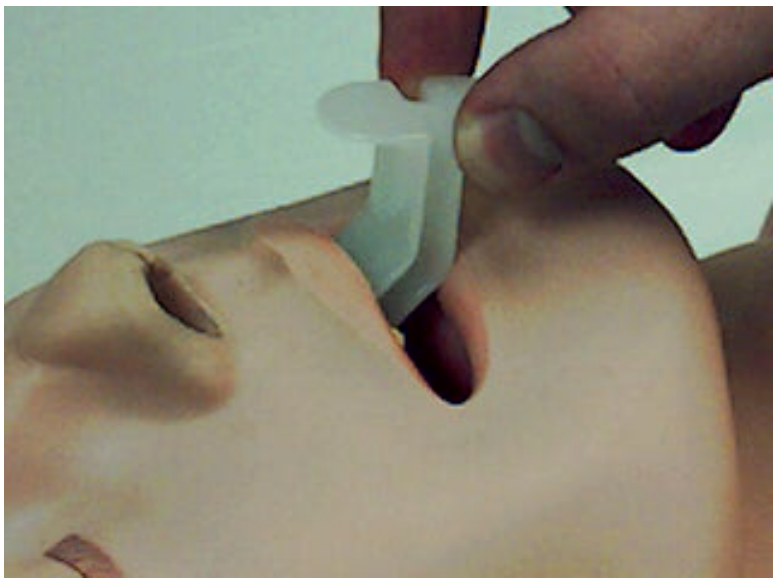
- Manually ventilate the patient until he/she is adequately pre-oxygenated and someone skilled in intubation is present and has equipment properly assembled
- If you cannot manually ventilate a patient with a BVM, a true airway emergency exists. Get as much help as possible and proceed to endotracheal intubation or placement of an laryngeal mask airway



Checking oral airway for correct size



Inserting the oral airway



Rotating the oral airway into position

Two-operator technique for manual mask ventilation

Chapter 3 How to be a Cardiac Arrest Team Leader

1) Pre-code responsibilities

- Know ACLS algorithms
- Know how to operate the defibrillator/pacer
- Walk quickly but calmly to the location of the cardiac arrest

2) General responsibilities

- Identify yourself as code leader
- Speak loudly in a calm voice
- Determine if patient is DNR
- Assign people, by name, to specific tasks (e.g. "Dick control the airway, Jane perform chest compressions, Ishmael operate the defibrillator")
- Code leader should not perform specific tasks but should stand back, observe entire situation and direct the team
- Code leader may need to calmly but firmly ask the team to lower their voices and direct all comments to the leader
- Constantly verify that ABCD goals are met (airway, breathing, circulation and early defibrillation)
- **Support circulation by performing chest compressions without interruption** (interrupt to defibrillate; not for frequent pulse or rhythm determinations

Most treatable cardiac arrests in the hospital are due to ventricular tachyarrhythmias or respiratory failure; therefore, you must administer adequate ventilation and, if indicated, defibrillation within seconds of your arrival

- Generate hypothesis about why arrest occurred (and treat underlying problem if possible)

3) Principles of airway management for cardiac arrest (also see previous chapter)

- Mask bag ventilation is more important than endotracheal intubation
- Do not sacrifice chest compressions for prolonged attempts to place an endotracheal tube
- A properly placed laryngeal mask airway (LMA) is a suitable alternative to intubation in a difficult airway situation

- For purely electrical arrests (VF and VT) place emphasis on prompt defibrillation and uninterrupted CPR. Endotracheal intubation can be delayed for the first 6 minutes (or 3 rounds of CPR)
- Ventilation in the first minutes is a higher priority for PEA/asystolic arrests and arrests due to respiratory failure or shock than in VF/VT arrests
- **Ratio of breaths to chest compressions prior to intubation is 2:30**
- **After intubation ventilate at 8-10 breaths/minute** – this correlates to a breath every 6 seconds
- Hyperventilation is detrimental during CPR
- Code Leader should count the delivered respiratory rate, and ask the airway operator to slow respirations if they are too fast

4) Basics of ventricular tachyarrhythmias

- Clinically stable, sustained VT: Consider synchronized electrical cardioversion or anti-arrhythmic therapy; e.g., amiodarone 150mg IV over 10 minutes
- Unstable VT with pulse: synchronized cardioversion biphasic 150J; consider additional anti-arrhythmic drug therapy
- Our defibrillators default to unsynchronized defibrillation after each shock, you must re-select synchronization in order to cardiovert
- Pulseless VT or VF: Biphasic defibrillator use 150 J followed by approximately two minutes of CPR prior to pulse/rhythm check
- Shock refractory pulseless VT or VF: Epinephrine 1mg IV (or vasopressin 40 units IV); repeat defibrillation then amiodarone 300mg IV (or lidocaine 1mg/kg IV); repeat defibrillation
- Success inversely proportional to time to defibrillation
- Maximize CPR and avoid frequent rhythm and pulse checks
- If successfully cardioverted/defibrillated, start appropriate maintenance infusion
- Polymorphic VT with long QTc (torsade): Mg infusion and overdrive pace if pause dependent
- VF and polymorphic VT are often caused by acute coronary syndromes; consider Aspirin, b-blocker (if stabilized) and reperfusion therapy
- Can give repeat doses of epinephrine (q 3-5minutes), and amiodarone (additional 150mg)

5) Principles of supraventricular tachycardia

- If unstable: synchronized cardioversion biphasic 100J
- If stable: rate control; consider chemical/electrical cardioversion

- Be careful when treating wide complex tachycardia as supraventricular with aberrancy (could be VT)

6)Asystole

- High quality chest compressions
- Avoid over-ventilation
- R/O "fine VF" by checking second lead (if in doubt: defibrillate)
- Epinephrine
- Consider pacing

7) Pulseless electrical activity

- High quality chest compressions
- Avoid over-ventilation
- Epinephrine

8) Outcome of CPR

- Success defined as neurologically intact patient who survives to hospital discharge
- Significantly better for tachyarrhythmias
- Prognosis worse for patients for patients with asystole, PEA, un-witnessed arrest, severe underlying disease or poor functional status

9) Terminating CPR

- Terminate if patient is DNR
- Terminate when you judge efforts to be futile; use your assessment of prognosis and reversible pathology, not rigid rules about duration of effort

10) Central Lines

- Central venous access is helpful but not necessary (if there are functioning peripheral IV's)
- Femoral venous catheters have a high rate of mechanical complications
- Subclavian vein catheterization is a good option during cardiac arrest
- Intraosseous catheters if unable to get adequate IV access

11) Miscellaneous

- Sodium bicarbonate not routinely indicated (unless known hyperkalemia, acidemia or tricyclic overdose)
- No known benefit to escalating doses of epinephrine

- NAEL drugs can be administered via endotracheal tube (naloxone, atropine, epinephrine, lidocaine) at one and one-half dose
- Keep the field free of contaminated sharps/needles

12) Care after return of spontaneous circulation (ROSC)

- Transfer patient to appropriate monitored setting
- Asses for appropriateness for moderate therapeutic hypothermia for anoxic brain injury[13, 14]
- Initiate cooling on hospital wards using ice packs, cold saline gastric and bladder lavage, and cold saline infusion and Arctic Sun cooling device in MICU
- Chart note should include: events immediately preceding code, initial rhythm, medications administered, estimation of time from loss of pulse to CPR and to restoration of spontaneous circulation, and neurological exam after ROSC (document the FOUR score)[15]
- Avoid hyperoxia goal SpO_2 94%
- If unresponsive obtain continuous VEEG monitoring
- Contact responsible team/attending and patient's health care proxy and/or family

Chapter 4 Hemodynamics

Cellular homeostasis requires constant perfusion.
The circulation provides oxygen, nutrients, immunoglobulins and the chemical mediators of cellular function and carries away CO_2, products of metabolism and mediators of cellular interactions. Cells require large amounts of energy to perform work and create organization. Cells, for example, consume one third of their ATP by pumping sodium against its concentration gradient to maintain tonicity, size and membrane potential.

Cells require a constant supply of oxygen However oxygen is highly toxic to cells and nucleic acids. Therefore the cellular oxygen tension is kept low (20-40 mmHg). In the mitochondria, where oxidation is linked to phosphorylation of ADP, the oxygen tension is approximately 2.4 mmHg. Oxygen flows into cells and mitochondria as it is consumed in cellular respiration. Blood serves as a reservoir of oxygen for the tissues. The oxygen tension of arterial blood (paO_2) is normally 90mmHg. Since 0.003ml O_2 are dissolved in 1 dl of blood for every 1mmHg of oxygen tension there is normally 0.27mlO_2 dissolved in every dl of blood. The amount of dissolved oxygen is usually negligible and we ignore it in physiologic calculations. Each gram of fully saturated hemoglobin carries 1.34mlO_2. Therefore the content of oxygen in arterial blood (CaO_2) is

$$CaO_2 = 1.34\ ml O_2 \times Hgb \times SaO_2$$

Normally $CaO_2 = 1.34 ml O_2 \times 15 gm/dl\ blood \times 100\% = 20 ml O_2/dl\ blood$

At rest, the lungs take up about 250mlO_2/minute. This term is called $\dot{V}O_2$ which is measured by a metabolic cart study using mass spectrophotometry analysis of inspired and expired gasses. $\dot{V}O_2$ Is often also called the oxygen consumption since consumption and uptake are equal over time for any person. For clarity we refer to the oxygen consumption by the cells as $\dot{Q}O_2$ and reserve $\dot{V}O_2$ for oxygen uptake by the lungs.

The rate of oxygen flowing in the systemic arteries is called oxygen delivery $\dot{D}O_2$. The $\dot{D}O_2$ is defined as

$$\dot{D}O_2 = CaO_2 \times \text{Cardiac output}$$

Normally $\dot{D}O_2 = 20mlO_2/dl$ blood x 5 L blood/minute = $1000mlO_2/min$

The oxygen tension of venous blood varies with the metabolic rate of the organ from which the blood returns. The renal veins carry blood with fairly high oxygen tension as the kidneys get 15% of the cardiac output for filtration but have low metabolic rates. Blood returning from the brain or exercising muscle is more hypoxemic. Blood mixes in the right-sided circulation and the pulmonary arterial blood can be sampled by right heart catheterization. The oxygen saturation of mixed venous (i.e. pulmonary artery) blood is called the $S\bar{v}O_2$. This mixed venous oxygen saturation serves a measure of the ratio between supply of oxygen by arterial blood and its use by the tissues. The normal resting $S\bar{v}O_2$ is 70%. If $\dot{Q}O_2$ increases due to exercise or fever the oxygen extraction ratio by the cells will increase and the $S\bar{v}O_2$ will drop to less than 70%. Normally, there will also be a compensatory rise in $\dot{D}O_2$. The minimum obligatory $\dot{Q}O_2$ to maintain homeostasis is around 250 mlO_2/min. The normal resting $\dot{D}O_2$ is significantly higher than this value. $\dot{D}O_2$ can decrease, therefore, without any decrease in $\dot{Q}O_2$ although $S\bar{v}O_2$ will decrease to <70%. Once $\dot{D}O_2$ decreases below a critical threshold, approximately $300mlO_2/min$, there is insufficient oxygen for basal $\dot{Q}O_2$ and severe organ failure develops[16].

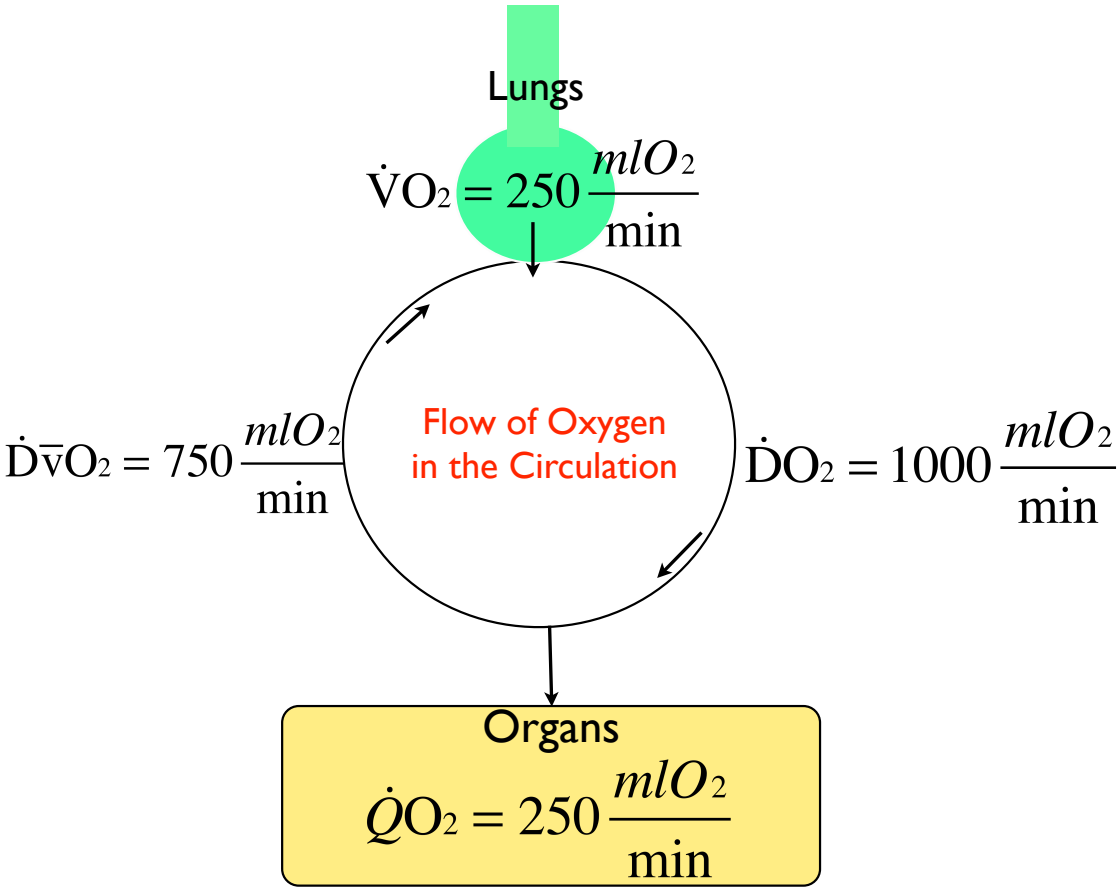


Figure1: Summary of oxygen flow in the circulation.

Cardiac output is proportional to pulse and stoke volume

CO = Pulse x Stroke Volume

The normal CO is approximately 5 L/min, although resting values vary widely and decrease with age.

Cardiac index (CI) is CO indexed to body surface area (BSA)

CI = CO/BSA (normal CI $\geq$ 2.5 L/min/m^2)

Stroke Volume is dependent on preload, afterload and intrinsic myocardial contractility In figure 2, factors that tend to augment stroke volume shown in green. Red denotes factors that usually decrease stroke volume[17].

