

CRITICAL CARE SURVIVOR MANUAL

1ST EDITION, 2022

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Introduction/Disclaimer to this Survivor Manual:

The ICU can be a daunting rotation. The sickest patients of the hospital are within this unit and it can be a very steep learning curve for a lot of learners. This manual was written in an attempt to give you some of the basics to build on - how the unit runs, review on some common presentations and basic physiology and walk through some of the fancy equipment within the unit. A lot of the content stems from what I felt I would've appreciated knowing going into my ICU rotations as a learner. Within the content, I've added some of the evidence to support our practice. This is not at all comprehensive. You are not at all expected to finish reading this prior to or during your rotation. It is made as a reference for some potentially helpful information. You will find that a lot of practice within the ICU is based on gestalt and the "art" of medicine, my hope is to provide some key foundations to start with.

Thank you for reading. Enjoy!
Open to any feedback.

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Introduction to the Intensive Care Unit:

Daily Rounds:

Handover typically begins at 0700 on weekdays, 0800 on weekends. Please be on time. Rounds will begin around 0830. Depending on the unit, we often round on our sickest patients first. On weekdays, residents are expected to use the time in between to pre-round on their patients. Quick tips on how to pre-round:

- It is reasonable to take patients in your first week that you are more comfortable with - e.g. surgical residents take surgical patients, etc. But your ICU rotation is meant to teach you things you may not often see so try to take on patients with presentations you are not as comfortable with!
- Rotate the patients around. Continuity is great but if the same patients are looked after by the same resident, you will see less variability and learn less. And on call you will know the unit better and be comfortable with troubleshooting and managing the issues.
- It is important to address **the reason why they are in the ICU first**. So, their first issue should not be “hypertension”, “diabetes” unless of course if it is “stroke” or “DKA”. There are really only 3 reasons why patients are in the ICU:
 - Shock
 - Respiratory Failure
 - Decreased LOC***PLEASE READ ON THESE PRESENTATIONS AND HAVE A SOLID APPROACH COMING IN***
- The structure of your patient issues should be similar to what you have done with your CTU rounds - Issue, followed by etiology and then plan. Example:
 - “Shock- Secondary to sepsis/distributive, source hospital-acquired pneumonia; On Piptazo/Vanco, norepinephrine and steroids, follow-up cultures and viral panel, maintain euvolemia”
- Review labs, *follow up micro*, recent radiographs and most importantly **EXAMINE YOUR PATIENT**. The nurses will report their head to toe exam but it is absolutely paramount for you to examine your patients yourself.
- Weekend rounding is usually more “rapid” in nature, with the attending/fellow handling the issues as there is a much smaller team around.
- Rounds structure will be:
 - Brief introduction to the patient provided by the resident. One liner - example: “This is patient X, 65M admitted for decreased LOC secondary to SAH from MCA aneurysm, s/p clipping, day 4 of admission”. Any pertinent overnight issues can be highlighted here. For example, “deterioration in neuro status last night, had a STAT CTA, presumed vasospasm, neurosurgery aware”.
 - The bedside RN and RT will present their exam.
 - The team will document pertinent findings in this - for example, if the patient is admitted for decreased LOC. It is important to document their

- neuro findings - e.g. PERL, withdraws to pain x 4. Or if shock - e.g. vasopressor dose, volume status, urine output, peripheral pulses, warm/hot, etc. Or respiratory failure - e.g. FiO2, level of ventilatory support, volume status, secretions, presence of cough
- Then the issues and plan will be addressed by the resident looking after the patient, and supported through by the attending/fellow.
- Lastly, it is important to go over the “Best Practices”. The “best practices” is a concept of going through a checklist to cover all the little but important aspects involved in an ICU admission. There are many approaches that you can find from various resources but a head-to-toe review is one systematic, organized method:
 - Head - HOB up/mobility, pain and agitation
 - Chest - weaning ventilator, fluid goals
 - Abdomen - bowel care, feeds, GI prophylaxis, glucose control
 - Legs - DVT prophylaxis
 - Family update
 - Goals of care
 - Medication review
 - Lines and tubes review
- There is also the acronym FAST HUGS that I have modified for simplicity:
 - Feeds
 - Analgesia
 - Sedation
 - Thromboprophylaxis/Tubes and lines
 - HOB up/mobility
 - Ulcer prophylaxis
 - Glucose control
 - Support - Goals of care, family, meds

Multidisciplinary Teams

- During rounds, you will round with your attending (+/- fellow), residents/medical students, bedside RN, RT (respiratory therapist), pharmacist, nutritionist
- There is also usually a speech language pathologist (SLP) and physiotherapist (PT) in the unit as well.
- **The allied health are invaluable members of the unit.** The ICU simply would not function without them. Introduce yourself, get to know their names. Listen to what they have to say. They are incredible resources, often very experienced and eager to teach. A lot of them will work in almost an auto-pilot mode. But at times, they will need an “MD” to sign off on their recommendations. Ask questions if you are not sure.

Approach to shock:

What is shock?

- Impaired end organ perfusion
- Not strictly hypotension - think about our heart failure patients who have normal systolic blood pressures (SBP) in the low 80s. But yes if your SBP is 60 you are probably in shock.
- Other classic findings of shock:
 - Altered mentation
 - Unwell/mottled appearance
 - Delayed capillary refill > 3 seconds
 - Decreased urine output < 0.5ml/kg/hr for more than 6 hours
 - Cold vs warm peripheries helps you differentiate the type of shock
 - Cold - classically cardiogenic, obstructive, end stage hemorrhagic/distributive
 - Warm - classically distributive
 - Respiratory failure
 - Biochemical markers:
 - Elevated lactate, decreased mixed venous oxygen
 - Abnormal end organ function:
 - Liver - transaminitis, increasing INR, PTT
 - Heme - decreasing PLT
 - Renal - Increasing Cr, metabolic acidosis

In general, there are 4 types of shock:

- Hypovolemic
- Distributive
- Obstructive
- Cardiogenic

Lactate vs mixed venous oxygen:

SvO₂ is the measurement of the oxygenation saturation of blood at the pulmonary artery (PA) and is measured through a PA catheter aka Swan-Ganz catheter. As the literature grew (PACMAN 2005), the use of PA catheters failed to demonstrate improved patient outcome, furthermore its use is associated with high mortality events such as PA rupture(1). These days, we can order a “poor man’s” mixed venous which is measured from a neck central line (i.e. IJ or subclavian) with the catheter tip within the SVC, ideally at the caval-atrial junction. This is described as a central mixed venous oxygen saturation (ScvO₂) and measures mostly the blood drained from the head and neck. ScvO₂ was made popular in the Rivers trial in 2001 for “Early Goal Directed Therapy” for management of sepsis with one of the goals as a ScvO₂ of 70%(2). The discrepancy between the ScvO₂ and SvO₂ is often within 3% so by and large, ScvO₂ has mostly replaced SvO₂. Today, ScvO₂ and SvO₂ are used almost interchangeably as “mixed venouses”. However again, the ScvO₂ still requires a neck central line which not all patients will have while a lactate can be measured through any peripheral/central/arterial sample. There is evidence to support that lactate clearance was non-inferior to ScvO₂ monitoring in the

management of sepsis in terms of in-hospital mortality (3). And thus, lactate has mostly replaced mixed venous as markers of end organ perfusion in the management of shock, particular in septic shock.

Nevertheless, mixed venous are important to understand as it encompasses basic physiology:

Fick's equation tells us:

- **oxygen consumption = cardiac output x arteriovenous oxygen difference**
- **Arteriovenous oxygen difference = arterial oxygen content - venous oxygen content (i.e. mixed venous)**
 - Oxygen content = oxygen carried by Hb and oxygen dissolved
 - Oxygen content = Hb x oxygen saturation x 1.34 + (PaO₂ x 0.003)
- Note dissolved oxygen has minimal contribution to oxygenation and thus **two biggest factors to oxygen content is Hb and oxygen saturation**. Unless you are hemorrhaging, the major determinant for oxygen content is oxygen saturation carried by your Hb.

Assuming oxygen consumption is kept constant, **measuring a low SvO₂ means the arteriovenous oxygen difference is HIGH and indicative of LOW cardiac output**

- By improving the cardiac output, this will decrease the arteriovenous oxygen difference and this will be measured by an increase in SvO₂.
- Furthermore, one can decrease this difference by increasing SaO₂ - this explains why patients in respiratory failure, when you improve their oxygenation, you improve their shock state.

Atypical shock presentations:

➤ High output shock:

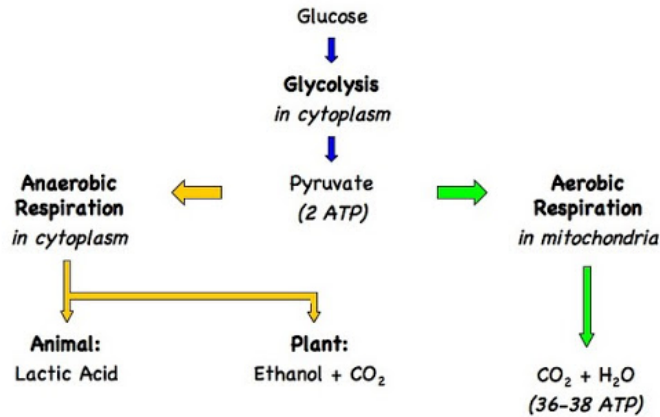
However there are times, especially in what has been described as “high output shock”, which can occur in sepsis where you may have a normal SvO₂ but an elevated lactate and other signs of shock. Clinical findings would be: hyperdynamic heart on echo, warm peripheries, low MAP, low systemic vascular resistance (SVR), the classic picture of distributive shock.

➤ Cellular shock:

Furthermore, especially in toxicology cases, we will have very sick patients with normal MAPs, a normal looking heart on echo but the patient will be in dense shock with elevated lactates and in multiorgan failure. This leaves us with the often forgotten 5th category for shock - **cellular shock**. Let's review the components of oxygen delivery:

- **Oxygen delivery = cardiac output x oxygen content**

Oxygen is the major substrate for tissues to generate ATP via aerobic metabolism. A refresher from a familiar diagram:



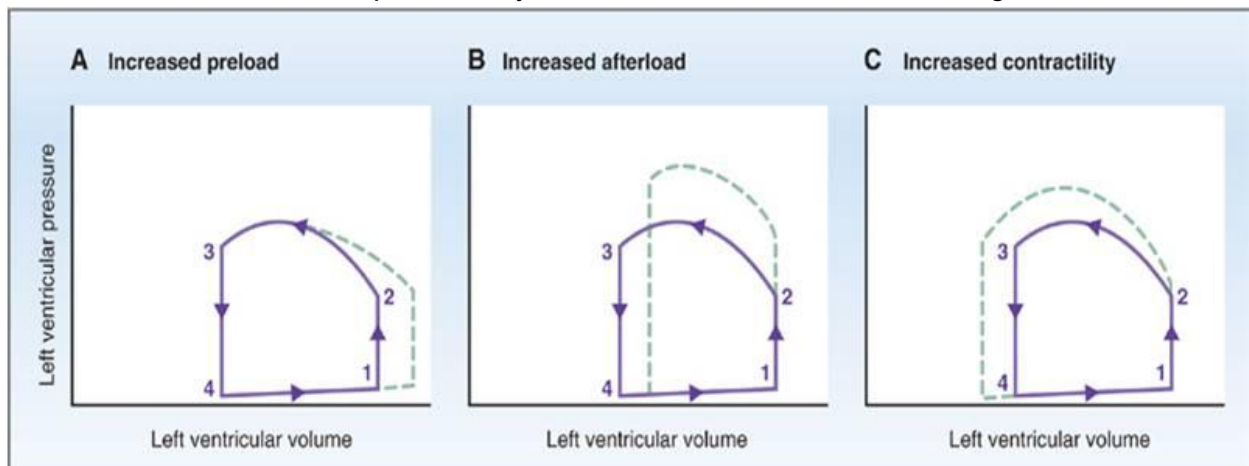
Poor cardiac output usually equates to poor oxygen delivery and thus anaerobic metabolism ensues and production in lactate. However, there are times where there is adequate oxygen delivery but inadequate oxygen consumption due the cellular dysfunction, most often mitochondrial dysfunction and you may have normal SvO₂, normal cardiac output but an elevated lactate and other signs of multiorgan dysfunction. Examples of mitochondrial poisons include: propofol, cyanide, iron, carbon monoxide, isoniazid. Certain inflammatory disease states such as sepsis, pancreatitis, burns, COVID-19, trauma, etc also release various cytokines and inflammatory mediators that can also disrupt mitochondrial/cellular function.

How to optimize cardiac output:

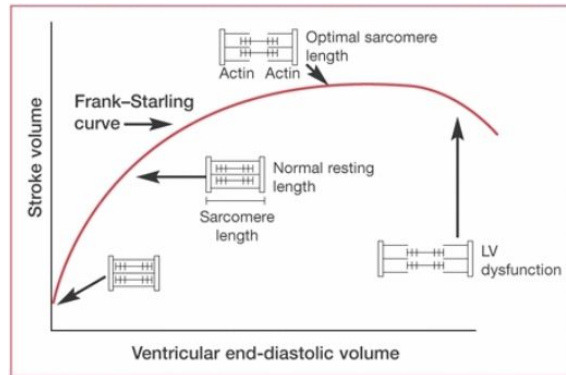
But more often than not, shock is due to decreased cardiac output where the classic 4 types of shock play in. Breaking down what determines cardiac output:

- **Cardiac output = heart rate x stroke volume.**
- **Stroke volume = end diastolic volume - end systolic volume**
 - **EDV determined by preload**
 - **ESV determined by afterload and contractility**

Stroke volume is best conceptualized by another familiar medical school diagram:



- 1) Optimize preload: First things first, make sure the tank is full. It is the easiest thing to do. Let's review the **Frank-Starling Curve**



Often the patient has already had 2-3L of fluids in the ED or on the ward before ICU is consulted. A question to consider would be: Does my patient need more fluid? Or is my patient fluid responsive?