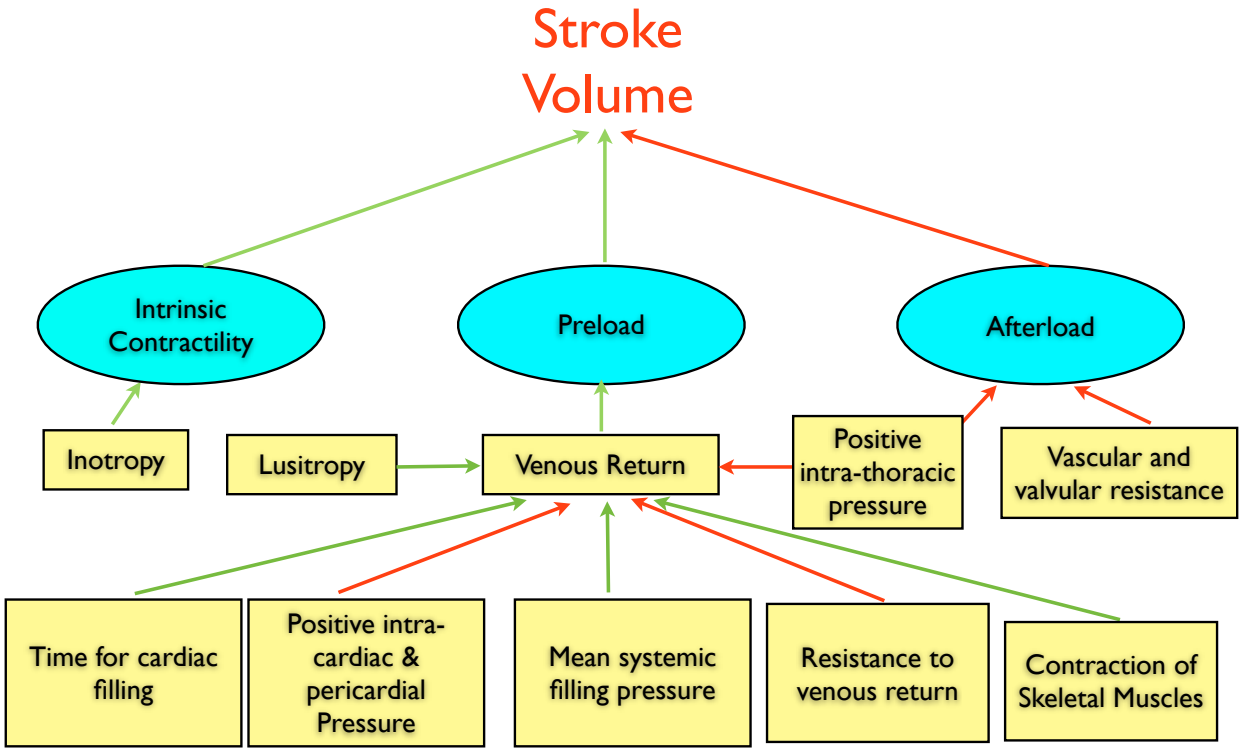


Figure 2

Preload is dependent upon the venous return to the left and right chambers of the heart. Increased venous return increases ventricular end-diastolic volume (i.e. preload). This increased myocardial stretch preceding contraction increases stroke volume. This mechanism insures that, within physiologic limits, the chambers of the heart match their output to the venous return. The venous return is dependent on the pressure gradient between the systemic vasculature and the right atrium. The right atrial pressure is also called the central venous pressure and the average pressure in the systemic circulation is estimated by a value called the mean systemic filling pressure (MSFP). The MSFP is the average pressure in the circulation if there is no pumping by the heart and is normally around 7mmHg (but can be up to 50mmHg). If RAP is constant, increases in MSFP such as by volume expansion or venoconstriction will increase the gradient for venous return. Decreasing venous tone or volume reduces MSFP (Figure 3 & 4). The plateau in the venous return curve at very negative pressures is due to collapse of the compliant veins[17].

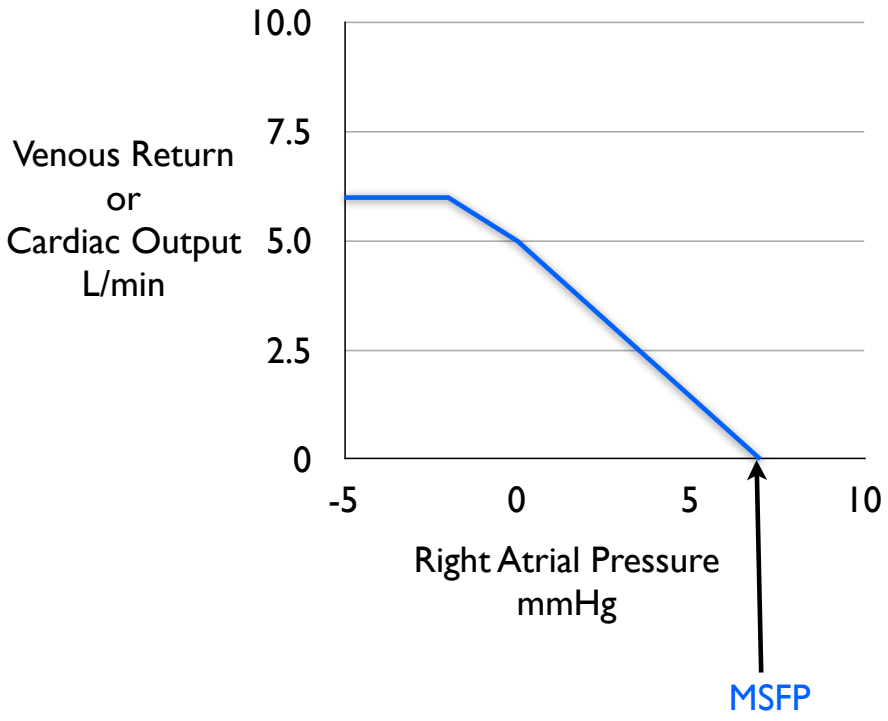


Figure 3: For a given MSFP venous return increases if RAP is low. If MSFP is equal to RAP there is no gradient for venous return and CO is zero. Adapted from Guyton AC, Jones CE and Coleman TG *Circulato Physiology: Cardiac Output and its Regulation.* 2nd edition. Philadelphia WB Saunders, 1973.

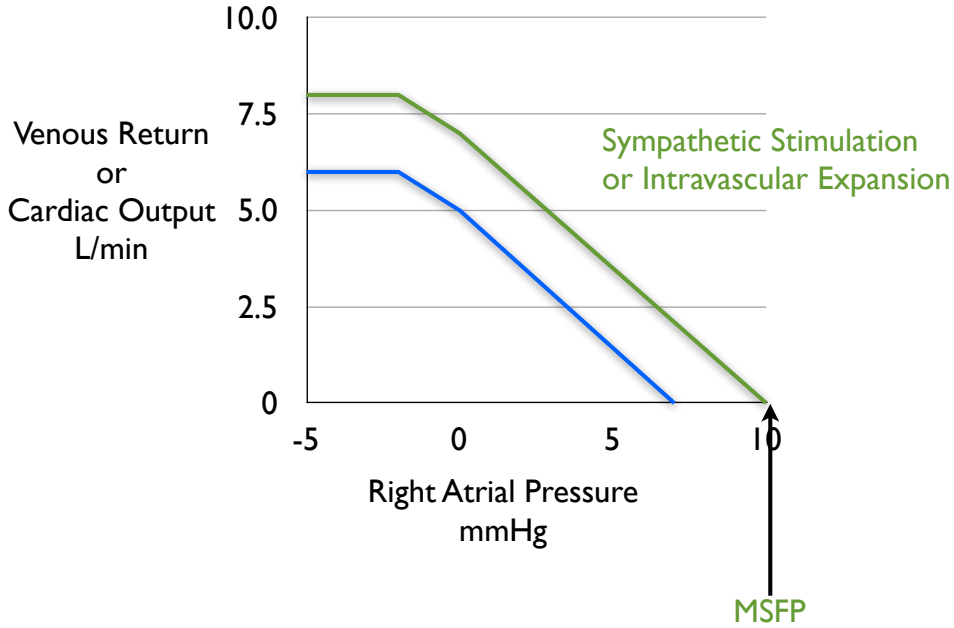


Figure 4: For a given RAP, increasing MSFP with vasoconstrictors or volume expansion will increase venous return Adapted from Guyton AC, Jones CE and Coleman TG *Circulatory Physiology: Cardiac Output and its Regulation.* 2nd edition. Philadelphia WB Saunders, 1973.

Resistance to venous return is due to the ratio of arterial and venous tone. Arterial tone offers increased resistance to venous return and an AV fistula reduces the resistance to venous return. Increased resistance to venous return reduces the slope of the venous return curve. Vasoconstrictors such as norepinephrine constrict veins and arteries and may improve cardiac output in volume expanded patients [17]. Pure arteriolar vasoconstrictors such as aldosterone increase the resistance to venous return and decrease stroke volume [18]

Elevations in intracardiac, intrathoracic or pericardial pressure will decrease the gradient for venous return. Normal exhalation (positive pressure) raises the pressure transmitted to the right atria and therefore decreases the gradient for venous return[17].

Intrinsic contractility of the heart is the degree of myocyte shortening for a given set of loading conditions (afterload and preload). This is typically demonstrated by a cardiac performance curve. The curve is represented as stroke volume vs. right atrial pressure. However it is important to remember that RAP is not an independent variable. The cardiac performance curve is most useful when graphed with venous return curves. The intersection of the two curves best describes the state of the circulation (Figure 5). Impaired systolic or diastolic function as well as increased afterload will rotate the cardiac performance curve down and to the right (Figure 6) [17].

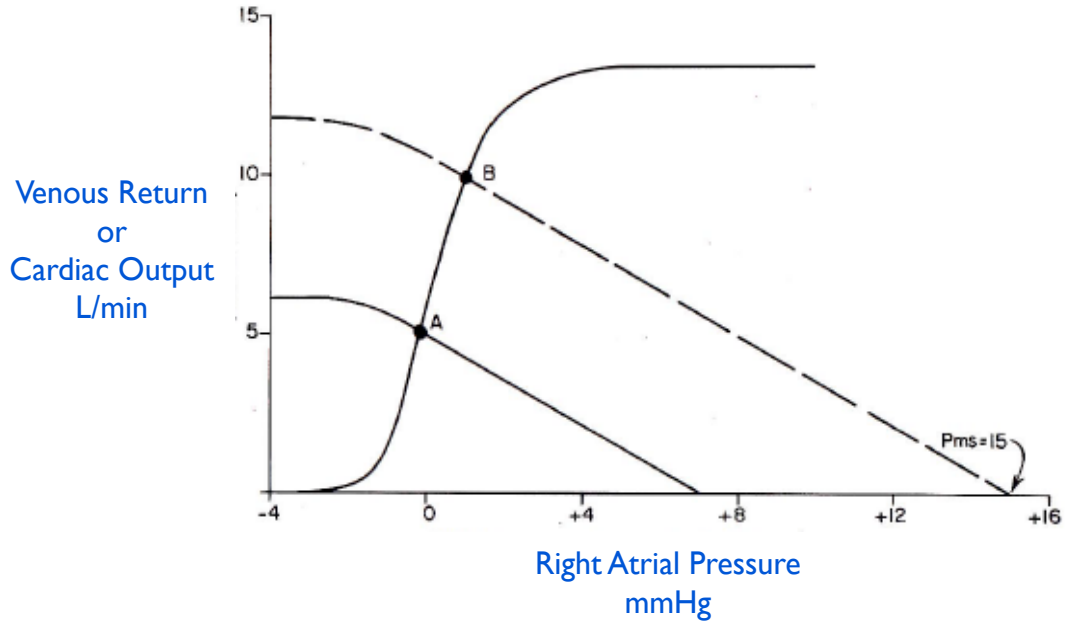


Figure 5: Cardiac performance curve graphed against venous return curves with 2 different MSFP. Point A and B are distinct values for CO although the intrinsic contractility is unchanged Adapted from Guyton AC, Jones CE and Coleman T *Circulatory Physiology: Cardiac Output and its Regulation.* 2nd edition. Philadelphia WB Saunders, 1973.

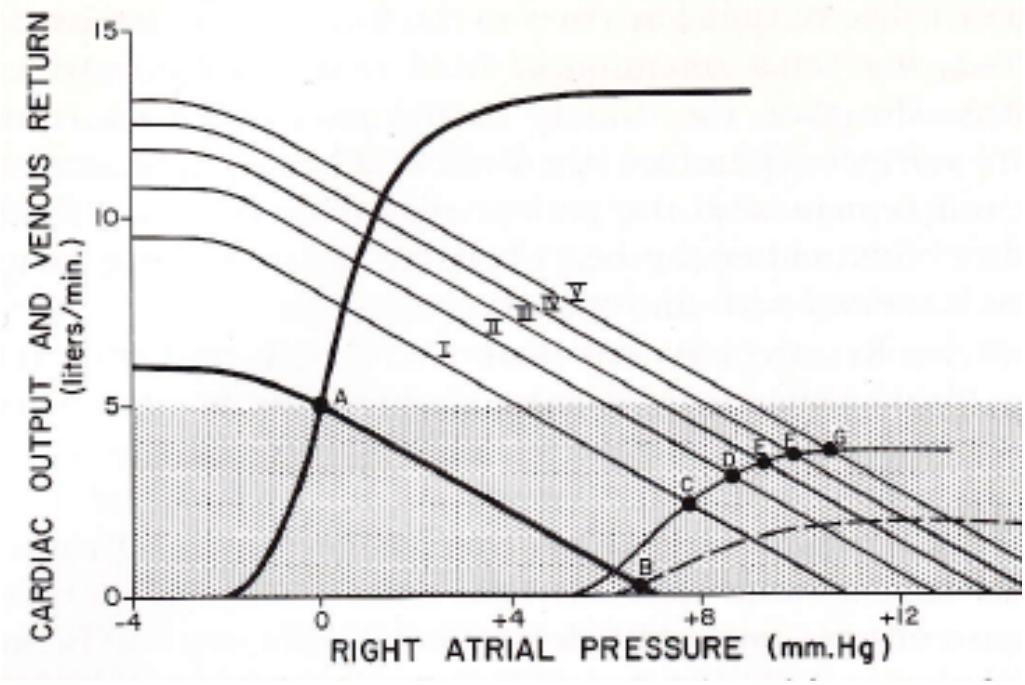


Figure 6: Three cardiac performance curves representing progressively deteriorating cardiac function graphed against multiple venous return curves. "A" is the norma situation. "B" is the result of reduced contractility but no compensatory increase in MSFP. Points C and D show that increasing MSFP recruits stroke volume for a failing ventricle. Points E, F&G show there is a limitation in in stroke volume recruitment from compensatory increases in MSFP. Adapted from Guyton AC, Jones CE and Coleman TG *Circulatory Physiology: Cardiac Output and its Regulation* 2nd edition. Philadelphia WB Saunders, 1973.

Ventilation affects cardiac output

Negative pressure during normal spontaneous breathing reduces the intrathoracic pressure. This lowers the right atrial pressure, which increases the gradient for venous return augmenting stroke volume. Positive pressure ventilation such as during forced exhalation increases intrathoracic and right atrial pressure which diminishes venous return (Figure 7)[17].

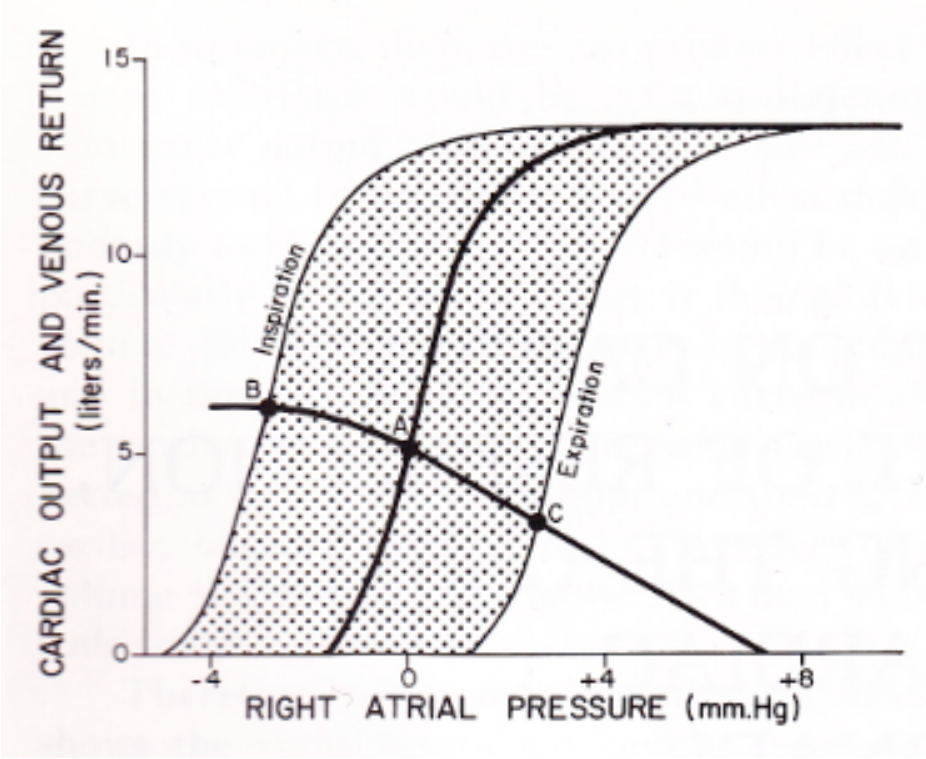


Figure 7 Transmural right atrial pressure varies with intrathoracic pressure. Cardiac output increases with inspiration. Adapted from Guyton AC, Jones CE and Coleman TG *Circulatory Physiology: Cardiac Output and its Regulation.* 2nd edition. Philadelphia WB Saunders, 1973.

Cardiac Output Regulation

In normal states the regulation of venous return is the most important factor regulating cardiac output. The heart pumps whatever blood is delivered to it. This is accomplished by the Frank-starling mechanism and the Bainbridge reflex (increased venous return stretches the sinus node which triggers an increased heart rate[17].

Autonomic control of the circulation is mediated in part through regulation of heart rate. Tachycardia increases cardiac output up to a rate around 150 per minute in normal hearts. Above this rate the inadequate time for filling lowers stroke volume. In patients with impaired lusitropy (relaxation) or mitral stenosis the threshold is lower. Sympathetic activation of B_1 myocardial receptors increases intrinsic contractility, rotating the cardiac performance curve upward and to the left. Sympathetic and catecholamine mediated venoconstriction can raise MSFP and augment venous return and cardiac output[17].