This can be tough to determine as isolated hypovolemic shock is a rare sighting these days in the developed world, furthermore most patients often already have had a reasonable fluid resuscitation prior to coming in. There is an obvious exception with hemorrhagic shock without source control. As one of the more common types of shock is distributive, specifically septic shock. The vasoplegia that occurs in sepsis leads to decreased venous return and compromised cardiac output. However the same inflammatory processes also result in leaky vasculature and third spacing mechanisms where the fluid given can creep into the interstitial space of organs, especially the lungs. There is good evidence that aggressive fluid resuscitation leads to higher incidences of ARDS, ventilator days and mortality(4). So how much fluid is enough?

➤ **Methods to determine fluid responsiveness:**

- JVP
- Pulse pressure variability on the arterial waveform
- Bedside POCUS - IVC distensibility on mechanically ventilated patients, or IVC collapsibility in spontaneously breathing patients.
- Improvement in MAP with Passive Leg Raise
- Improvement in MAP / end organ perfusion with fluid challenge of 500ml

- 2) Increase contractility: this is where bedside echo can be very useful. Before this, they were floating Swans in to measure cardiac index which again as mentioned before, PA catheters have become a rare sighting in the ICU in the last 20 years. Take a look at the RV and LV contractility and determine if the patient may benefit from an inotropic agent like milrinone or dobutamine. If you don't have much experience with bedside echo, grab a probe and ask someone to teach you and practice, practice, practice! There are a ton of FOAMed resources online as well - thepocusatlas.com is a good, free one to start!

- 3) Minimize afterload: Well, a lot of our patients in septic shock have already self-managed their afterload reduction with vasoplegia.

If improving cardiac output usually from those 3 things - ie. increasing preload, decreasing afterload and increasing contractility - why is norepinephrine, predominantly a vasopressor, the first line agent for shock?

One must review **Ohm's Law**:

- **Pressure = Flow x resistance (V = IR)**
- **where Flow = Pressure / resistance**

That is, in order to have flow towards tissue - you need a pressure gradient. Vasopressors also act on the venous system, increasing systemic venous pressures and thus the pressure gradient for venous return back to the right atrium. From a tissue perfusion perspective on the arterial side, vasopressors are also often titrated to MAP targets (**MAP = DBP + 1/3 pulse pressure**). In general, albeit mostly an arbitrary number, the MAP goal is set as 65 mmHg.

Overview of vasopressors and inotropic agents:

This has been taken from the Internet Book of Critical Care: <https://emcrit.org/ibcc/pressors/>

Drug Typical dose range	Target	Effect on - Heart rate - Inotropy - Ectopy	Effect on systemic vascular resistance	Effect on cardiac output	Effect on blood pressure	Effect on pulmonary vascular resistance	Main uses	Safe for peripheral use?
Inodilators								
Dobutamine 2-20 mcg/kg/min	αββββ	↑↑↑↑	↓	↑↑↑↑	Variable	↓	Cardiogenic shock	
Milrinone 0.375-0.75 mcg/kg/min	cAMP	↑↑↑↑	↓↓↓	↑↑↑↑	Variable	↓↓↓	Cardiogenic shock	
Isoproterenol 2-10 mcg/min	ββββ	↑↑↑↑↑↑	↓	↑↑↑↑	Variable		Bradycardia	Yes
Pure Vasopressors								
Vasopressin 0.01-0.06 U/min	V1 & V2	↓	↑↑↑↑	↔/↓	↑↑↑↑	↓	Distributive shock, Pulmonary HTN	No.
Phenylephrine 40-180 mcg/min	αααα	↓	↑↑↑↑	Variable	↑↑↑↑	↑↑	Distributive shock	Yes
InoPressors								
Norepinephrine 0-40 mcg/min*	αααβ	↑	↑↑↑↑	↔/↑	↑↑	↔	Shock (most types)	Yes, for short period with monitoring
Epinephrine 0-20 mcg/min*	αβββ	↑↑↑↑	↑	↑↑↑↑	↑↑		Bradycardia, cardiogenic shock, sepsis, anaphylaxis	Yes
Dopamine, low 1-4 mcg/kg/min	Dopa-R	↔	↓	↑	↓		Zombie apocalypse (absence of better agents).	Probably not
Dopamine, medium 4-10 mcg/kg/min	αβββD	↑	Variable	↑↑	Variable			
Dopamine, high 10-20 mcg/kg/min	αααβD	↑↑	↑↑	↑	↑↑↑↑	↑		

My take on pressors:

Norepinephrine:

- Go-to pressor in undifferentiated shock. Why? It provides alpha squeeze but also some beta 1 (chronotropy) and beta 2 (inotropy). Start at 5-10mcg/min. It is easy to titrate. There is a plateau threshold where escalating doses yield minimal effect. This is usually around 0.5mcg/kg/min or 30-50mcg/min.

Phenylephrine:

- Pure alpha squeeze. Can be given peripherally and a great “push dose pressor” in acute resuscitation and during procedures where you may anticipate acute changes in hemodynamics - most notably intubation. Phenylephrine also has good venosqueeze and thus helps provide a quick “bolus” through venous return to the heart. Good starting dose would be 100-200mcg boluses. Due to its popular use in codes, phenylephrine now comes in pre-mixed syringes and available in most codes with the code RN.

Vasopressin:

- Pure systemic squeeze but at the V1 receptor level. One pro is that there are no V1s in the pulmonary circulation and thus favorable in RV failure. There is a paucity of evidence for any mortality benefit in septic shock (VASST 2008, VANISH 2016) but it is safe to use at lower doses (0.02-0.04 units/min), will lower your norepinephrine requirements and may provide some renal benefit (VANISH 2016) (5,6). Typically vasopressin will be started in refractory distributive shock; my threshold is at norepinephrine doses of 10-20mcg/min.

Dopamine:

- Dopamine is the only pressor that has evidence going against its use. It is associated with increased adverse events (mostly arrhythmia), increased mortality in patients with cardiogenic shock and pediatric septic shock(7,8).
- Works on dopamine receptors and has indirect alpha, beta 1 and 2 effects but also some endocrine effects and thus called a “dirty” drug due to its variable responses at variable doses; Furthermore it is notoriously associated with tachyarrhythmias.
 - 2-5mcg/min - renal perfusion dosing
 - 5-10mcg/min - more inotropy and chronotropy
 - >10mcg/min - vasoconstriction
- The only time I use dopamine is that dopamine has a long shelf life and is pre-mixed and ready for use in all crash carts. In a code situation where a patient needs pressors and the RNs are mixing norepinephrine, I may temporize with dopamine - generally start at 10 mcg/min. Another pro is that dopamine can be run peripherally.

Epinephrine:

- Alpha, beta 1,2. First line for anaphylaxis. A part of ACLS cardiac arrest management. Know your doses well. They show up on exams and save people in real life. Anaphylaxis: 0.3mg IM of 1:1000 epi. Cardiac arrest: 1mg IV/IO of 1:10,000 epi.
- There is also “push dose epi” that has been well described by the EMCrit guys. I like it in code situations as a quick ionopressor. Dose is 10-20mcg boluses. You can make it by mixing a syringe of cardiac epi (1mg in 10ml) into a 100ml NS bag = 10mcg/ml.
- Otherwise, for patients in dense shock that need inotropy who may not tolerate the vasodilatory effects of dobutamine and milrinone, as the alpha effect of epi certainly helps counter this.

- NB: epinephrine will notably increase HR and thus are associated with tachyarrhythmias and due to the prominent beta effect, can cause type B lactic acidosis.

Dobutamine and Milrinone:

- A lot of anecdotal debate but there is not a ton of evidence to point to either. A new NEJM study further supports this in cardiogenic shock (DoReMi 2021)(9,9). Here are some common pros and cons to this debate:
 - Milrinone - inhibits PDE3 and will increase myocardial contractility but smooth muscle relaxation; it tends to have more of a pulmonary vasodilatory effect and thus favorable for the RV. Difficult to titrate and takes time to work and thus not easy on and off. It is renally cleared so caution in use in patients in renal failure, it will take a time to wear off. Good starting dose would be 0.25 mcg/kg/min
 - Dobutamine - beta 1, 2; quicker onset, easy to turn on and off, easier to titrate. May have desensitization with prolonged use; Good starting dose would be 2.5 mcg/kg/min
 - Both will cause systemic vasodilation and thus will likely increase your norepinephrine requirements. Both can cause tachyarrhythmias, anecdotally milrinone tends to do so less

Common/Important Presentations of Shock:

Sepsis:

Sepsis is one of the most common presentations you will see in the ICU. Patients of all types can end up extremely sick with multiorgan failure from sepsis. Furthermore, we are seeing increasing incidences of sepsis and more severe illness in part by our advances in medicine, aging population and surge of multidrug resistant organisms. And thus, It has been and will continue to be extensively studied. It is easy to get into a rabbit hole with all the literature and studies but I think for the most part, it is best to keep things as simple as possible.

First, what is sepsis? The definition of sepsis changed in 2016 with the Sepsis-3 guidelines.

- **Sepsis = life-threatening organ dysfunction caused by a dysregulated host response to infection**
- **Septic shock = Sepsis + shock defined as “despite adequate resuscitation, requires vasopressors to maintain a MAP of at least 65 and a lactate of >2mM”**

Sepsis-3 also came out with a scoring system that helped risk-stratify patients early in terms of their mortality risk. This is the quick Sequential Organ Failure Assessment (qSOFA) score, where 2 points or higher have increased mortality:

- RR greater than or equal to 22/min
- Altered mentation
- SBP < 100

There is also the long and convoluted SOFA scoring which can help prognosticate and risk stratify patients (great for research!) but not necessarily change clinical management.

In medical school, we were taught the SIRS (Systemic Inflammatory Response Syndrome) criteria as a method to identify sepsis. Despite what Sepsis-3 tried to do, I don't think SIRS is a lost cause and is still very helpful in **screening** for patients who may have sepsis but recognize that patients who meet SIRS criteria may not be septic - e.g. pancreatitis, trauma, burns. Another scoring system that is used more in pediatric care is NEWS (National Early Warning Score).

This is my approach to Sepsis:

1. Stabilize ABCs.
2. **Recognize it early.** Use SIRS, NEWS, qSOFA, clinical gestalt whatever you choose.
3. Start empiric management
 - Hard to confirm the diagnosis of sepsis as you need to know you have an infection - cultures take time to grow, in general in the ICU, our patients are sick. **Start big guns early** and dial back when you can. Piptazo is a good antibiotic to start in the following patients:
 - i. Undifferentiated sepsis
 - ii. Hospitalized patients
 - iii. Intra-abdominal sepsis
 - iv. Immunocompromised
 - If you know the source:
 - i. CAP - Ceftriaxone and Azithromycin
 - ii. GU - Ceftriaxone
 - iii. GI - Piptazo
 - iv. Meningitis - *Meningitic dosing* of Ceftriaxone, consider Vancomycin for extended gram positive coverage, consider acyclovir if concern for HSV; consider ampicillin if concern for Listeria; use Meropenem if hospital-acquired.
 - v. Skin and Soft Tissue - Cefazolin; Vancomycin if concern for MRSA, Clindamycin and IVIG if concern for necrotizing infection or toxic shock; use Piptazo instead of cephalosporin if concern for polymicrobial especially in vasculopathies and diabetics
 - vi. **REVIEW their previous micro / cultures** - a lot of patients are recurrent presenters and have had antibiotic resistant patterns in the past:
 1. ESBL - use meropenem
 2. MRSA - use vancomycin / linezolid / daptomycin
 3. Pseudomonas - first consider if this is colonization - use Meropenem
4. Determine the source. **It's all about source control.**
 - Get as much history as you can
 - Head to toe exam
 - Consider CT imaging
 - Talk to your surgeons once identified a surgical source
5. Follow-up on cultures. Look for alternative diagnosis or sources or broadening if the patient is not improved in 24-48 hours.

***Note:** sick patients do not always need meropenem. If it is an obvious community acquired pneumonia or urosepsis in a patient with no history of ESBL, it is very reasonable to use ceftriaxone. We need to be astute physicians and have some insight into antibiotic stewardship. The key for sepsis is early administration of antibiotics, particularly use of a beta-lactam which will cover the bugs that can kill their hosts quickly or make them very sick through toxin-mediated mechanisms - i.e. group A strep and gram negatives. Not everyone needs piptazo or meropenem especially if the source is known.

The Surviving Sepsis Campaign recommends this 1 hour bundle, I think it provides a good framework to start:

1. Get initial lactate
2. Get blood cultures
3. Start empiric antibiotics
4. Fluid resuscitate with 30ml/kg of crystalloid for hypotension or lactate > 4
5. Start vasopressors if still hypotensive

Back to #1. Stabilize the ABCs. Let's talk about C. **In shock, it is best to optimize C, before you deal with A and B.** Sepsis is most often a distributive type of shock but consider cardiogenic as well.

1. Optimize preload - Surviving Sepsis recommends 30ml/kg but again how much fluid is enough fluid. ^Go back to previous section to review
2. Optimize forward flow
 - a. Is my patient vasoplegic? - needs peripheral squeeze - start norepinephrine
 - b. What are my ventricles doing - needs inotrope - start dobutamine
3. Optimize A and B
4. Patient status will flux. Always go back and reassess your patients.
5. **Refractory shock:**
 - a. What is refractory? Escalating doses of norepinephrine - I would say around 20mcg/min this would be a reasonable starting threshold to consider adding another vasopressor - vasopressin. And adding steroids.
 - b. A lot of work done on steroids. Overall mostly safe to use and has mortality benefit (APROCCHHS 2018) especially in patients with refractory septic shock(10). Hydrocortisone is often given for its additive mineralocorticoid effect - start at 200-300mg/day (50mg q6h or 100mg q8h depending how sick the patient is). Have a low threshold in patients who would have adrenal insufficiency - i.e., patients on chronic steroids.

Pulmonary Embolism

Pulmonary Embolism can result in a wide spectrum of disease. There are patients that can be treated as outpatients and patients who end up on ECMO or die. PE is a diagnosis that can be challenging to make without a CT chest PE. We often do not use V/Q scans in the ICU as the majority of our patients will not have a normal CXR rendering the V/Q scan less helpful. One

can look up the risk factors easily for VTE but going back to **Virchow's triad of stasis, endothelial injury and hypercoagulable state** helps remind us of those risk factors.