The summation of local tissue metabolic needs regulates cardiac output
With the exception of the pulmonary and glomerular capillary beds, hypoxia causes vasodilation. Acidosis and the byproducts of metabolism also vasodilate the local microvasculature. Therefore hypoxic and catabolic tissues are able to increase their blood flow. When there is a generalized increase in vasodilation, such as occurs during exercise, there is a reduction in the resistance to venous return and afterload. This mechanism increases cardiac output. Therefore the peripheral tissues exercise a great deal of control over the circulation. As tissues require more perfusion they vasodilate which increases cardiac output[17].

Adequate tissue perfusion requires an appropriate distribution of blood flow in addition to sufficient cardiac output. Mediators such as catecholamines, NO ADP, oxygen tension, hydrogen ion concentration influence the relative perfusion of capillary beds. These factors direct blood flow to tissues that require more perfusion. For example the kidneys normally accept 20% of the cardiac output. A normal cardiac output can be insufficient to sustain renal function if flow is diverted away from the glomerular capillary beds. This situation happens in hepato-renal syndrome in which a markedly increased cardiac output is shunted away from the kidneys through splanchnic and cutaneous vessels. In shock states, endothelial dysfunction and sludging of the microcirculation with neutrophils, sloughed endothelial cells and fibrin impair perfusion.

Thermodilution can measure cardiac output. Cool saline is injected into the right atrium via a side port in a pulmonary artery catheter. A thermistor at the distal tip of a pulmonary artery catheter (or axillary/femoral artery PiCCO catheter) measures the fall and recovery of the temperature of blood in the pulmonary artery. The area under the idealized thermodilution curve is proportional to the cardiac output. Tricuspid regurgitation adds error to this calculation because cooled blood flows back up into RA with RV systole.

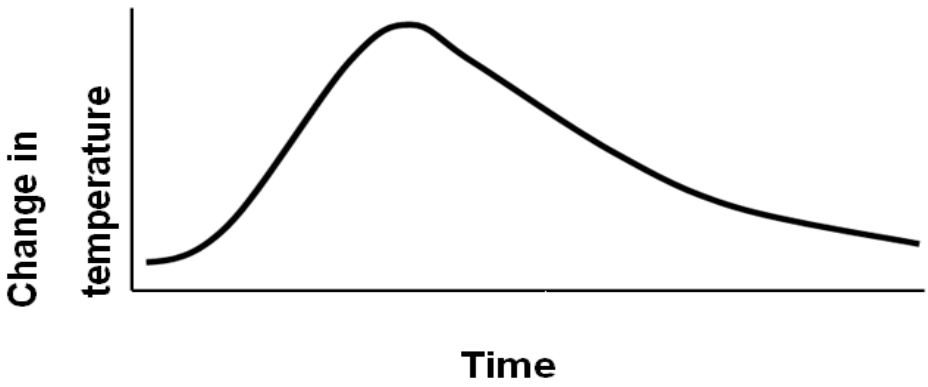


Figure 8 Idealized thermodilution curve. The drop in temperature is plotted as positive.

The Fick method can also derive cardiac output.

The Fick method states that the rate of oxygenated blood flow away from the lungs ($\dot{D}O_2$) is equal to the rate of oxygen flowing in mixed venous blood to the lungs plus the rate of oxygen added to blood by the lungs. The rate of oxygen flow away from the lungs is equal to the cardiac output times the content of oxygen in arterial blood (CaO_2). The rate of oxygen flowing to the lungs is equal to the cardiac output times the content of oxygen in mixed venous blood in the pulmonary artery ($C\bar{v}\ O_2$) The figure below is a schematic representation of the Fick principle.

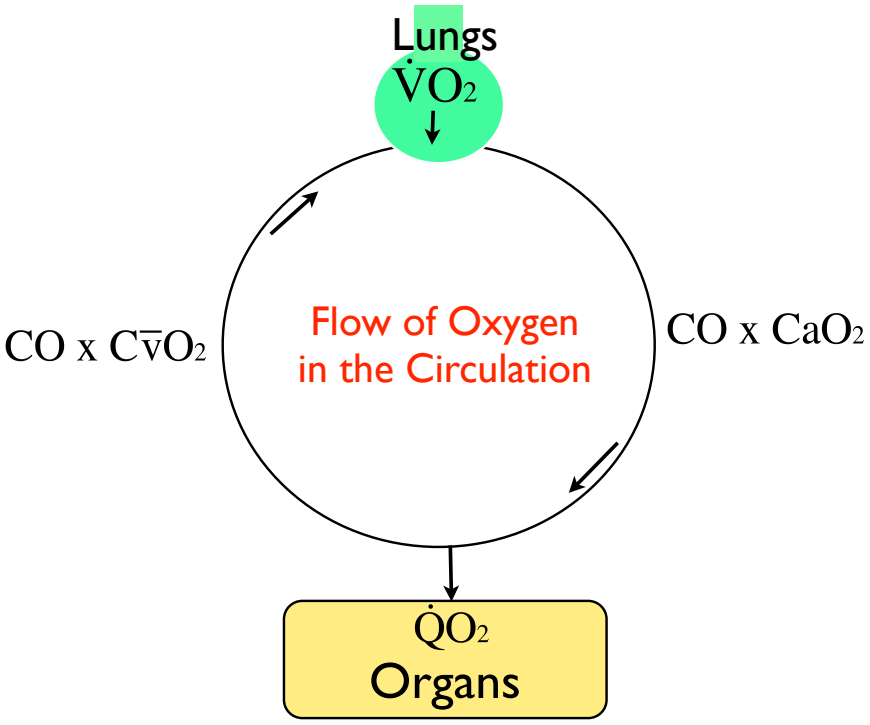


Figure 9 The Fick principle used to determine cardiac output. Measure $\dot{V}O_2$ with a metabolic cart and obtain a sample of mixed venous blood from the pulmonary artery.

$$(CO \times C\bar{v}O_2) + \dot{V}O_2 = (CO \times CaO_2)$$

$$CO = \frac{\dot{V}O_2}{CaO_2 - C\bar{v}O_2}$$

Stated another way: Cardiac output equals the rate of oxygen uptake by the lungs divided by the arterial-mixed venous oxygen difference. Using normal resting values

$$\mathrm{CO} = \frac{\frac{250 mlO_2}{\min}}{20\frac{mlO2}{dl\ \text{blood}} - 15\frac{mlO2}{dl\ \text{blood}}} = 5\frac{L\ blood}{\min}$$

Chapter 5 Shock

Shock is a syndrome of acute circulatory failure associated with ineffective tissue perfusion and cellular injury.
Cellular injury manifests as multi-system organ dysfunction that is initially reversible. Persistent shock leads to irreversible organ failure and death. The physiological derangements of shock include circulatory failure, microvascular and endothelial dysfunction, and dysregulation of the clotting and inflammatory cascades. Cellular homeostasis fails and cells lose their ability to perform work and ultimately die.

Clinical Assessment of Perfusion

Surrogate Markers of Perfusion

Clinical	Indices of Oxygen Delivery
Blood Pressure	DO_2
Urine output	SvO_2
Pulse	Lactate concentration
Capillary Refill	
Absence of Encephalopathy	
Acidosis/Base excess/Anion Gap	

Blood pressure is the most commonly used marker of perfusion. It is governed by

BP = CO X Systemic vascular resistance

BP, therefore, is also proportionate to stroke volume and pulse. BP reflects the perfusing force of blood in the large arteries. However blood pressure is an unreliable indicator of perfusion in the microvasculature. Healthy young people with severe hypovolemia can have significant hypoperfusion even though their BP is maintained by catecholamine-induced compensation (raising pulse and SVR). Similarly patients with shock whose blood pressure is normalized with vasoconstrictors can suffer from severe hypoperfusion of the microcirculation. Catecholamines constrict arterioles that are upstream from the capillaries which can remain under-filled. However, a mean arterial pressure of 60mmhg or a drop in systolic BP of 30mmhg from baseline is generally suggestive of hypoperfusion.

Indices of oxygen delivery as surrogate markers of perfusion

Obviously shock occurs if $\dot{D}O_2$ falls below the critically low value. The stressors of critical illness such as fever and high work of breathing raise VO_2 requirement. One model of shock suggests that patients may not be able to efficiently increase oxygen extraction to meet the demand of increased QO_2 and therefore patients in shock require high levels of $\dot{D}O_2$. Indeed, survivors of critical illness have higher $\dot{D}O_2$ values. Clinicians therefore often attempt to augment $\dot{D}O_2$ by increasing its constituents (CO, Hgb, and SaO_2) to keep it above its critical value. There is no way to determine critical $\dot{D}O_2$ and therefore clinicians often use the oxygen saturation of mixed venous blood ($S\bar{v}O_2$) to determine if $\dot{D}O_2$ is adequate.

$S\bar{v}O_2$ is an indirect marker of oxygen delivery and perfusion

$S\bar{v}O_2$ reflects the balance between the amount of oxygen delivered and what is consumed. If the $\dot{D}O_2$ is relatively low compared to QO_2 then the extraction ratio will be high and $S\bar{v}O_2$ will be low. Therefore a low $S\bar{v}O_2$ is often used to determine if $\dot{D}O_2$ is low in shock states (as occurs in cardiogenic shock or severe hemorrhage). There are multiple problems with using $S\bar{v}O_2$ to assess adequacy of perfusion. One is that is that $S\bar{v}O_2$ is very low in normal healthy exercise. Another is that its measurement requires a pulmonary catheter. Moreover $S\bar{v}O_2$ can be normal in vasodilatory shock. Therefore many clinicians use other markers to assess the adequacy of perfusion.

End-organ function as surrogate markers of perfusion. In the presence of hypotension or a clinical scenario that may cause shock (e.g. major hemorrhage or infection) clinicians look for shock induced organ dysfunction.

Important abnormalities include:

Respiratory system: Patients in shock will be tachypneic or in respiratory distress even if oxygenation is normal. Minute ventilation increases in response to the metabolic acidosis of shock, but a respiratory alkalosis will also occur due to cytokines and hypoperfusion of medullary receptors. Hypoperfusion of respiratory centers in the brain stem and of respiratory muscles at a time of increased demand can lead to respiratory failure requiring intubation to prevent sudden death. In an animal model of cardiac tamponade apnea preceded cardiac arrest[19]. As shock progresses, ventilation/perfusion mismatches and non-cardiogenic pulmonary edema from endothelial dysfunction commonly cause severe hypoxia (ARDS).

Renal: oliguria (<1/2 ml/kg/hr) is an important early sign of hypoperfusion (except for patients who have oliguric renal failure prior to the onset of critical illness). As shock progresses acute tubular necrosis and acute renal failure may develop.
Metabolic acidosis: due to accumulation of lactate and/or other unmeasured anions.
CNS: encephalopathy manifested as agitation or obtundation

Other abnormalities are common but are less useful for immediate assessment. They include: ischemic hepatopathy (shock liver), ileus, erosive gastritis, pancreatitis, myocardial depression, coagulopathy, thrombocytopenia, hyperglycemia, and immune dysfunction.

Classification of Shock

I) **Hypovolemic shock:** The hallmark of hypovolemia is the loss of intravascular volume leading to decreased venous return. Decreased preload reduces stroke volume and cardiac output. The BP equation predicts that the compensatory mechanisms to maintain perfusion are tachycardia and elevated SVR. Therefore, the patient in hypovolemic shock will be cool and clammy due to peripheral vasoconstriction. The compensation includes sympathetic and catecholamine constriction of the large reservoirs of blood in the venous system to raise MSFP and increase the gradient for venous return. Splenic constriction also mobilizes a large volume of blood[20]. Young healthy patients with intact circulatory reflexes will defend their systemic blood pressure despite severe intravascular fluid deficit. Patients can be in severe shock with a relatively normal BP. They will have tachycardia, narrow pulse pressure, cold and clammy extremities, tachypnea, academia and will be in distress. Ultimately they will lose consciousness typically in the moments before death.

The classic hemodynamic profile of hypovolemic shock is decreased CVP, PCWP, CO, SvO_2 and increased SVR.

Hypovolemic shock is caused by hemorrhage or fluid loss (GI losses, or loss of fluid into the interstitial space such as occurs in pancreatitis, traumatic tissue injury and sepsis).

In hemorrhagic shock the fluid deficit exceeds the amount of shed blood. This is because the hypoperfused cells are unable to maintain their resting membrane potential. Sodium flows into the cells as the ion pumps fail causing intracellular fluid sequestration. This causes severe interstitial fluid deficit which tends to pull more fluid out of the intravascular space[21].

If prompt fluid resuscitation is not administered the patient can develop an irreversible shock state. At that point no amount of fluid or blood resuscitation will

correct the hemodynamic collapse[22]. Irreversible shock is characterized by severe and persistent vasodilatation and reduced cardiac output[23].

II) **Cardiogenic Shock** .The primary disturbance is an inadequate cardiac output despite adequate venous return. Filling pressures are usually pathologically elevated resulting in JVD and pulmonary edema (typically occurring when PCWP is > 19 mmHg). The BP equation predicts an elevated SVR as the compensation for decreased CO; therefore, the skin will be cold and clammy. The arterial pulse pressure will be narrow. The typical hemodynamic profile is elevated CVP, PCWP, SVR and decreased CO and SvO_2.

Etiologies include massive MI, cardiomyopathy, acute valvular disease, tachycardia and bradycardia.

III) **Vasodilatory shock** also called distributive shock. The primary circulatory disturbance is decreased SVR. This failure of vascular smooth muscle contraction occurs despite extremely elevated levels of endogenous catecholamines and can persist despite infusions of massive doses of exogenous catecholamines (i.e. vasopressors). The pathogenesis of this phenomenon includes activation of ATP sensitive potassium channels in vascular smooth muscle as well as vasopressin deficiency and elevated NO activity[24].

The causes of vasodilatory shock include sepsis, pancreatitis and anaphylaxis. Importantly, vasodilatory shock is a common endpoint of prolonged shock of any etiology such as massive hemorrhage or after prolonged cardiopulmonary bypass or cardiac arrest.

Because of vasodilatation and loss of intravascular fluid to the interstitium (capillary leak), most cases are initially complicated by hypovolemia which can diminish CO and $ScvO_2$[4]. Volume resuscitation can restore venous return and allow the typical compensation for vasodilatation: increased CO. CVP and PCWP vary depending on volume status. SvO_2 may be normal in vasodilatory shock, as tissues are unable to utilize the delivered substrates and oxygen. This process, called cytopathic hypoxia, may be due to inflammatory up-regulation of P(ARP)-1 polymerase which depletes cytoplasmic NAD, a limiting reagent of oxidative phosphorylation. Cells therefore, may be unable to synthesize sufficient ATP despite adequate cellular oxygen[25].

The patient in vasodilatory shock will be warm and flushed (due to peripheral vasodilatation) and have a wide arterial pulse pressure and hyperdynamic precordium.

Prolonged vasodilatory shock results in progressively diminished cardiac function in part due to myocardial under perfusion and circulating myocardial depressant factors (including TNF)[26].

IV) **Obstructive shock** Many consider this a variant of cardiogenic shock. The primary disturbance is a low cardiac output due to an obstruction of diastolic filling (e.g. tension pneumothorax, pericardial tamponade, high intrathoracic pressures from positive pressure ventilation) or an outflow tract obstruction (massive pulmonary embolism). The typical profile is decreased CO and SvO_2 and elevated SVR and CVP.

Shock due to Right ventricular failure

The RV failure syndromes are a distinct form of shock that are often unrecognized and a common cause of death. 10% of all hospitalized patients die of RV failure due to acute pulmonary emboli. The RV is a thin walled structure that is unable to tolerate elevations in PVR. Figure 1 demonstrates classic experiments showing the effect of progressive increase in PVR on a normal RV. Initially PA pressures rise as CO is maintained. Systemic BP and right atrial pressures are defended. Once a critical level of PVR is reached the RV develops failure and blood wells up in the RV and RA. The rising RA pressure is an ominous sign in RV failure. CO and systemic blood pressure begin to fall, which reduces RV perfusion worsening its performance. Normally the RV receives perfusion from the right coronary artery in systole and diastole. As intra-ventricular RV pressure rises the systolic perfusion gradient from the aorta/RCA begins to fall creating ischemia. A vicious rapidly deteriorating cycle is created (figure 2). Note that PA pressures begin to fall after the point of maximum compensation is reached. The RV cannot generate systolic pressures higher than 50-60mmHg in the acute setting. Rising RA pressures and PVR, CO, and $S\bar{v}O_2$ are likely more useful markers of RV failure than PA pressure. Importantly administration of epinephrine shifts the point of maximum compensation to the right. This explains why adrenergic and sympathetic blockade are poorly tolerated in RV failure[27-29].