There are many ways to classify PE:

- Acute vs chronic
- Submassive vs massive
- Provoked vs unprovoked
- Peripheral vs central
- Saddle vs segmental vs subsegmental

What's most relevant for us in the ICU is thinking about how the PE affects the patient's hemodynamics - **is this a submassive or massive PE?** And lastly **what is the clot burden and pattern** because this will help guide us in it's management of relieving that clot burden.

Definition of massive and submassive PE:

- **Massive = patients who are hemodynamically unstable** defined by sustained hypotension (SBP < 90 for >15 min or requiring vasopressor support not explained by alternative diagnosis) or associated with persistent bradycardia or pulselessness
- **Submassive = patients who do not have hypotension but have RV dysfunction or myocardial injury** defined by:
 - RV dysfunction:
 - Echocardiogram findings: RV dilation, Septal bowing, McConnell's sign, TAPSE < 17
 - Electrocardiogram findings: New incomplete/complete RBBB, Anteroseptal STE/D or TWI, classic S1T3Q3
 - Biochemical findings: BNP > 100
 - Myocardial injury:
 - Troponin elevation > 0.4

Approach to workup and management of PE:

1. Everything starts with stabilizing the ABCs. See below for a primer on acute RV failure.
2. Get the information you need:
 - a. CT Chest PE, echocardiogram (bedside and formal), blood work - ABG, troponin, BNP, coag panel, CBC, renal function
3. **Anticoagulation:**
 - a. In the ICU, we tend to use UFH due to the higher chance of use of lytics / interventional procedures / surgery. However, early therapeutic anticoagulation stabilizes clot and is the mainstay of management. Thus, if the patient is stable and would be a good candidate for LMWH, there is no reason not to use it as there is no faster way to achieve therapeutic anticoagulation. If a patient has a history of HIT, this usually buys a Heme consult and the patient would likely need an alternative agent like argatroban or fondaparinux.
 - b. Be aware of any contraindications to anticoagulation - in general this is like significant BLEEDING. That is bleeding that would be catastrophic (brain, spinal

cord), difficult to control (noncompressible site), or life-threatening (GIB, RPH, pulmonary hemorrhage). You will die from bleeding a lot faster than from a VTE.

4. **Antifibrinolytic:** There is quite a bit of literature out there regarding indications, dosing, timing, and type of antifibrinolytics in these patients (i.e. submassive and massive PEs). In general, you would never give a lytic to a patient without consultation with your attending unless perhaps if the patient has been arrested. Here is a brief and simplified review:

For massive, generally indicated especially if ongoing instability and without interventional radiology or cardiothoracic surgery for catheter-directed lysis or surgical embolectomy options:

- a. If the patient has arrested:
 - i. Give 50 mg as bolus over 15 minute and repeat x 1 if no effect.
- b. If the patient is not arrested:
 - i. Give 100mg over 2 hours OR 20mg a bolus then infuse the rest of 2 hours

For submassive:

- a. Evidence is less clear. PEITHO 2014 showed improved hemodynamics but increased risk of bleeding and unchanged mortality(11). TOPCOAT 2014 showed better functional outcome (12) and MOPETT 2013 showed lower rates of pulmonary HTN and trend to lower mortality when using lower dose of lytic (13).
 - i. Consider stability of the patient, clot burden and bleeding risk. Is the patient amenable to catheter-directed lysis instead? EXPRESS 2019 showed better outcomes.
 - ii. If the patient starts to crash, this patient is no longer submassive and really is now massive -> would give lytic - with MOPETT trial and especially if higher risk of bleeding, start with lower dose at 50mg - first 10mg as bolus then 40 mg over 2 hours.

^NB: if you are going to lyse, there is equipoise on what to do with anticoagulation, but North American guidelines tell us to hold anticoagulation during lytic administration and 2-3 hours after; Europeans do not hold.

Primer on RV Failure:

The RV is a very fragile, thin-walled ventricle. It is accustomed to the low pressure pulmonary system in otherwise healthy individuals. RV systolic pressures are usually in 20-30 mmHg range in comparison to the LV at 90 to well above 100. As with obstructive shock, the significance of interventricular dependence becomes emphatically highlighted. A failing RV will balloon out, compress the LV and thus lower systemic cardiac output. There are not many things that will cause an RV to acutely fail, but acute PE is definitely one of them.

Breaking down the elements of cardiac output helps simplify an approach to managing RV failure.

- Stroke volume:

- **Optimize preload** - this is very challenging to ascertain as this really needs to be a "Goldilocks" concept. Not too empty, not too full, needs to be just right. In an unstable patient with an acute PE, giving too much volume may cause further

ballooning out of that RV. However, without adequate preload, there is no forward flow. This is a patient I would trial small boluses to see if they are fluid responsive - 250-500ml of IVF. OR a passive leg raise. If you feel this patient is volume overloaded, a trial of diuretic can be done but recognizing the effect is not immediate.

- **Contractility:** Consider starting an inotrope to promote forward flow - dobutamine has a quicker on/off but milrinone has better pulmonary afterload reduction
- **Afterload:**
 - There is an obvious afterload burden with an acute PE - this is where antifibrinolytics should come in - systemic vs catheter-directed.
 - **Minimize pulmonary vascular resistance:**
 - Things that will increase PVR: hypoxia, hypercarbia, acidosis, sympathetic drive, high airway pressures
 - Starting pulmonary vasodilator - common one would be inhaled nitric oxide
 - **Optimize systemic vascular resistance:**
 - Keep MAP goal at 65 - to offset the increasing right sided pressures, you need to have adequate LV pressures to promote forward flow and perfuse the coronaries. Using a vasopressor like vasopressin is favorable as it has less effect on the pulmonary vasculature. Avoid phenylephrine as it will increase both. Can use norepinephrine as you have some mild inotropic and chronotropic effect.
- **HR: Target a HR of 80-100.** Too fast, the coronaries will not fill. Too slow, you may overload the RV during filling. Sinus rhythm ideally.

I hope it is much more clear that intubation and positive pressure ventilation can potentially kill your patient in acute RV failure - this will decrease preload and increase afterload. These are patients who have extremely delicate hemodynamics so call for help early. Furthermore, these are patients who if meet the right indications, i.e, young with reversible disease, should be considered for VA-ECMO should medical therapy not suffice.

Cardiogenic shock

As shock will result in multi-organ dysfunction, it is more common to manage cardiogenic shock in the ICU rather than the CCU. This does not mean the cardiology team is not involved with their care but we are often the MRP in their management as it includes ventilator management, pain/sedation/agitation, and often CRRT.

Once you have identified the patient is in the cardiogenic shock. The approach to their management is again the same: preload, stroke volume and afterload.

Stroke volume:

- **Preload:**
 - Especially in patients with known heart failure, especially in the heart failure with reduced ejection fraction (HFrEF) population, understanding their volume status is important:
 - What is their weight change? Medication and diet compliance? Examine for organomegaly, JVP/IVC, edema
 - If overloaded - then diuresis is important. It may seem odd to diurese someone who is on vasopressors and inotropes but again going back to the **Frank-Starling curve** you are trying to realign those sarcomeres to optimize contraction of the ventricles.
 - Dosing of diuretics can be difficult. DOSE trial 2011 showed no difference in symptoms or worsening renal function between intermittent bolus vs continuous infusion. High dose (2.5x home dose) vs low dose (home dose) had similar findings but intuitively, high dose achieved better diuresis and weight loss but trends towards worsening renal function. In general, if your goal is to get fluid off, get fluid off first. If home dose is furosemide 20mg BID - I would start with 20-40mg IV BID. The kidneys are resilient and most often there is some cardiorenal syndrome at play, and diuresis may improve renal function. Lastly, if the prescribed dose is not effective, reassess the patient to see if your suspicion of volume overload holds, and double up your dose in 2 hours.

- **Afterload:** Systolics in the 80-90 range. This will lower your MAP but often a traditional MAP goal of 65 is ambitious. One needs to balance minimizing afterload and work of the heart to perfusion of the end-organs. We often lower our MAP goals to 55-60 and assess if this provides adequate perfusion to our end organs - mentation, urine output, cap refill, lactate, mixed venous etc.

- **Contractility:** An inotrope is often necessary. Milrinone vs dobutamine, pick one.

HR - any new arrhythmia? Review their old ECGs to compare.

- New bradyarrhythmia? - Consider pacing:
 - Electrically - transvenous preferred. IF in a pinch, transcutaneous asynchronously at 80-100bpm and 70mA and call for help.
 - Chemically - try isoproterenol at 2-10mcg/min
- New tachyarrhythmia - *common culprit is rapid atrial fibrillation*
 - This is where we love our amiodarone - start at 150mg IV boluses and then infusion at 1mg/min. The goal is to obtain a load of 900mg so if the patient is not yet responding, one can repeat the bolus dosing.
 - Amiodarone initially acts as a gentle beta blocker; allows us to rate control our patients without having to use an actual beta blocker which is less than ideal for patients in shock as it is an negative inotrope.
 - Digoxin can be a reasonable option however digoxin takes a long time to work and has a long half-life; and a lot of the times these tachyarrhythmias are short-lasting.

- There is minimal downside to giving MgSO₄ to patients - low threshold to top off their magnesium with 2g or 5g IV. Consider having Mg goals of > 1; K goal of > 4 to keep the heart less irritable.

Ascertain the etiology behind the failing heart:

A cardiologist once broke down cardiology very simply to me: there is the pump, the pipes and the electricity. Common things being common, a driver to all of these problems is often the pipes aka ischemia.

- Ischemia is not always obstructive and thus there are various types of myocardial infarction to consider: Type 1 vs type 2, etc. Review of these types:
 - **Type 1 = primary coronary event - classically plaque rupture, or from other causes like dissection, vasospasm *these patients need a cath***
 - **Type 2 = demand >>> supply *correct this imbalance***
 - Type 3 = sudden unexpected cardiac death
 - Type 4 = associated with PCI
 - Type 5 = associated with cardiac surgery
 - ^Type 3-5 no change in management.
- By in the large, it is critical to rule out Type 1 causes and we do this by clinical features, ECG findings, biochemical aka troponin findings and echocardiogram findings (*caution use if inexperienced*).
- However, there are many type 2 causes to consider: Sepsis, trauma, burns, pancreatitis, PE, aspiration, hypoxemia, etc.

Other causes of pump failure to consider are: a metabolic etiology like hyperthyroidism/thyroid storm, post-viral, mechanical - valve failure, volume overload, right sided from pulmonary disease

GI Bleed

1. Consider upper vs lower. This often changes management in terms of how you will get source control.
 - a. Upper clues: hematemesis, melena
 - b. Lower clues: Hematochezia or BRBPR, no hematemesis.

2. Upper GIB:

DDx: ulcer, gastritis/esophagitis, MW tear, Dulofuy's lesion, varices.

- a. Low threshold to activate massive transfusion protocol. You do this by calling the blood bank. This mobilizes blood in an expedited fashion and the blood bank will send O negative uncrossmatched blood until we ask them to stop. We are often involved as the patient is becoming unstable; so this is not the time to wait an hour for blood and transfuse the blood over an hour as we usually tolerate on the ward. Transfuse with balanced blood - 1:1:1 ideally or 1:1:2 (PROPPR trial) (14). This means 4 units FFP: 1 pooled PLT (1 pooled PLT = 4 units of PLT): 4 or 8 units of RBC

- i. Do not forget to keep the patient warm and replace calcium (1 amp or 1g for every 4 units of blood product as citrate in the blood product will chelate calcium).
 - ii. Reasonable targets would be:
 - Hb > 70 - more restrictive strategy has better mortality than liberal; i.e. Hb target > 90 - (Villanueva 2013 NEJM); unless active coronary disease then > 80
 - PLT > 50
 - INR > 1.5
 - Fibrinogen > 1.5
- b. Ensure adequate IV access:

$$Q = \frac{\Delta P \pi r^4}{8 \eta l}$$

- i. Back to Poiseuille's law: And thus, long and narrow = bad.
 - ii. So peripheral 18G will provide about 90ml/min in comparison to a triple lumen central line about 50ml/min. A 8.5Fr cordis is the best choice at 300ml/min.
- c. Reverse any coagulopathy:
- i. **For the NOACs:** the only antidote that is available is **Idarucizumab (Praxbind) for dabigatran**; if Praxbind is unavailable, dialysis may work as dabigatran is less protein bound. Otherwise despite the lack of evidence, it is PCC (Octaplex) for all others in life-threatening bleeds. This is off-label use but give **PCC 5000 units IV**.
 - ii. **Warfarin: Vitamin K 10mg IV and PCC 2000 units** to start if unknown weight and INR; otherwise look up dose (from Thrombosis Canada):

PCC Dosing Table

	INR 1.6-1.9	INR 2.0-2.9	INR 3.0-5.0	INR > 5.0
Weight Less than 100 kg	5,00 units	1,000 units	2,000 units	3,000 units (maximum)
Weight More than 100 kg	1,000 units	1,500 units	2,500 units	3,000 units (maximum)

- iii. **Heparin and LMWH: Protamine;** look up dose, will depend on timing of last bolus vs infusion.
 - iv. Antiplatelets: not much can be done. PATCH 2016 trial showed platelets in the context of ICH related bleeding showed worse outcomes.
 - v. TXA in GIBs: HALT-IT trial in 2020 did not show a 5d mortality benefit and potential trend to harm of increased VTE (15). Evidence for TXA use in GIB is not as robust as the Trauma and postpartum literature.
- d. Start pantoprazole infusion. There is no mortality benefit with the 80mg bolus or 8mg/hour infusion (compared to 40mg IV BID or intermittent dosing) but will

reduce ulcer bleed. In general this protocol is used unless you are really short on vascular access.