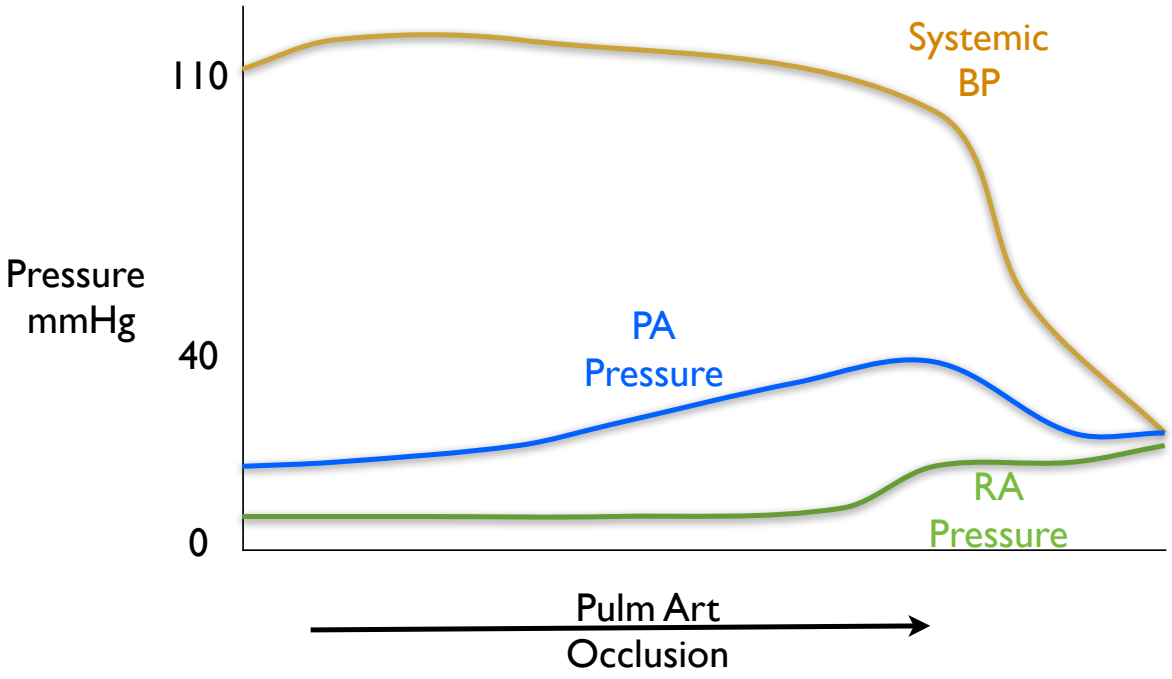


Figure 1: Adapted from Guton AC et al The limits of right ventricular compensation following acute increase in pulmonary circulatory resistance *Circulation Res.*195 2; 326-332

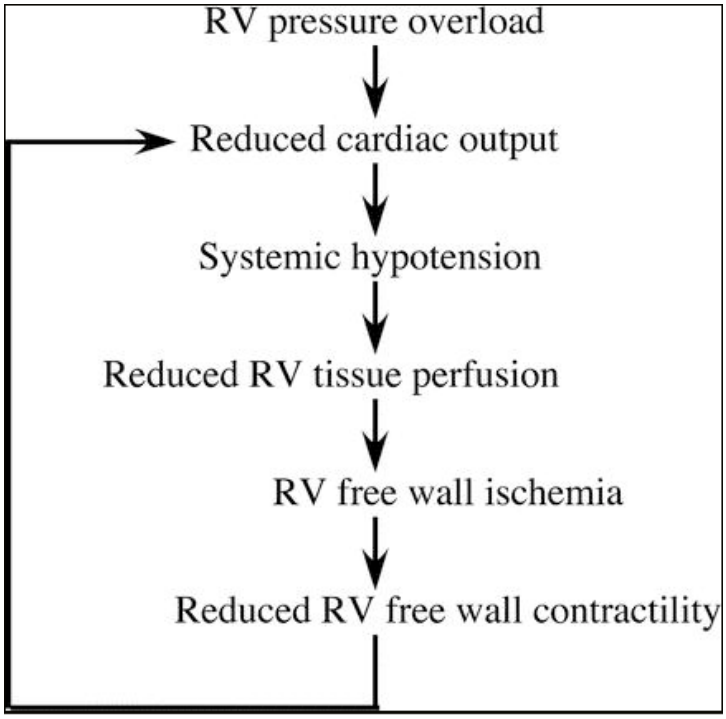


Figure 2: The vicious cycle of RV failure.
Greyson *Crit Care Med* 2008 Vol. 36, No. 1 (Suppl.)

Shock due to Positive Pressure Ventilation

Positive pressure ventilation will reduce preload and LV afterload, which may help LV failure and pulmonary edema. However the reduction in venous return may decrease cardiac output especially if autonomic reflexes are blocked (such as by anesthesia). In one study all sedated patients with a right atrial pressure less than 10mmHg became hypotensive with the application of 10cmH_2O continuous airway pressure[30]. The hypotensive effects of positive pressure are blunted by vasoconstriction and intravascular volume expansion. A less common cause of shock from positive pressure is hyperinflation of the lungs. Nearly the entire cardiac output must flow through the pulmonary capillary beds. Excessive lung inflation with airway pressures that exceed pulmonary vascular pressures can dramatically increase PVR. Severe elevation of PVR by hyperinflation causes a form of acute cor pulmonale. This is common in patients with ARDS and large tidal volumes. PVR has a J shaped relationship with lung inflation. When end expiratory pressures are low there may be atelectasis and high PVR (Figure 3). PVR falls with increasing expiratory lung volume but then rises dramatically with hyperinflation[31].

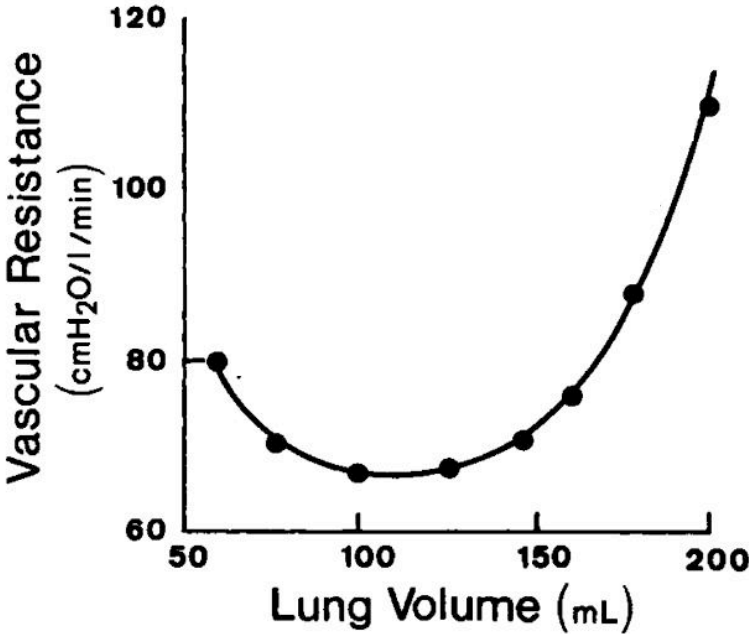


Figure 3: PVR is elevated at low lung volumes due to atelectasis causing hypoxic vasoconstriction. Hyperinflation compresses alveolar capillary beds and increases PVR. Adapted from West, J.B. *Respiratory Physiology - The Essentials.* Baltimore: Williams & Wilkins, 1974.

From the perspective of the circulation it does matter if the airway pressures such as the PEEP are deliberately set on the ventilator or if they are unintentional due to auto-PEEP. Therefore the evaluation of any hemodynamically unstable patient must include examination for auto-PEEP[32].

Hemodynamic instability from positive pressure ventilation is usually due to diminished venous return and less commonly from RV outflow obstruction with high PVR. Fluid resuscitation is beneficial in former but harmful in latter. Echocardiography will show a dilated RV with septal flattening and dilated IVC in acute cor pulmonale[33].

Cardiac Tamponade

Tamponade occurs when pericardial pressure is higher intracardiac and systemic venous pressure. It is obstructive shock because the pericardial pressure impedes venous return. The pericardial pressure becomes the minimum pressure in the heart. This leads to so called "equalization of diastolic pressures" when measured by right hear catheterization. The pericardial compliance is such that the rate of fluid accumulation is important. Small volumes of fluid that accumulate rapidly can raise pericardial pressures to higher levels than large effusions which accumulate more slowly. Cardiac output may be preserved despite high pericardial pressures if circulatory reflexes are intact. However low systemic venous pressures (e.g. due to volume depletion or vasodilation) will diminish venous return.

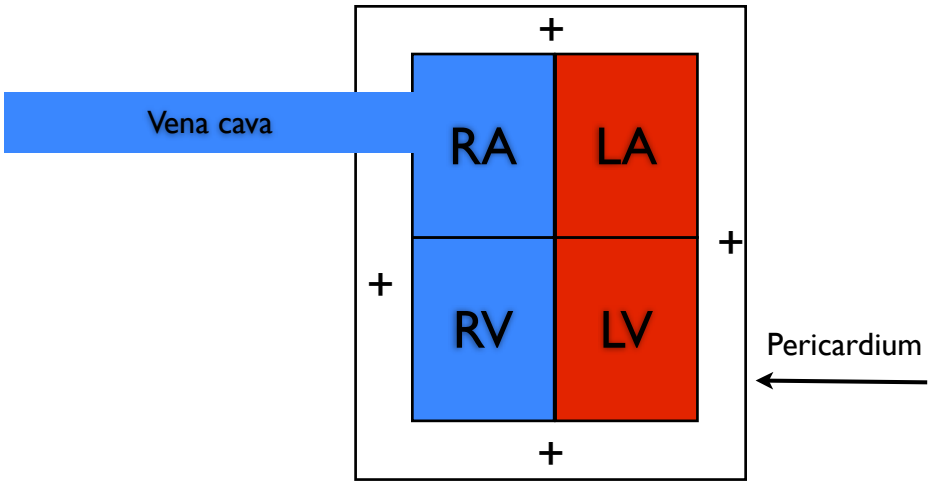


Figure 4: Positive pressure around the heart decreases the gradient for venous return

The effects of ventilation are important diagnostic tools. During normal spontaneous inspiration the negative pressure in the thorax increases the gradient for venous return. Right atrial and ventricular volumes will increase during

inspiration. Since pericardial fluid limits the total volume of the heart, the rise in right-sided volumes leads to impairment of diastolic filling of left atria and ventricle and a drop in LV output. This is the cause of the characteristic increase in the magnitude of systemic hypotension during inspiration (increased pulsus paradoxus).

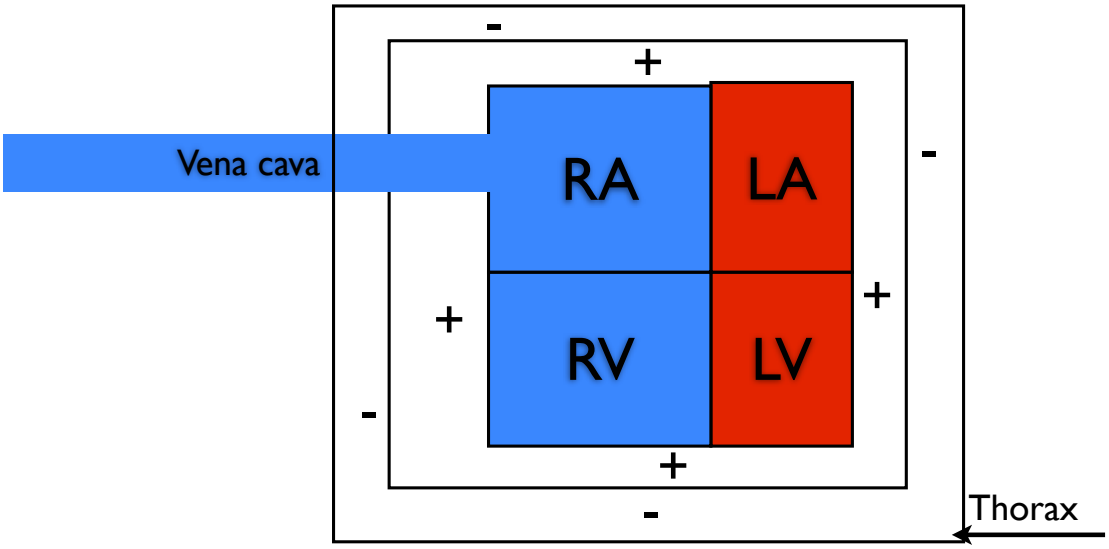


Figure 5: Negative intrathoracic pressure enlarges the RA & RV limiting left filling

Cardiac tamponade causes low stroke volume, and $S\bar{v}O_2$, high SVR, narrow arterial pulse pressure and tachycardia. The diagnosis is clinical but echocardiography is invaluable to demonstrate pericardial fluid. 2-D imaging the high pericardial pressures may cause diastolic collapse of the RA and RV. Less specific is the Doppler imaging, which shows increased flow across the tricuspid valve and decreased flow across the mitral valve during negative pressure inspiration.

Management of Shock

1) Secure airway
2) Guarantee adequate oxygenation and ventilation
3) Resuscitate circulation
    - Large bore IV access
    - Optimize intravascular volume
    - Monitor adequacy of resuscitation
4) Continuous presence of trained clinician at bedside
5) Vasopressors if shock is refractory to fluids
6) Treat underlying cause

Prompt recognition of shock and diagnosis of its etiology are essential if the patient is to survive. The airway must be secured and ventilation supported. Supplemental oxygen is given for hypoxemia. If respiratory distress or severe acidemia is present the patient will require mechanical ventilation to assume the work of breathing[19]. Nearly all patients require a Foley catheter to follow hourly urine output, continuous cardiac and oxygen saturation monitoring, and most will require an arterial line. CVP monitoring is a flawed measure of fluid responsiveness but helpful marker of RV function. Cardiac output can be monitored in our unit with PA catheter, PiCCO and NICOM.

Survival requires appropriate fluid resuscitation. Most patients require fluid resuscitation but some, particularly those in decompensated RV failure and elevated right atrial pressures, will deteriorate with fluid. You need to use clinical criteria to determine which patients will respond to volume expansion by increasing stroke volume. The history is most helpful. For example healthy outpatients who present with severe sepsis will almost uniformly require fluid resuscitation, as do patients with pancreatitis, burns, recent surgery or hemorrhage. Hemodynamic monitoring can be helpful. Traditionally, the profile of low stroke volume, low $S\bar{v}O_2$, and normal filling pressures of CVP and PCWP dictated the administration of fluid. For example in cardiogenic shock from myocardial infarction, a PCWP 14-18mmHg is associated with the highest stroke volume[34]. New data, however, challenge the power of isolated values of CVP and PCWP to predict which patients will recruit stroke volume from a fluid bolus. Use of dynamic assays of the circulation seem to be better predictors of fluid responsiveness than static filling pressures[35]. We use three dynamic assays in our MICU: passive leg raising (PLR), pulse pressure variability, and IVC variability.

Stroke volume augmentation by PLR is highly suggestive of fluid responsiveness. The PLR test requires a stroke volume monitor but is validated in positive or negative pressure breathing. Measure the baseline stroke volume and

then perform PLR as shown in the figure 6. After one minute measure stroke volume again. If the SV rises by 10% this predicts that a subsequent fluid bolus will augment the patients stroke volume. The positive and negative predicted values for this test are both >90%[36].

Figure 6: Measure stroke volume in both positions. A 10% rise predicts fluid responsiveness. Adapted from Monnet X et al. Passive leg raising predicts fluid responsiveness in the critically ill *Critical Care Medicine* - Volume 34, Issue 5 (May 2006)

Respiratory variability of arterial pulse pressure of more 13% also predicts that stroke volume will increase in response to a fluid bolus. Pulse pressure variability is only valid if the patient has a regular cardiac rhythm, and is passively ventilated with large tidal volumes (>8ml/kg/IBW) and has no sign of RV failure[37, 38]. In figure 7 the thick black vertical lines represent the maximum and minimum arterial pulse pressures during mechanical ventilation (PPmax and PPmin)[35].

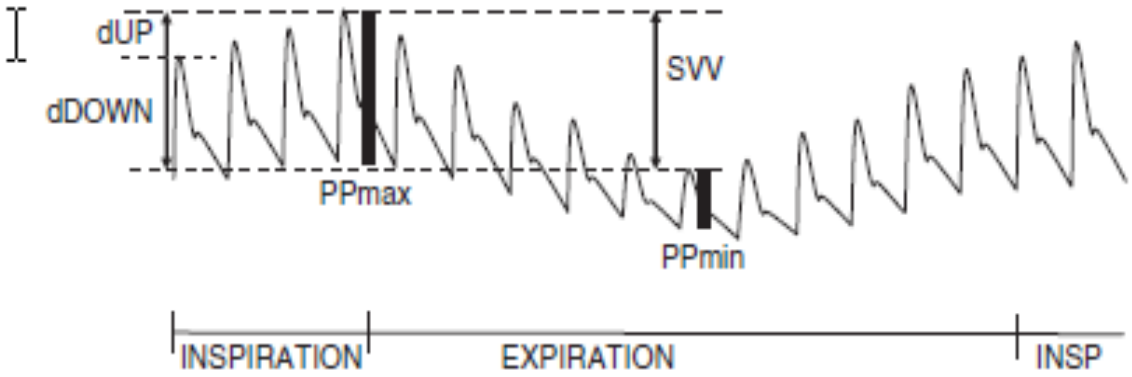


Figure 7 Pulse pressure variation is equal to the difference divided by the mean of the maximum and minimum pulse pressure. Adapted from Durairaj and Schmidt *Chest* 2008 133; 252-263

The pulse pressure variation is:

PPV = Pmax - PPmin/ [(PPmax + PPmin)/2]

Observation of the inferior vena cava with ultrasound is useful in 2 distinct situations. In spontaneously breathing patients, a narrow IVC diameter that collapses >50% with negative pressure inspiration predicts a normal CVP. Cyclical dilation of the IVC diameter with passive positive pressure inspiration on mechanical ventilation predicts fluid responsiveness in patients with sepsis. This is only valid with passive, large tidal volume (>8ml/kg/IBW) ventilation. RV failure gives a false positive result. In clinical trials, IVC variability had a >90% positive and negative predictive value for predicting that a subsequent fluid challenge would significantly increase stroke volume. One trial used a threshold of 12% variability and another used 18%. IVC variability is determined by difference in inspiratory and expiratory diameter/mean IVC diameter[29, 39, 40].

When fluid resuscitation is indicated, administer isotonic crystalloid (LR or NS) in 500ml-1L boluses and re-evaluate the patient after each fluid bolus to determine response. Most patients with vasodilatory shock will require 4-5 L of volume in the first few hours (and may ultimately require three times this amount)[4]. Use a fluid warmer for crystalloid and blood products to prevent hypothermia.

Typical end points of volume resuscitation include restoration of blood pressure without the need for vasoconstrictors and restoration of normal urine output (although urine output may not correct if patient is in oliguric ATN). For hemorrhagic shock many intensivists continue volume resuscitation until the acidosis is corrected. For sepsis consider normalization of SvO_2 or oxygen saturation of central venous blood ($ScvO_2$) or serum lactate concentration during first 6 hours of resuscitation[3, 4].

Other resuscitation end points include evidence of symptomatic fluid overload.

Although it remains controversial we do not routinely resuscitate patients with colloid[41]. We use Lactated Ringers as our main resuscitation fluid as NS leads to significant electrolyte abnormalities (Figure 8). Avoid LR when you need to avoid hyponatremia such as in cerebral injury or if you need to avoid any potassium load. LR is inflammatory in lab models[42]. Indications for blood transfusion remains controversial[43]; we generally correct the Hgb to around 8 mg/dl for shock. We also use albumin for resuscitation in patients with cirrhosis[44].

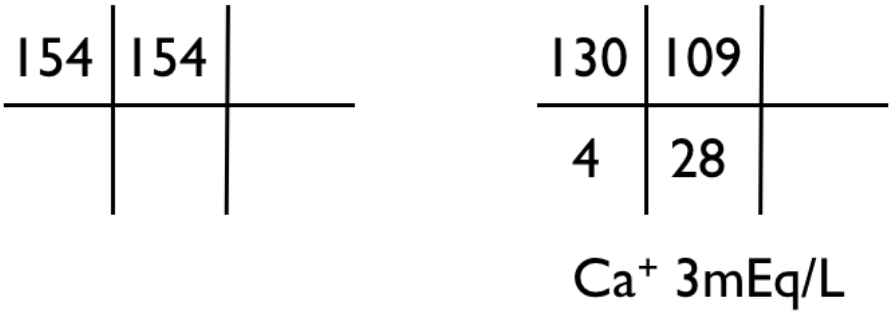


Figure 8: Components of Normal saline left and Lactated ringers on right

Correct choice of intravascular catheters is essential. Flow through the catheter is independent of the size of the vein but inversely proportional to the length of the catheter. Flow is proportional to the fourth power of the radius of the catheter. Therefore short, large bore catheters are essential for rapid fluid administration. For example:

22 gauge angiocath: maximum infusion rate: 35 ml/minute
20 gauge angiocath: maximum infusion rate: 60 ml/min
18 gauge angiocath: maximum infusion rate: 105 ml/min
16 gauge angiocath: maximum infusion rate: 205 ml/min
14 gauge angiocath: maximum infusion rate: 333 ml/min

Therefore, small IV's and long PICC lines are inadequate for rapid volume resuscitation. Long triple lumen central lines may also be inadequate (large lumen allows 34 ml/min, other two lumens each allow 17 ml/min). Large bore central venous introducers are ideal. Electric pumps and micro-drip IV tubing will *slow* infusion rates through large bore catheters (maximum rate 1L/hr). Rapid infusions require only gravity and plain IV tubing (the way blood products are infused). Place central venous access if adequate peripheral access is not possible or the patient requires vasopressors, or hemodynamic monitoring.

Massive fluid resuscitation causes many complications. This is especially important in hemorrhagic shock because massive resuscitation causes hypothermia, hypocalcaemia, and dilution of clotting factors all of which worsen coagulopathy and perpetuate bleeding. The combination of injury from bleeding and the complications of resuscitation leads to a “vicious bloody triad” of acidosis, hypothermia and coagulopathy[45].

Complications of Massive Resuscitation

Fluid Overload	Causes of coagulopathy
Decreased respiratory compliance	Hypothermia
Pulmonary edema	Dilution of clotting factors
Abdominal compartment syndrome	Hypocalcaemia
Complications of 0.9% Saline	**Infectious risks of PRBC**
Metabolic acidosis	viral infection (very rare)
Hypernatremia	Nosocomial Pneumonia
Hypokalemia	

Resuscitation from hemorrhage The term "damage control resuscitation" refers to the approach of preventing over-resuscitation and its complications when active bleeding is severe enough to cause shock and require massive transfusion (>4units PRBC/12 hours or expected to lose a circulating volume of blood within 24 hours). The principles are to target fluid resuscitation to maintain the minimum blood pressure required for perfusion (warm skin, urine output, absence of acidosis, absence of distress/encephalopathy) and avoid dilution of clotting factors. Traditionally, physicians treated the interstitial fluid deficit created by severe hemorrhage by infusing large volumes of isotonic crystalloid. This was the basis of the 3:1 rule of trauma (administer 3ml of LR for every one ml of shed blood). This approach frequently led to over-resuscitation.

The current paradigm is use blood products instead of crystalloid as the resuscitation fluid. The ratio of the different blood products should approximate the relative amounts of the constituents of whole blood. Transfuse PRBC and thawed plasma (FFP) in a 1:1 ratio. The goal hemoglobin is around 8gm/dl and PT/PTT < 1.5 X control values. Transfuse platelets to keep platelet count >75K. Maintain fibrinogen >100 with cryoprecipitate[46]. Page the blood bank resident to help the blood bank deliver the correct ratio and amount of components expeditiously. If the patient is in imminent danger of death from exsanguination and cross-matched blood is unavailable ask the blood bank for the "least incompatible PRBC". It is important to use that phrase as opposed to "O negative blood" as the blood bank may by able to give ABO or Rh specific blood even if full cross matching is unavailable. The hospital has a massive transfusion protocol the blood bank resident can activate if needed. Alert the nurse to use a rapid infuser device

(Belmont rapid infuser) to deliver warmed blood products and medications. Check complete blood count, coagulation profile and serum chemistries as frequently as once per hour in massive hemorrhage. Over correction of blood pressure may increase the risk of ongoing bleeding from injured vessels. It is important to remember that blood products contain a large volume of anti-coagulants and contribute to resuscitation injury. Therefore early intervention to control hemorrhage is essential[45, 46].

You should tailor the full implementation of the aforementioned approach to the clinical scenario. For example, there is likely no need to give clotting factors to a patient who requires 4 units of PRBC slowly for severe isovolemic anemia.

Prompt treatment of the underlying cause of the shock is essential: antibiotics and drainage of infected foci for sepsis, thrombolysis for PE, pericardiocentesis for pericardial tamponade, control of bleeding, re-perfusion therapy in acute MI, tube thoracostomy for tension pneumothorax, cardioversion or pacing of arrhythmias, and placement of intra-aortic balloon pump or ventricular assist device for refractory cardiogenic shock. Also consider using activated protein C for patients in septic shock[47]. Consider low dose steroid replacement for septic shock. Consider low tidal volume ventilation if the patient develops ARDS[48].

Vasoactive drips: Vasoconstrictors can restore the blood pressure to a normal value without normalizing perfusion and they do not correct the misdistribution of blood flow that characterizes shock. Vasoactive drips should never be used in place of adequate volume resuscitation or treatment of the underlying etiology of the shock. The patient who is on these vasoactive drips is unstable and the clinician should constantly attempt to liberate the patient from the drips. Nonetheless experience suggests these medications can be life sustaining in patients in shock.

Vasoactive drips target various receptors:

Alpha predominantly found in the vasculature; activation causes vasoconstriction

$Beta_1$ Predominantly found in heart; activation causes increased inotropy and chronotropy

$Beta_2$ predominantly found in vasculature; activation causes vasodilatation

Dopaminergic: One subtype causes vasodilatation of splanchnic, cerebral and coronary vasculature; another subtype causes vasoconstriction

The catecholamine vasopressors are administered in central venous catheters. If extravasation into soft tissues occurs consider administration of phentolamine to counteract to prevent tissue necrosis. The onset of action and the elimination half-lives of the catecholamines are all within minutes.

Norepinephrine (Levophed) potent alpha agonist (vasoconstrictor) also some B_1 activity but no B_2 stimulation. The effect on cardiac output is variable and depends multiple factors[18, 49]. Used in vasodilatory shock, it is the most potent and our most commonly used vasopressor[50].

Phenylephrine (Neosynephrine): Pure alpha agonist causes vasoconstriction (increases SVR). May cause reflex bradycardia. Useful in vasodilatory states especially in setting of tachyarrhythmia. The presence of pure vasoconstriction without any inotropic or chronotropic effects may reduce cardiac output. Phenylephrine might be more immediately available as we have prefilled syringes available for emergencies that you can administer as a bolus. You can administer these 100mcg IV bolus injections intermittently through a peripheral IV until central venous access is established. Commonly used to counteract vasodilation induced by anesthesia. Vasopressor of choice in hypertrophic obstructive cardiomyopathy with dynamic outflow tract obstruction.

Dopamine dose responses for various receptors vary;
1-3 mcg/kg/min dopaminergic receptors predominate with dilation of renal and splanchnic vessels. Some vasodilatation and tachycardia
5-10 mcg/kg/min : Beta predominates with some alpha activity
>10 mcg/kg/min: alpha predominates with some Beta activity

In summary, at mid doses dopamine causes tachycardia and modest increase in CO. Vasoconstriction increases with increased dose. Controversy exists over the use of renal dose dopamine (1-3 mcg/kg/min) to preserve renal perfusion. Dopamine does increase urine output at low doses that is likely transient and due to naturesis. However, it is relatively certain that it does not improve renal function or mortality[51]

Epinephrine At low doses epinephrine activates *B* receptors and has less *alpha* activity. The net result is increased CO with variable vasoconstriction and effect on BP. At higher doses >10mcg/min alpha effects predominate increasing vasoconstriction and BP. Epinephrine is used in anaphylaxis and for circulatory support immediately after coming off bypass. Given its greater *B* effects it causes more hyperglycemia, elevated blood lactate concentrations, rise in oxygen consumption, bronchodilation and leukocytosis then other catecholamines[49].

Vasopressin Peptide (non catecholamine) used as vasoconstrictor for vasodilated states. There is a physiologic rationale for vasopressin replacement therapy in situations when endogenous vasopressin levels are deficient such as in sepsis or the irreversible shock state of hemorrhage. Moreover, vasopressin does not increase

PVR and at low doses does not constrict the renal circulation. However the vasoconstriction increases afterload and causes reflex bradycardia which typically reduces cardiac output. Therefore it is essential to ensure that vasopressin therapy does not worsen hypoperfusion from reduced cardiac output. Vasopressin is commonly used for refractory septic shock but a large randomized trial did not confirm a benefit. It is commonly used to support vasodilated states after cardiopulmonary bypass and to counteract inotrope induced hypotension. There are multiple vasopressin receptors and there appears to be heterogeneous effects at different doses of vasopressin. Vasopressin is known to cause mesenteric, coronary and limb ischemia[52-55]. Mix 25 units/250cc D5W infuse at 0.04 units/minute (24ml/hour), do not titrate to higher dose; must taper off slowly.

Dobutamine Potent stimulator of β receptors increases cardiac output and vasodilatation. Commonly used in cardiogenic shock (characterized by decreased CO and high SVR) its effects include vasodilatation and hypotension as well as tachyarrhythmias. Long-term inotropic support increases mortality; it is presumed that short-term isotropic support does not increase mortality although there is no clinical trial data to support this. You can add dobutamine to other vasoconstrictors if additional cardiac output needed to augment perfusion. Start at 2.5mcg/kg/min if no adverse effects increase to 5mcg/kg/min, if the patient tolerates this dose but if response is inadequate increase to 7.5mcg/kg/min.

Milrinone is a phosphodiesterase inhibitor and a potent inotrope approved for decompensated heart failure. It is a more potent vasodilator of the systemic and pulmonary circulations than dobutamine. Arrhythmias are common and there is no clinical outcome data supporting its use. Much longer half-life then the catecholamines and dosage must be reduced in renal failure. Loading can decrease time to onset of action but is commonly complicated by hypotension.

Treatment of Right Ventricular Failure

Reduce PVR	Improve RV Contraction
Avoid Hypoxemia	Optimize Filling Volumes
Avoid Acidemia	Systemic Vasoconstrictors
Avoid Atelectasis	Inotropic Support
Avoid Hyperinflation	Unload Left Ventricle
Pulmonary Vasodilators	Right Ventricular Assist Device

When confronted with a patient in shock from the vicious cycle of RV failure you must immediately increase systemic blood pressure with vasoconstrictors to maintain RV perfusion gradient. We favor vasopressors with some inotropic activity such as NE or Epinephrine. You should attempt to normalize gas exchange (i.e. avoid permissive hypercapnia and hypoxemia). This may prove difficult, however, if the patient is on mechanical ventilation, as attempts to improve gas exchange with increasing airway pressures may cause hyperinflation, which can also increase PVR. The process of intubation, which combines the effects of positive pressure ventilation and the systemic vasodilation due to sedation, may cause rapid deterioration. Pulmonary vasodilators such as inhaled NO can reduce PVR.

The right ventricle is extremely sensitive to volume status. In the face of normal PVR and impaired RV contractility, such as occurs during RV infarction, cautious volume expansion may improve RV stroke volume by the Starling mechanism. As the RV fails, RV end-systolic volumes rise. The RV pressure will rise dramatically creating RV ischemia. If RA pressure is markedly elevated (>15mmhg) and echocardiography reveals a dilated RV chamber with septal flattening diuresis may improve stroke volume.

In the setting of acute RV failure from acute pulmonary embolism it is essential to support the systemic BP with vasoconstrictors and inotropes. In the absence of RV distention, consider a cautious (250ml) fluid bolus. Thrombolytics can rapidly reduce PVR. If there is a contraindication to thrombolysis consider surgical embolectomy[29, 33, 56-58].

Chapter 6 Mechanical Ventilation

Basic Principles

Air flows from areas of high pressure to lower pressure. By convention, all pressures are referred to atmospheric pressure. Normal unassisted ventilation is driven by negative pressure. When we inspire, our muscles expand our thoracic cavity, which lowers the intra-thoracic pressure and allows air to flow in passively from the pharynx. Standard mechanical ventilation is positive pressure ventilation. The ventilator will create airflow if the ventilator pressure exceeds the pressure inside the conducting airways and lungs.

Positive pressure ventilation has many physiologic consequences. It can recruit atelectatic alveoli (figure 1), decrease right-to-left-shunt fraction, and improve oxygenation[59]. Positive intra-thoracic pressure can decrease preload by reducing the pressure gradient for the venous return of blood to the heart. This is the most common reason for hypotension associated with the use of mechanical ventilation[30]. Excessive lung inflation may also compress pulmonary capillaries and raise pulmonary vascular resistance which can precipitate acute cor-pulmonale.[31]

Positive pressure can also reduce left ventricular wall tension (i.e. afterload)[60]. These effects may be life saving for patients with congestive heart failure and left ventricular dysfunction.