- e. If concern for variceal (i.e. liver disease or cirrhotic history):
 - i. Add octreotide 50mcg bolus then 50 mcg/hr IV infusion
 - ii. **Cetrixone for SBP prophylaxis (1g daily) *mortality benefit*(16)**
 - iii. If hemorrhaging and difficult to control - watch a YouTube video on Blakemore/Minnesota esophageal balloon insert. LITFL also has a good page on it. And call for help.
- f. **Call GI for endoscopy.**

3. **Lower GIB:**

DDx: hemorrhoids, diverticular disease, ischemic colon/bowel, mass, brisk UGIB

- a. Same as above. Unlikely will benefit from PPI or octreotide infusion but if sick and unstable, minimal harm until more differentiated.
- b. Involve GI but these patients usually need a CTA to assess for blush or active arterial source that is amenable to IR for embolization.
- c. If failing IR, usually will not be amenable to lower endoscopy due to poor visualization - next step is to involve general surgery.

Introduction to decreased LOC:

This is where examination and documentation of the neurological exam is very important. Unlike most organs, the brain and rest of the nervous system have very few measures of function. Compared to the heart, there are biochemical markers like troponin, ECGs, echocardiograms, angiograms, nuclear scans, CTs, MRIs etc to measure its structure and function. There sadly isn't a blood test yet available for brain function. We have clinical exams, EEG and radiographic findings.

Let's start with clinical exam:

1. Level of consciousness: Everything is great if the patient is alert, conversing and obeying commands x 4. Often our patients are not. There are many ways to assess their LOC but I like the Glasgow Coma Scale (GCS). Although mostly validated in the trauma literature, the GCS provides an objective measure and a scoring system that nearly all health care providers can use and understand. Reminder of the GCS:

	Eyes	Voice	Motor
1	No eye opening	No speech	No movement
2	Eyes to painful stimulus	Incoherent speech	Extending Decerebrate
3	Opens eyes to voice	Inappropriate words	Flexing Decorticate
4	Spontaneously opens eyes	Confused	Withdraws from painful stimulus
5		Oriented	Localises to painful stimulus
6			Obeys commands

2. Motor exam: focality is important so examine all 4 limbs.

- It was always a bit confusing as to what is localize vs withdraw vs flexion:
 - Localize - limb must cross midline: e.g. patient grabs for endotracheal tube (ETT) to self-extubate, or you pinch the shoulder and the contralateral limb responds towards the pain stimulus
 - Withdraw - the limb will have sustained efforts away from the stimulus
 - Flexion - more reflexive, the limb will have effort away but not sustained.
3. Eyes:
- comment on pupillary size and reactivity. The term “sluggish” gets used at times, but to me, reactivity is binary - reactive or not. Sluggish always concerns me that the pupils are not reactive but the examiner is too nervous to call it nonreactive.
 - Comment on ability to track; eye opening/closing can be reflexive
4. Brainstem reflexes: pupils, corneals, cough and gag. These are especially important in patients who have loss of cortical function - i.e. no longer obeying or localizing. Also, if the patient is on the ventilator - are they triggering breaths?
5. Tone/Clonus/Reflexes - I don't tend to do them in all exams but can be very helpful in certain situations. E.g. in patients with generalized weakness, looking for signs of GBS or spinal cord injury with areflexia; or with drug overdose, looking for signs of neuroleptic malignant syndrome or serotonin syndrome with signs of clonus, hyperreflexia, increased tone, etc.

Keeping it simple, I still use the old medical school **DIMS approach for decreased LOC:**

1. Drugs:
 - Think about sedatives/hypnotics/narcotics - the urine drug screen is plagued with false positives and false negatives; furthermore not helpful in narrowing the timing of the ingestion but can be helpful if all other causes ruled out and the history fits - e.g. younger patient found down in downtown eastside with drug paraphernalia and a positive urine fentanyl.
 - Serum tox panel includes ASA, ethanol, and APAP (acetaminophen) - have a low threshold to order these. It also includes a serum osmolality and osmolar gap that can be helpful to screen for toxic alcohols. Any fire/enclosed spaces/multiple patients - think CO poisoning
 - Review their pharmanet/medications and get as much history as possible of timing, dose and ingestion.
2. Infection/Inflammatory process:
 - Sepsis can cause altered mentation but should not alone cause coma in a patient with a structural normal brain. We must also ask ourselves if there is a CNS infection present? Meningitis and encephalitis can certainly result in coma. How to best assess this? History and physical exam +/- a lumbar puncture (LP). In an alert immunocompetent patient, one can rule out meningitis/encephalitis with a normal neuro exam and no neck pain or headache. Unfortunately in an altered patient, this can be much more difficult. A concern for infection - fever, unexplained high WBC/CRP + CNS involvement (altered LOC, preceding headache or neck pain) + Rash (vesicular for HSV, or purpuric for

meningococcus) = LP. Anyone of the age > 40 years should get a noncontrast CT head first prior to an LP to assess for any space occupying lesion.

- Send the cerebrospinal fluid (CSF) for cell count, gram stain, C+S, glucose, protein, HSV PCR; plus others if clinically suspicious: AFB stain, VZV, adenovirus, cryptococcus, etc
- ALWAYS give antimicrobials first if suspicion is high as the sensitivity for cultures is quite poor and cell count is often where we make the diagnosis for meningitis.

3. Metabolic

- Glucose, sodium, urea, and calcium are probably the most important metabolic derangements to assess for but don't forget to add TSH as well as a blood gas for hypercarbia.
- Hepatic encephalopathy is a diagnosis of exclusion; measuring ammonia level is neither sensitive nor specific but can still be helpful in some scenarios.
- Temperature! T<34 can cause altered levels of consciousness.

4. Structural/Seizures

- CT noncontrast is a good starting point. Anything acute (<6h in general) and/or focal definitely warrants a CTA arch to vertex - ie. hot stroke protocol. MRI typically added if CT is not helpful and still concerned for structural abnormality. MRI noncontrast will most often provide the information needed. Contrast (gadolinium) is typically used for malignancy/mass workup.
- Consider EEG:
 - i. patients with severely depressed LOC without a clear cause
 - ii. Patients with known seizure hx and now in status / persistent altered LOC
 - iii. Drug or alcohol use
 - iv. Patients with structurally abnormal brain but nothing acute on most recent imaging with persistent, unexplained altered LOC

major caveat is that there may be more than one process occurring which may confound our workup and management - e.g. polytrauma patient from MVC with decreased LOC from small SDH and ethanol level of 100

Traumatic Brain Injury (TBI):

With trauma, it is very important to think about 4 factors that will impact the severity of injury, injury pattern and prognosis:

- Mechanism: blunt vs penetrating, MVC high speed vs low speed, restrained vs unrestrained, fall from height vs standing, industrial injury, burns, electrical injury, etc
- Anatomy/location of injury: obvious skull fracture, basal skull fracture, flail chest, distended abdomen, degloving injury, long bone fractures, pelvis #, burns to face, etc
- Physiology: GCS, tachypnea, hypotension, tachycardia
- Patient factors: elderly, pediatric, pregnancy, comorbidities, medication - use of anticoagulants, etc

For example, an elderly man on warfarin fall from ladder with an obvious skull # and GCS of 3 is painting a significantly different picture than 20 yo M otherwise healthy fall from standing, GCS

14, abrasion to face. And thus, those 4 historical and physical parameters are very important to obtain when doing really any trauma consult.