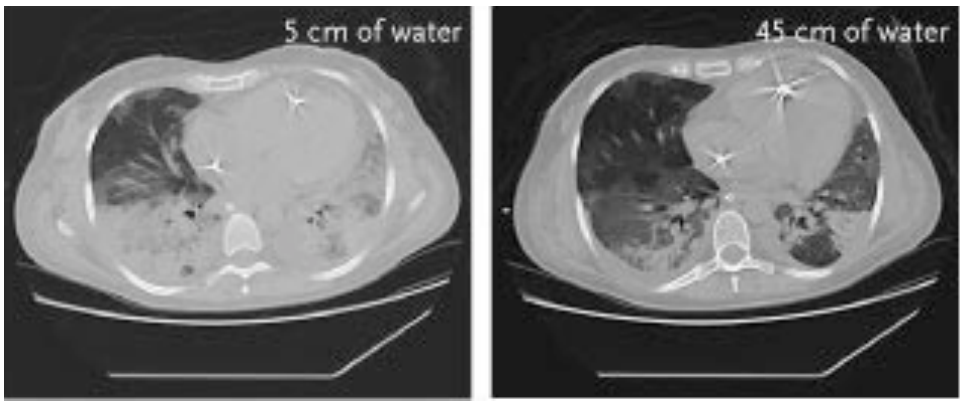


Figure 1
CT scans of the lungs from the same patient with acute lung injury inflated with lower and higher inflation pressures. The higher pressure resulted in recruitment of atelectatic alveoli. Adapted from Gattinoni et al N Engl J Med. 2006 Apr 27; 354(17): 1775-86.

Ventilator Modes

The number of different modes available on modern critical care ventilators is daunting and ever-expanding. However, it is important to realize that the same basic principles govern all of the modes[61]. A ventilator has separate inspiratory and expiratory valves that interface with the flexible tubing of the airway circuit. These two flexible limbs, which are outside the ventilator, meet at a junction and interface with an endotracheal or tracheostomy tube. When the

ventilator cycles to inspiration, the expiratory valve closes and the ventilator pushes air into the inspiratory limb. This inspiratory phase is what varies the most between the different modes. Depending on the mode, the ventilator usually targets an airway pressure or a tidal volume to deliver. At the end of inspiration, the ventilator cycles over to exhalation by closing the inspiratory valve and opening the exhalation valve. The cycling over to exhalation occurs after a volume has been delivered (volume cycling) or the inspiratory limb has been opened for a defined time (time cycling). An alternative is flow cycling, in which the ventilator recognizes the end of inspiration by a decline in inspiratory airflow rates. During exhalation, air flows out of the lung passively as long as the pressure in the lung exceeds the pressure in the ventilator. To promote alveolar recruitment, clinicians usually set the ventilator to maintain positive pressure in the expiratory limb throughout the cycle. This is called extrinsic positive end-expiratory pressure (PEEP).

The ventilator delivers breaths depending on the frequency set by the clinician. The patient may also trigger breaths by generating sufficient respiratory effort to exceed the sensitivity trigger set by the clinician[62].

Given the inherent similarity of the modes as well as the absence of clinical trials or consensus guidelines demonstrating the superiority of one mode over another, I recommend that physicians be familiar with and use only a few modes. Each ventilator company uses different terminology to describe their modes, and the algorithms for each mode will vary between brands and models of ventilators. The following discussion deals with the PB-840 our most common ventilator.

The most commonly used mode in critical care units is **Assist Control -volume control ventilation** (**AC-VC**)[61]. The ventilator delivers breaths that are volume-targeted and volume-cycled and initiated by the patient or the machine. This mode allows the best analysis of respiratory mechanics using ventilator graphics. The clinician sets a minimum respiratory rate, as well as the tidal volume and peak inspiratory flow rate. The inspiratory flow pattern can be a square wave or a decelerating wave. (Figure 2) The former allows inspiration to be shorter while the later more closely mimics normal unassisted ventilation. On AC-VC, if patient effort increases, the ventilator will not deliver increased tidal volumes or higher flow rates. This can result in significant distress[62].

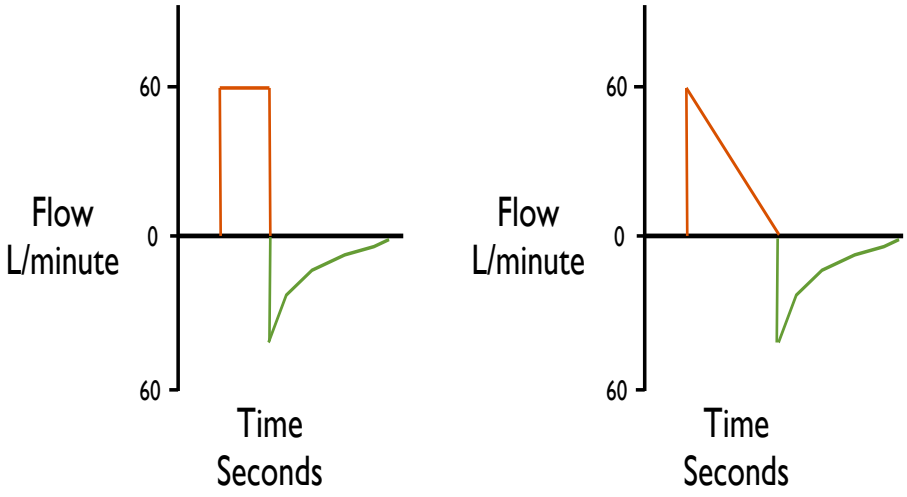


Figure 2 Flow vs. time curves for AC-VC. Inspiration brown and exhalation is green. Square wave on left and decelerating ramp on right. The peak inspiratory flow rates are identical but the square wave delivers the same tidal volume more rapidly.

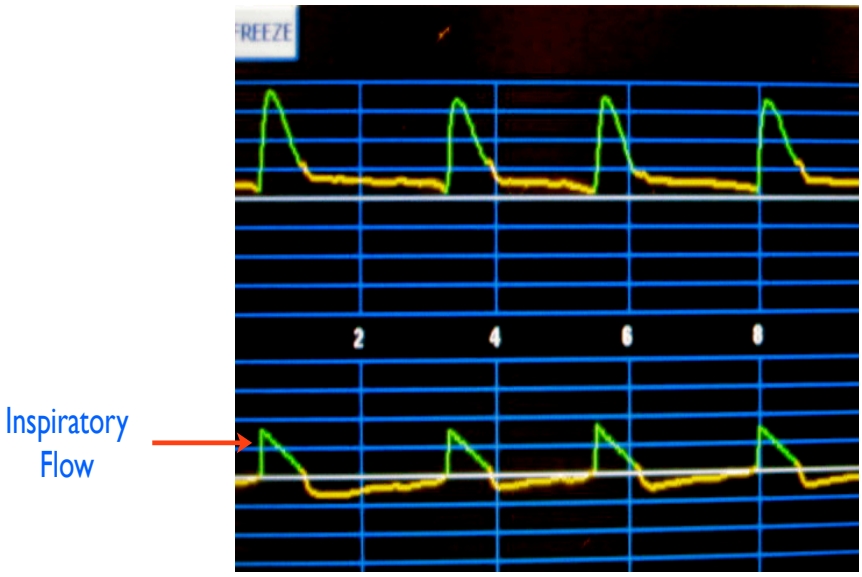


Figure 3 Pressure vs. Time (top) and flow vs. time (bottom) curves in a patient breathing comfortably on AC-VC. Green represents inspiration. The white lines at X-axis represents 0cmH_2O (top) and O L/min flow (bottom). This patient has a normal fall in the expiratory flow rate to 0 L/min prior to initiation of the subsequent breath.

AC-Pressure control (AC-PC) is machine- or patient-initiated, pressure-targeted, time-cycled ventilation. The ventilator forces sufficient air into the inspiratory limb to maintain a constant pressure target that has been set by the clinician. If the respiratory system is non-compliant, the pressure will rapidly equilibrate between lung and ventilator and the ventilator will deliver small tidal volumes. Respiratory effort by the patient increases the pressure gradient and the delivered tidal volume (Figure 4).

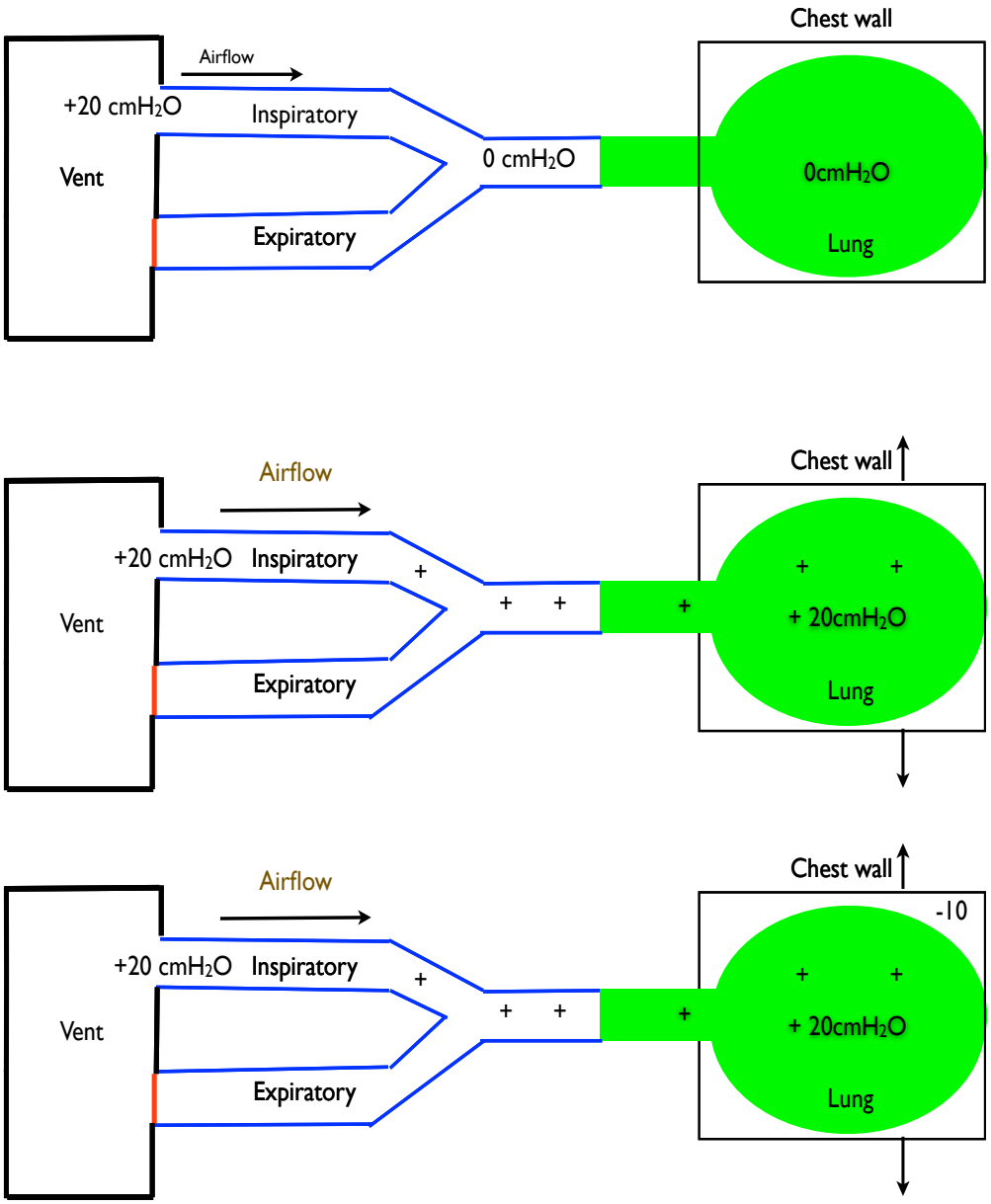


Figure 4 Pressure targete ventilation. Top is the onset of inspiration with the lung at PEEP 0 cmH_2(The exhalation limb is closed and the inspiratory limb is open. The inspiratory pressure targe has been set arbitrarily to $20cmH_20$. The ventilator blows in air to keep pressure at the ventilator opening $20cmH_20$. In the middle panel airflow will stop when there is equalization of the pressure throughout the airway. In bottom panel the pleural pressure is $-10cmH_20$ from patient effort. Therefore the inspiratory flow rate and tidal volume will be greater then if the patient is passive.

A common source of asynchrony on AC-PC occurs when the inspiratory time set by the clinician differs from the patient's neural inspiratory time. The patient may attempt to continue to inhale after the ventilator cycles over to exhalation if the inspiratory time set is too short or may actively exhale against a closed expiratory valve if the time set is too long. (Figure 5) Most patients tolerate a set inspiratory time of 0.8- 1.2 seconds. Changing the inspiratory time will have variable effects on exhaled tidal volume. If there is inadequate time to complete exhalation then lengthening inspiratory times may worsen air trapping and reduce exhaled tidal volumes. Alternatively, the pressure in the lung may not equilibrate

with the inspiratory pressure target of the ventilator prior to the completion of the inspiratory time interval as seen in Figure 6. In this situation lengthening the inspiratory time interval may increase the delivered tidal volume[62, 63].

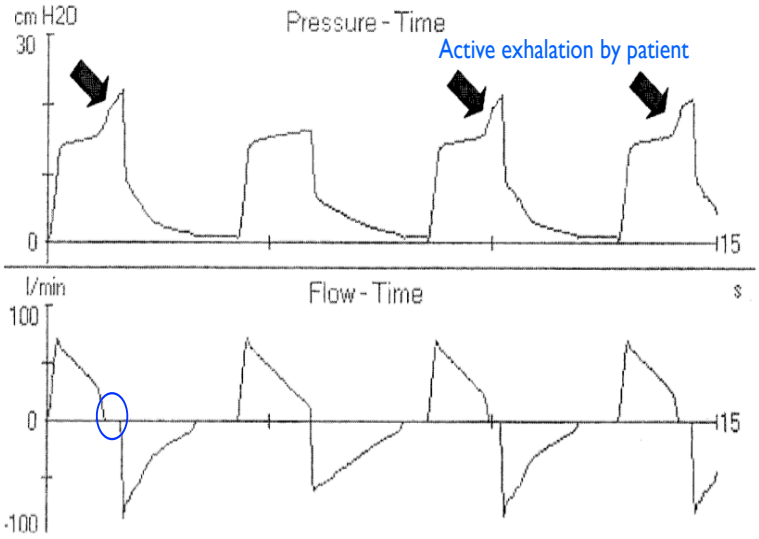


Figure 5 Asynchrony in PCV due to inspiratory time set too long. There is no flow for a brief duration at the end of inspiration (circle). The patient is actively trying to exhale while the inspiratory limb is still open. Adapted from Nilsestuen J and Hargett K Respir Care 2005; 50(2): 202–232.

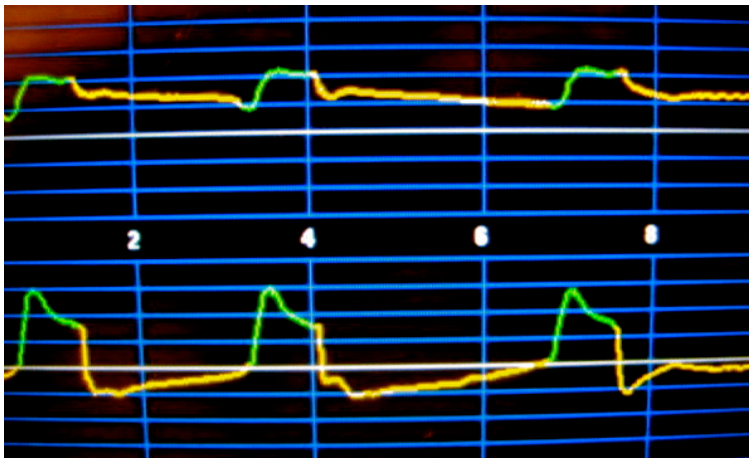


Figure 6 Pressure (top) and flow (bottom vs. time curve in PCV. Note that the pressure is constant in inspiration. Inspiratory flow is not set directly but naturally assumes a decelerating pattern as the pressure gradient between ventilator and lung dissipates as the lung fills with air. In this patient there is still inspiratory flow just prior to the cycling over to exhalation. Therefore lengthening the inspiratory time will increase delivered tidal volume.

Another common mode is **pressure support ventilation** (**PSV**). This is patient-initiated and pressure-targeted ventilation. On the PB 840 ventilator this mode is called "spontaneous mode". The patient must have an intact neuromuscular circuit of the respiratory muscles in order to trigger the ventilator. The mode is flow-cycled; when the inspiratory flow rate decreases to a set threshold, the ventilator cycles over to exhalation. You can change the expiratory sensitivity (which is the % of peak inspiratory flow rate that flow falls) to trigger cycling over to exhalation sooner or later (see Figure 7). Patient effort will result in the ventilator delivering

larger tidal volumes and faster inspiratory flow rates. Since the patient must trigger the ventilator to cycle to inspiration, many clinicians consider this mode to provide less support. However, a common source of asynchrony with PSV is setting the inspiratory pressure target too high in patients with normal or increased respiratory system compliance, leading to hyperinflation and tachypnea. Because the patient has significant control over the inspiratory flow rate and the cycling to exhalation many clinicians consider this mode more comfortable than AC modes. As with any mode, however, there are substantial opportunities for asynchrony and the patient is most definitely not "breathing on their own" with this mode.[62, 64, 65].

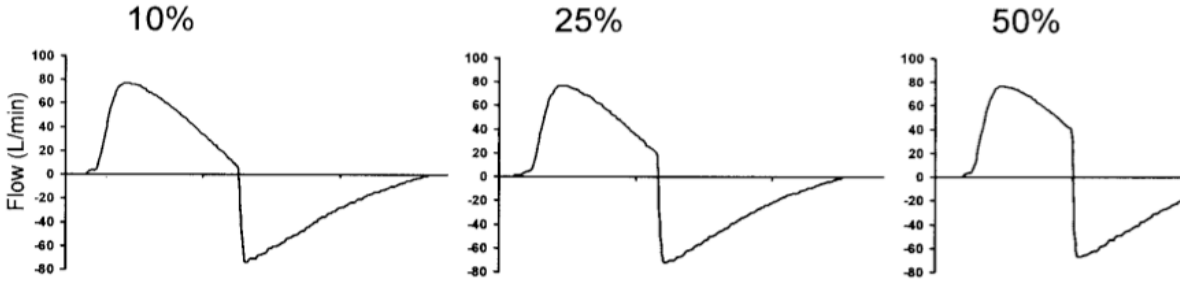


Figure 7 PSV with three different settings of expiratory sensitivity. 25% is the default settin
Adapted from Hess RESPIRATORY CARE FEBRUARY 2005 V 50 NO 2

Synchronized Intermittent Mandatory Ventilation **(SIMV)** is a mixed mode. It was designed to improve weaning from mechanical ventilation, but it is less effective than other weaning strategies in clinical trials.[66] The machine-initiated breaths are volume-targeted and volume-cycled. The patient-initiated breaths are pressure-targeted and flow-cycled (Figure 8). It combines both the virtues and the problems of the constituent modes already discussed[62].

Figure 8 SIMV Note the mixture of the breaths

Table (1) lists a few of the most commonly used modes and lists their key characteristics.

Mode	Machine Triggered Breath	Patient Triggered Breath	Inspiratory Airflow Target	Inspiratory Flow Rate	Expiratory cycling	Set FiO_2	Set PEEP
AC-VC	Yes	Yes	Volume	Set	Volume	Yes	Yes
AC-PC	Yes	Yes	Pressure	Not set	Time	Yes	Yes
PSV	No	Yes	Pressure	No set	Inspiratory Flow Decrement	Yes	Yes
SIMV	Yes	Yes	Volume/ Pressure	Set/ Not set	Volume/ Inspiratory Flow Decrement	Yes	Yes

Initial settings If rapid sequence induction with neuromuscular blockade is used for intubation, the clinician should choose a mode with machine-initiated breaths. Assist control ventilation is a reasonable choice. The initial tidal volume should be 8ml/kg/ideal body weight. Chose the FiO_2 on the basis of the oxygen requirement prior to intubation. Many clinicians start with FiO_2 1.0. However this may be incorrect in situations when high concentrations of inspired oxygen are deleterious such as after resuscitation from cardiac arrest[67]. The extrinsic-PEEP is typically set at 5cmH_20. Consider setting a higher PEEP if the patient required high pressures on non-invasive ventilation prior to intubation. On AC-VC, the inspiratory flow rate is initially set at 60 L/min[68, 69]. The respiratory rate can be set at 12 breaths/min. The rate should be set higher if there is a need to compensate for metabolic acidosis.

Evaluation of the Patient on Mechanical Ventilation

The physician should evaluate the patient on the initial settings and as soon as the effect of sedation and neuromuscular blockade wears off. Re-evaluate if the patient develops distress or hemodynamic instability or experiences any significant clinical change. To focus the evaluation, the clinician should answer the following five questions.

1) Is the patient comfortable? Nasal flaring and retractions of intercostal and neck muscles are evidence of inspiratory effort. A negative deflection of the pressure-time curve on the ventilator graphics suggests inspiratory distress. (Figure 9). Excessive effort throughout inspiration is often due to inadequate inspiratory flow rates, set tidal volumes, or inspiratory pressure targets. If effort occurs mainly at the onset of inspiration, the patient may be having difficulty triggering the ventilator. Difficulty triggering the ventilator may be due to inadequate trigger sensitivity or auto-Positive End Expiatory Pressure (auto-PEEP). Expiratory effort is noted by contraction of the rectus abdominus. The abnormal effort may be due to asynchrony with the ventilator cycle or due to exhalation against obstructed airways[62].

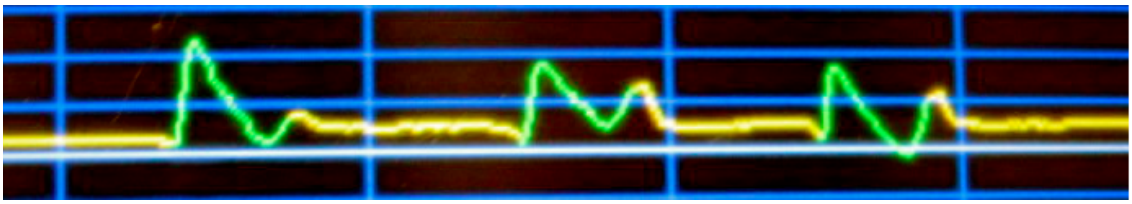


Figure 9
Pressure vs. Time curve from a patient making strong inspiratory efforts on AC-VC. Note that the airway pressure becomes negative even though the patient is on positive pressure ventilation

2) Is the positive pressure having any deleterious hemodynamic consequences? Excessive positive pressure may decrease venous return or create right ventricular outflow tract obstruction. Excessive patient effort may divert perfusion to the muscles of respiration during hypo-perfusion[5].

3) Is gas exchange adequate? Adequacy of oxygen-carrying content in the blood is determined by the hemoglobin saturation with oxygen. Pulse oximetry is sufficient as long as there is no increased met-hemoglobin or carboxyhemoglobin. Increasing FiO_2 or extrinsic set PEEP in increments of 2.5 cmH_2O can increase oxygenation. Excessive PEEP may worsen oxygenation, however, by reducing cardiac output and mixed venous oxygen saturation. Adequacy of ventilation is best assessed by arterial blood gas analysis determination of pH and pCO_2. The clinician should consider addressing hypercarbia or acidemia by increasing exhaled minute ventilation. The respiratory rate may be increased, and either the tidal volume or inspiratory pressure target can be increased as long as there is sufficient time to exhale[62]. Hypercapnia may be well tolerated if it is chronic but may be deleterious in patients with intracranial hypertension or elevation in pulmonary vascular resistance[56, 70].

4) Is significant auto-PEEP present? This occurs if there is dynamic hyperinflation and successive tidal volumes are delivered despite incomplete exhalation. The rapid respiratory rate creating the auto-PEEP may have been set on the ventilator or initiated by the patient. With dynamic hyperinflation the end expiratory lung volume and airway pressures rise with each breath. The total PEEP in excess of the PEEP set on the ventilator is the auto-PEEP. Auto-PEEP is common when respiratory rate and tidal volumes are high, and expiratory times are short. Expiratory airflow obstruction will contribute to auto-PEEP. It is diagnosed by noting the onset of inspiration prior to the completion expiratory flow on ventilator graphics (Figure 10). Physical examination can also detect patient efforts to inspire during the ventilator's exhalation phase[71].

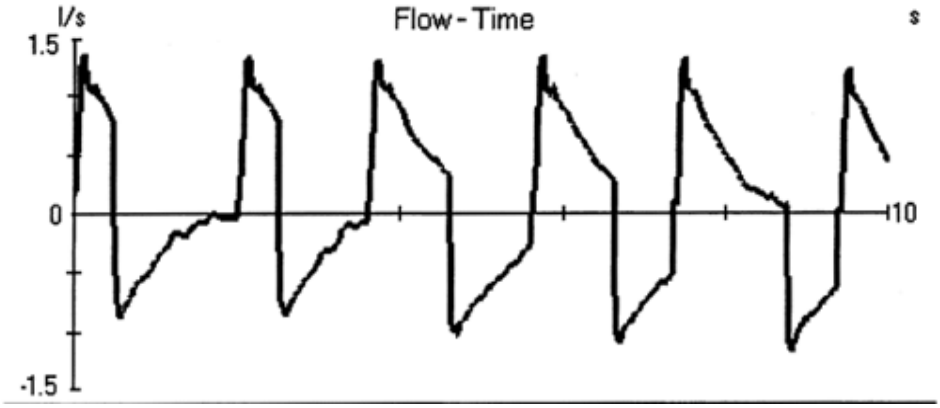


Figure 10 Flow vs. time curve in a patient with dynamic hyperinflation leading to auto-PEEP. On the two breaths at left there is a normal return of flow to 0 L/min prior to cycling over to inspiration. On the curves at right, expiratory flow persists at the onset of inspiration. Adapted from Schmidt Gregory A, "Chapter 32. Ventilator Waveforms: Clinical Interpretation" (Chapter). Hall JB, Schmidt GA, Wood LDH:Principles of Critical Care, 3e: http://www.accessmedicine.com/content.aspx?aID=2286647.

Unfortunately current ventilators are unable to reliably detect the presence of auto-PEEP. The pressure –time curve will continue to display the expiratory pressure as the set PEEP because the ventilator measures pressures at its airway opening. The actual PEEP inside the lungs may be significantly higher. If the patient is completely passive with neuromuscular blockade you can set an expiratory pause to allow time for equilibration between the lung and ventilator. During this pause the ventilator graphics will display the actual total PEEP. Manifestations of auto-PEEP include hyperinflation, severe dyspnea and difficulty triggering inspiration on the ventilator. The hyperinflation may be sufficient to precipitate shock and cardiac arrest.

Treatment of auto-PEEP includes limiting minute ventilation, lengthening expiratory time, and treating expiratory airflow obstruction [32,

72]. Limiting minute ventilation may require opiates to suppress respiratory drive. On AC-VC, consider reducing respiratory rate and tidal volume and increasing the inspiratory flow rate. On AC-PC consider reducing respiratory rate and inspiratory time. On PSV consider reducing inspiratory pressure target and increasing expiratory sensitivity. If auto-PEEP is life threatening consider detaching the endotracheal tube from the ventilator circuit for 30 seconds to allow more complete emptying with exhalation.[73]

5) Are there excessive tidal volumes, airway pressures, Fio_2, or sedation that the clinician can reduce? High concentrations of oxygen are toxic to the lung, as is excessive lung stress by large tidal volumes and pressures. Because it is dependent on the speed with which the ventilator pushes air into the conducting airways, peak inspiratory pressure does not accurately predict the distending pressure of the lung. The best diagnostic test to estimate the distending pressure in the alveoli is to perform a 0.5 second pause at the end of inspiration that prevents expiratory flow. This allows time for the ventilator circuit to better equilibrate with the lung. The pressure measured during this end inspiratory pause is the plateau pressure which should be limited to less than 30cm H_20 to prevent barotrauma[61]. The peak airway pressure and the plateau pressure are both dependent upon the PEEP. Higher PEEP shifts the curve upward. The plateau pressure is dependent on the PEEP, the tidal volume and the respiratory system compliance. The peak airway pressure is determined by the PEEP, the plateau pressure and the pressure generated by resistance to inspiratory airflow. Higher airway resistance and faster inspiratory rates increase the peak pressure. (Figures 11-13)

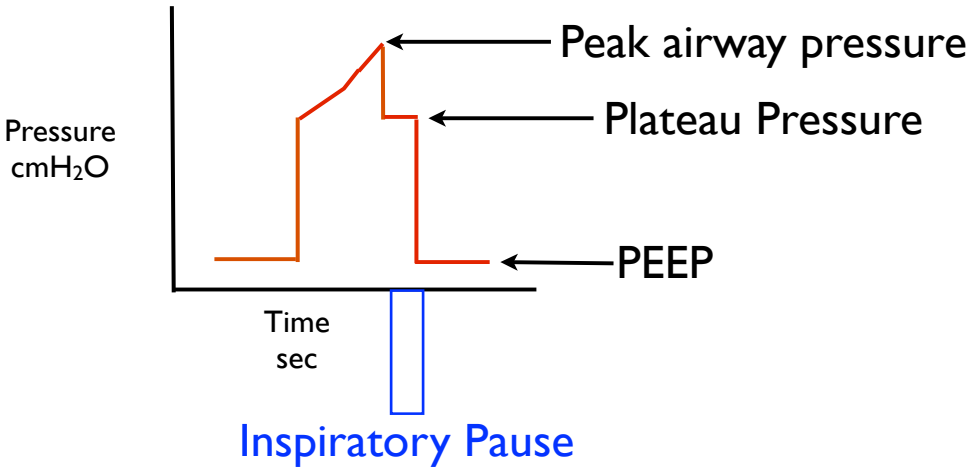


Figure 11 Use of an inspiratory pause to measu plateau pressure. The blue interval on the X-axis is th duration of the pause

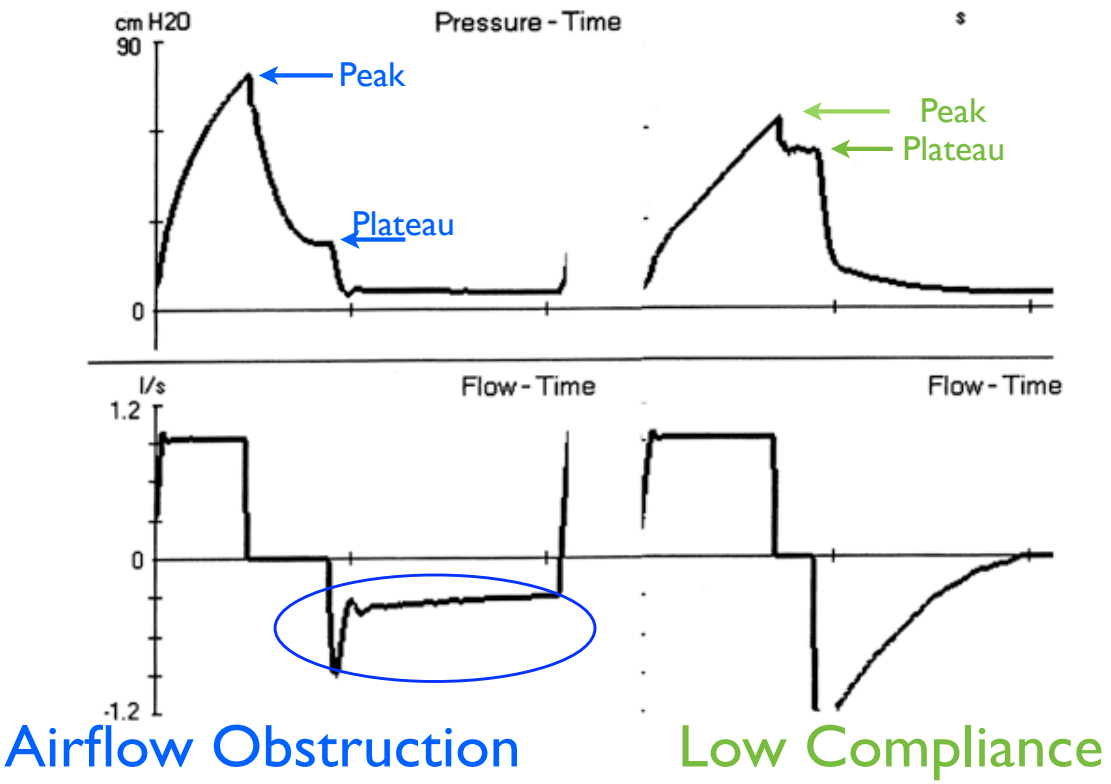


Figure 12 Use of inspiratory pause on AC-VC to determine the cause of elevated peak airway pressure. The patient on the left has expiratory airflow obstruction and therefore a large peak-plateau gradient. The blue circle shows the presence of dynamic hyperinflation which is common with airflow obstruction. On the right there is reduced respiratory system compliance causing elevation of the plateau pressure. There is no significant airflow obstruction and therefore little Peak-plateau gradient Adapted from Schmidt G in Principles of Critical Care Eds Hall et al 3rd edition on Access Medicine

Figure 13 Normal rat lung on left and rat lung ventilated at 45cmH20 for 5 minutes (center) and 45 minutes (right) Adapted from Dreyfuss and Saumon Am J Respir Crit care Med 157 1 1998 295-323

Ventilator Strategies for Specific Situations

Acute Lung Injury (ALI)

This syndrome in its most severe form is called acute respiratory distress syndrome (ARDS). It is defined as the new onset of severe hypoxemia with bilateral lung consolidation that is not due to cardiogenic pulmonary edema. Well-designed clinical trials reveal that survival is significantly improved by limiting plateau pressures to 30cmH_20 and tidal volumes to 6ml/kg/ideal body weight. During the first 24 hours of limiting the distending pressure and volume, there is often deterioration in oxygenation and a worsening of ventilation[48]. Tidal volumes should be lowered in steps while carefully monitoring gas exchange. If the patient becomes severely asynchronous and double triggers the ventilator you can use 8ml/kg/IBW as long as the Pplateau is <30cmH_2O. We typically use high dose opiates, sedatives and neuromuscular blockade to enforce lower tidal volumes in the early stages of severe ARDS [6]. Higher extrinsic PEEP should be applied for ARDS than for other lung diseases. Diffusely infiltrated lung tends to be more recruitable than lungs with a focal infiltrate. The ideal amount of PEEP is unknown; therefore, use the FiO_2 to PEEP ratios in the ARDS Network clinical trials[48]. (Figure 13) Patients may not tolerate these levels of PEEP until they are well resuscitated.[30]

Ventilator mode	Volume assist–control
Initial tidal volume (ml/kg of predicted body weight)†	6
Plateau pressure (cm of water)	≤30
Ventilator rate setting needed to achieve a pH goal of 7.3 to 7.45 (breaths/min)	6–35
Ratio of the duration of inspiration to the duration of expiration	1:1–1:3
Oxygenation goal	PaO_2, 55–80 mm Hg, or SpO_2, 88–95%
Allowable combinations of FiO_2 and PEEP (cm of water)‡	0.3 and 5 0.4 and 5 0.4 and 8 0.5 and 8 0.5 and 10 0.6 and 10 0.7 and 10 0.7 and 12 0.7 and 14 0.8 and 14 0.9 and 14 0.9 and 16 0.9 and 18 1.0 and 18 1.0 and 20 1.0 and 22 1.0 and 24

Figure 14
Ventilation strategy for ALI and ARDS
Adapted from: Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrom
The Acute Respiratory Distress Syndrome Network. *N Engl J Me* 2000, 342(18):1301-1308

Asthma and Chronic Obstructive Pulmonary Disease

These diseases are characterized by expiratory airflow obstruction. Large tidal volumes and high respiratory rates may lead to dynamic hyperinflation and significant auto-PEEP. Therefore, use small tidal volumes at slow respiratory rates to allow sufficient time for exhalation. If using volume cycled ventilation, set faster inspiratory flow rates (70-90 L/min) to prolong exhalation. High peak airway pressures are acceptable as long as the plateau pressure is kept to 30cmH_20. Deep sedation and opiates may be needed to suppress the respiratory drive. The clinician may need to allow hypercapnia and acidemia to limit minute ventilation. In extreme cases the patient may require neuromuscular blockade to limit minute ventilation sufficiently to prevent dynamic hyperinflation[72, 74]. The case fatality rate of young patients intubated for status asthmatics far exceeds the in-patient case fatality rate for myocardial infarction[75].

Shock and Metabolic Acidosis

Patients with these conditions will have a significant central drive for minute ventilation. Given the high drive, the patient may exert excessive energy toward the work of breathing despite mechanical ventilation [76]. If AC-VC is employed, it is important to provide sufficient inspiratory flow rate and tidal volume to satisfy patient demand. Pressure-targeted ventilation may be better tolerated as greater patient inspiratory efforts result in larger delivered tidal volumes at faster flow rates. If high minute ventilation results in excessive tidal volumes or auto-PEEP, the only recourse may be to administer opiates and sedatives to decrease patient demand and, ultimately, a neuromuscular blocking agent if the auto-PEEP is life threatening.

Liberation from Mechanical Ventilation

After the initial phase of resuscitation and stabilization it is essential to keep patients as awake as they can tolerate. Adjust the ventilator for comfort whenever possible. Address discomfort, anxiety and pain with non-pharmacological interventions. Preferentially use bolus sedation/analgesia as opposed to continuous infusions. Implement adequate nutrition and physical therapy as soon as possible[9, 77]. Hold sedation every morning unless the patient is extremely unstable [11]. The value of the rapid-shallow breathing index as a screening tool has been validated on a T-piece device[78]. Protocol based screening for the resolution of respiratory failure was effective in clinical trials[79]. In a clinical trial, a once daily trial of unassisted breathing via T-piece was superior to slowly lowering pressure support or incrementally reducing the frequency of machine initiated breaths on SIMV[66]. While there are no definitive trials proving the superiority of one version of spontaneous breathing trial over another (e.g. T-piece, PSV 5cmH_2O PEEP 5cmH_2O, PSV 0cmH_2O PEEP 0cmH_2O) there may be significant physiologic differences between the different methods. It is important to use a T-piece in situations (i.e. CHF) where a switch to negative pressure ventilation may be deleterious. In my opinion the use of PSV for the spontaneous breathing trials may lead to false failures of due to asynchrony and over-support[80].

Our approach:

a. Trial of awakening each AM
b. Screen all patients each morning for ability to tolerate FiO_2 0.5 PEEP 5cmH_2O
c. If patients pass screen use clinical reasoning (using mental status, hemodynamics, work of breathing, etc.) to determine the pre-test probability for extubation success.
d. If pre-test probability of extubation success is very high >90% proceed to extubation.

e. If pre-test probability is intermediate place on unassisted breathing trial via T-piece for 30-120 minutes and monitor carefully for respiratory and hemodynamic deterioration. Consider extubation if the patient tolerates the trial.

Chapter 7 Critical Care Sedation

I) Determine etiology of problem: Pain, dyspnea, anxiety, drug withdrawal, fear, delirium, hypoglycemia, etc.

II) Treatments: Analgesia, hypnotics, anxiolytics, anti-psychotics
- Also repositioning, re-orientation, reassurance, adjustment of ventilator settings
- Not all patients on mechanical ventilation need sedation

III) Drug therapy should include:
- Induction: Rapidly achieve effect using bolus of short-acting agent
- Maintenance of desired effect; in general requires constant infusion or intermittent dosing of longer acting agents.

IV) Sedatives (especially intravenous agents) can cause life threatening respiratory depression.
- Resident physicians may not administer intravenous sedatives for the purpose of performing procedures to patients not on mechanical ventilation (including radiology, venous access, etc.)

V) Under-treatment of pain and over-sedation of mechanically ventilated patients are common ICU problems

VI) In general, interrupt continuous sedation every day and allow the patient to awaken. This prevents over-sedation and decreases the duration of mechanical ventilation

VII) Hypnotics and sedatives can paradoxically precipitate agitation in patients with delirium

VIII) Elderly and debilitated patients are much more sensitive to sedatives and the lowest possible doses should be used

IX) All sedatives may cause hypotension in patients who are dependent on endogenous catecholamines for maintenance of a minimal blood pressure

X) A combination of agents may be helpful (e.g. combining an opiate with a benzodiazepine)

Order sedative medications to use the minimum effective dose to achieve a target score of the Richmond Agitation and Sedation Scale (RASS).

Figure RASS scale adapted from Sessler[81]

+4	**Combative**	Combative, violent, immediate danger to staff
+3	**Very agitated**	Pulls or removes tube(s) or catheter(s); aggressive
+2	**Agitated**	Frequent nonpurposeful movement, fights ventilator
+1	**Restless**	Anxious, apprehensive but movements are not aggressive or vigorous
0	**Alert and calm**	
-1	**Drowsy**	Not fully alert, but has sustained awakening to voice (eye opening & contact > 10 sec)
-2	**Light sedation**	Briefly awakens to voice (eye opening & contact < 10 sec)
-3	**Moderate sedation**	Movement or eye opening To voice (but no eye contact)
-4	**Deep sedation**	No response to voice, but movement or eye opening to physical stimulation
-5	**Unarousable**	No response to voice or physical stimulation

XI) 1. Sedative agents

Benzodiazepines: Potent anxiolytic and soporific effects; also cause anterograde amnesia. NOT ANALGESIC. Cause respiratory depression and mild hypotension

- **Midazolam (Versed):** Very short onset to and duration of effect.
  - Indicated for short-term sedation (< 24 hrs.)
  - Useful for procedures and immediate treatment of agitation.
  - IV bolus (1-2mg) q 3-5minutes to intubated patients to rapidly induce sedation.
  - Active metabolites accumulate during continuous infusion causing prolonged sedation
  - Re-bolus every time you increase drip rate to achieve desired effect more quickly.
- **Lorazepam (Ativan)** Onset within 15-30 min and effect lasts for hours).

- Can be used for > 24 hrs.)
- Dose intermittently IV or PO to maintain sedation.
- If patient becomes agitated on a lorazepam infusion re-bolus 1-4 mg
- High intravenous doses associated with hyperosmolar metabolic acidosis due to accumulation of its carrier molecule[82]

Propofol (Diprivan) An intravenous short acting sedative.

- No analgesia
- Anticonvulsant
- Reduces ICP
- Indicated for short-term sedation (< 24 hrs.)
- Excellent induction of sedation with repeated 20-30mg boluses.
- Also used for maintenance by continuous infusion.
- Discontinuation of the infusion allows rapid emersion from anesthesia
- Causes **severe hypotension**. Other side effects include bradycardia, severe respiratory depression (and should only be used in intubated patients), pain on injection and hypertriglyceridemia/pancreatitis.
- Prolonged use (>48 hrs.) of high doses (> 5mg/kg/hr.) has been associated with lactic acidosis, renal failure, heart failure, lipemia and bradycardia. Risks for Propofol Infusion
- Phospholipid emulsion provides 1.1 kcal/mL.

Etomidate.

- A potent intravenous hypnotic that rapidly induces sedation with bolus injection. (0.3mg/kg)
- Ultra-short acting with no analgesia.
- Not used for maintenance of sedation.
- Adverse effects: Adrenal suppression, nausea, vomiting on emergence from anesthesia, pain at injection site, myoclonus (33%)
- Minimal cardiovascular effects

Dexmedetomidine. Selective alpha-2 agonist

- FDA approved for the sedation of mechanically ventilated patients and procedural sedation

- Decreases the dose requirement of other sedative and analgesic drugs
- Not analgesic when used alone
- Not an anti-convulsant
- Rapid-loading infusion of dexmedetomidine may cause hypertension and bradycardia because of peripheral alpha-2 adrenoreceptor stimulation
- During dexmedetomidine-induced sedation, patients are usually rousable into an awake and alert state

2. Analgesic Agents

Opiates:
Relieve of dyspnea and cause mild sedation. All opiates cause respiratory depression, constipation, mild hypotension due to sympathetic withdrawal, nausea, decreased GI motility, urinary retention, and muscle rigidity. Consider adding benzodiazepine or propofol if patient requires more sedation.

Morphine sulfate:
- Intravenous bolus of 1-4mg to rapidly induce analgesia
- Morphine causes more severe hypotension by vasodilation than other opiates (because of histamine release).
- Active metabolite may cause prolonged sedation in the presence of renal insufficiency.

Fentanyl: Rapid onset and short duration, but may accumulate with repeated dosing
- Administer intravenous bolus to intubated patients (usually 50 mcg) up to q3minutes

Meperidine (Demerol):
- Avoid because of drug interactions and an epileptogenic active metabolite that accumulates in renal failure.

Hydromorphone (Dilaudid):
- Duration of action is similar to Morphine, but without active metabolite or histamine release.
    - Use in place of morphine when concerned about hypotension

Ketamine
- NMDA receptor antagonist. Dissociative analgesia and sedation.

- IV bolus effective in approximately 30 seconds and effect lasts 5-10minutes.
- Little respiratory depression. Sympathomimetic and may increase heart rate, blood pressure, and induce coronary ischemia.
- Causes nystagmus, raises intracranial pressure and lowers seizure threshold. Emergence delirium with vivid dreams are common. Has bronchodilator effect. Increases salivation. Increases intraocular pressure
- Continuous infusions used at times for refractory pain syndromes and status asthmaticus.

3.Neuromuscular blocking agents (NMBA)

These agents block the nicotinic acetylcholine receptor of the myoneuronal junction of skeletal muscle. They create paralysis; therefore it is essential to provide concurrent analgesia, amnesia and sedation. They are used in our ICU for rapid sequence induction of anesthesia for endotracheal intubation. We also use them to reduce respiratory muscle activity to facilitate low tidal volume/low transpulmonary plateau pressure ventilation[6], stop shivering during therapeutic hypothermia, and to prevent hemodynamic crises from ventilator patient asynchrony. Also used as a rescue intervention for refractory hypoxemia by decreasing the high oxygen consumption from the work of breathing on mechanical ventilation (25% of total oxygen consumption).[5] This raises the $S\bar{v}O_2$ which helps abnormal lungs achieve an adequate SaO_2. Use of NMBAs increases the risk of critical illness polymyoneuropathy. Electrolyte abnormalities and neuromuscular diseases may potentiate or antagonize NMBA effect.

- **Succinylcholine** A depolarizing agent which causes initial fasciculation. Rapid onset (60-90 seconds) and offset (9-13 minutes). Used mainly for rapid sequence induction intubation. Can cause hyperkalemia especially in settings of burns, myodegenerative disorders, chronic abdominal infections. Fasciculation theoretically could raise ICP but this is unproven. Can raise intraocular pressure and cause familial malignant hyperthermia. Cleared by plasma esterase

- **Rocuronium** Non-depolarizing. Rapid onset (60-90 seconds) but effect lasts for 30 minutes. Longer effect in renal or hepatic failure. May increase PVR. Effect prolonged with hepatic dysfunction.

- **Cis-atracurium** Non-depolarizing slow onset (2-3 minutes) longer duration of effect (45-60 minutes). Cleared by plasma esterase so little effect from renal or hepatic failure. Used as continuous infusion in patients with MODS. May cause bradycardia.

Protocol for prolonged neuromuscular blockade (ICU fellow or attending required)

- Set ventilator with sufficient rate of machine initiated breaths
- Ensure secure endotracheal tube
- Sedate patient to RASS-5; ensure sedation will last for the duration of neuromuscular blockade
- Treat pain or dyspnea if present
- Consider Bispectral monitoring to ensure depth of sedation goal 40-60 (unitless value) during neuromuscular blockade
- Order artificial tears to prevent exposure keratopathy
- Monitor baseline peripheral twitch monitor & record amplitude that generates 4 twitches to train of four monitoring. Maximum allowable blockade is 2/4 twitches. (see NYPH policy https://webvpn.med.cornell.edu/Nursing/Standards/N/,DanaInfo=.aiohrrjzGv7zK04u+Neuromusular-Blocking-Agents.pdf)
- Ensure no hard objects impinging on skin/soft tissues
- Review side effects and drug interactions of the chosen agent
- Administer correct dose of drug after pre-procedure time out
- Use lowest dose sufficient to achieve the intended goal (cessation of shivering or limitation of extreme respiratory effort). There is usually no need for full blockade.
- In most situations hold or halve the dose of continuous infusion of blocking agent once per shift and assess if patient still requires blockade

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Part II: Daily Presentation on Attending Rounds

1) Review events of previous 24 hours (e.g. procedures, intubation, extubation, spontaneous breathing trials, dialysis, hypotension,)
2) Current BP, Pulse
3) Current drips (Norepinephrine in mg/min; Dopa and DBA in mcg/kg/min; Neo in mcg/min, vasopressin in units/min)
4) List central and arterial lines, drains and tubes
5) CVP
6) Other Hemodynamics: Cardiac Index, Mixed venous sat, PA pressure, PCWP,
7) Oxygen saturation, Respiratory rate and FiO_2
8) Current vent settings: Mode of ventilator, Tidal Volume, RR set on machine, PEEP, Peak airway pressure
9) ABG
10) Max and current Temp
11) Type and rate of IV fluid
12) Urine output last 2 hours
13) Total amount in and out past 24 hours
14) Last 4 Finger sticks
15) Type of Dialysis If on CRRT: Ultra filtration rate, component and rate of replacement fluid, component and rate of dialysate
16) Type and rate of nutrition
17) Abnormalities on physical examination
18) CBC, Chem-7, LFT
19) Drug levels and other pertinent labs
20) Blood, urine and sputum culture results
21) List each medication and the reason you are prescribing it (antibiotics with length of therapy)
22) Type of DVT prophylaxis
23) GI prophylaxis
24) Head of bed elevated/not elevated at 45 degrees
25) Type of advance directives