More specific to TBI, it is prudent to gather the following information in your consult/presentation:

1. History:

- Mechanism
- Patient: Age, comorbidities, use of anticoagulants, occupation or functional baseline if elderly

2. Physical:

- GCS at the scene. Initial GCS is a major prognosticating factor for TBI. Intuitively, a lower GCS typically leads to worse neurological outcomes. In fact we often classify the severity of a TBI based on their best GCS:
 - i. Mild = 13-15
 - ii. Moderate = 9-12
 - iii. Severe = 3-8
- Neurological exam: see above for specific findings to look for; and trend of neurological exam. A patient who was alert and talking and now is in a comatose state may change management vs a patient who was already in a comatose state. What sedation and/or paralytic has the patient received? As well as dose and timing. It will significantly confound your neurological exam.
- Vitals at the scene and trend since their presentation: **presence of hypoxia or hypotension will double your mortality in TBI.**(17)
- Is the patient intubated? If so, what is the patient doing on the ventilator? Spontaneously breathing or in a control mode. Much more on ventilators later.

3. Radiographic findings:

- What kind of TBI? The major TBI patterns are:
 - i. Subdural hematoma (SDH)
 - ii. Epidural hematoma (EDH)
 - iii. Contusions
 - iv. Subarachnoid hemorrhage (SAH)
 - v. Diffuse Axonal Injury (DAI)
- *SDH and EDH are typically managed surgically; however, in general all TBIs should warrant a neurosurgical consult.*

4. What other injuries have the patient sustained?

5. Key bloodwork parameters to look for:

- Glucose, lytes - specifically Na
- Blood gas - O₂, CO₂
- CBC and coag panel

Management of Moderate to Severe TBI:

Mild TBIs do not often end up in the ICU, unless of course there is another injury accounting for their critical illness.

A key concept to recall is the Munro-Kellie doctrine where the skull is a fixed cavity and thus volumes of the brain, CSF and intracerebral blood will remain constant. An increase in one will result in decrease in either or both of the remaining two.

As with management to all patients, step #1 is to stabilize the ABCs. Again, hypoxia and hypotension are your enemies with any brain injured patient. A brief review of the concept of “neuroprotective intubation” is described later.

Brain Trauma Foundation (BTF) came out with guidelines in 2016 that in general provide a framework to how we manage moderate to severe TBI:
https://braintrauma.org/uploads/13/06/Guidelines_for_Management_of_Severe_TBI_4th_Edition.pdf It is a 244 page document; here are my Cole's notes:

I like to compartmentalize TBI management into 3 aspects:

- Preventing any further secondary injury to the brain
- Minimizing intracranial pressures (ICP)
- Optimizing oxygen/substrate delivery to the brain

1. Preventing secondary injury to the brain:

- Think normal everything:
 - Normoxia - PaO₂ 60-100
 - Normocapnia - PaCO₂ 35-45
 - Normoglycemia - *caution hypoglycemia much more*
 - Normal lytes - see below for concept of Na goals
 - Normal temperature - hyperthermia is bad for all brain injured patients. Hypothermia is controversial. There are select cases for TBI where we may use hypothermia to lower the metabolic demand and thus ICP of the brain.
 - Normotension - hypotension is bad. It is unclear if hypertension is beneficial, there is a paucity of evidence to support driving MAPs over 80. BTF recommends (Level III) to have at least SBP of >100 if age 50-69 years or > 110 if <49 or >70 years old
- Seizure prophylaxis: the BTF guidelines recommend 7 days of phenytoin to prevent early post-traumatic seizures. Our local centers are not as aggressive with this, as perhaps it is a culture thing. This is only a Level 2a recommendation. Patients to consider this regimen for would be:
 - Patients with seizure history
 - Patients who have seized within 24 hours
 - GCS < 10
 - Penetrating injury
 - Depressed skull fracture
 - SDH, epidural or intracerebral hematoma
 - Cortical contusions
 - Chronic alcoholism

- Pneumonia prophylaxis: It is not uncommon to assume a TBI or really any brain injured patient has aspirated given their altered LOC state. However, there is no evidence to support giving empiric antibiotics to prevent pneumonia.
- DVT prophylaxis: obviously if there is intracranial bleeding, it would be unwise to cause further bleeding. Stick with SCD (sequential compression devices) for now until DVT chemophylaxis (i.e. Enoxaparin or heparin SC) until repeat CT head in 24-48 hours is stable or cleared by neurosurgery.
- TXA use: TXA gained popularity particularly in the CRASH-2 trial for hypotensive trauma patients where there was a mortality benefit to using TXA early(18). TXA for TBI was studied in the CRASH-3 trial and there was a mortality benefit in the mild-moderate TBI population if given within 3 hours. Much less of a benefit seen in the severe TBI group, perhaps more if pupils are still reactive(19). Regimen is 1g IV bolus over 10 minutes then 1g over 8 hours. This is not yet endorsed in the BTF guidelines as CRASH-3 came out in 2019. Furthermore CRASH-3 was a negative study as the primary outcome showed no difference. It is the subgroup analysis that found a mortality benefit in the mild-moderate TBI group. Overall, not standard of care yet but can consider use especially in the mild-moderate TBI patients.
- Steroids: It is a Level 1 recommendation to NOT use steroids in TBI.

2. Minimize ICP: I try to break things down anatomically:

- Brain parenchymal level:
 - **Minimize metabolic demand**:
 - Sedation - GABAergic agents: Propofol, Benzodiazepines, Barbiturates
Note: Opioids don't really lower cerebral metabolism
Caution using barbiturates before speaking with your fellow/attending. Barbiturate comas will lower ICP but commit your patient to a prolonged comatosed state due to their long half-life and will make their neurological exam unreliable due to their potent effect as a CNS depressant.
 - Hypothermia - not great evidence for patient outcome but hypothermia will lower your ICP - for every 1 deg C will decrease cerebral blood flow by ~10%
 - Osmotherapy - for acute rises in ICP and signs of herniation: mannitol or hypertonic saline (HTS). No great evidence to lead us to either but mannitol may cause hypotension so caution use in patients who have a borderline/low blood pressure
 - Doses: Mannitol is 0.5-1.0g/kg IV. RNs may often ask you how much volume to give. The mannitol bags are of 25% concentrate and in 500ml bags = 125g per bag. Most patients, I give half a bag or 250ml. This is easy to remember because it is roughly the same volume for 3% HTS (dose is 2-3ml/kg).
 - Serum Na goals: acute hyponatremia causes cerebral edema and so I would avoid hyponatremia or acute drops in Na. In general start with normal Na goals 135-145. However, physiologically we can "shrink the brain more" by driving Na higher into 140-150 zone but there is little evidence to support this.

- CSF level:
 - EVD placement can help transduce to measure your ICP but also drain CSF; more on EVDs below
- Vasculature:
 - Avoid hypercarbia and hypoxia - both will cerebral vasodilation and will increase ICP
 - Optimize venous drainage:
 - Head of the bed (HOB) up > 30 deg
 - Neutral neck
 - Avoid restrictive devices at the neck like hard C-spine collars; can use sandbags or 1L saline bags instead to immobilize the neck
 - Avoid high intra-thoracic pressures and intra-abdominal pressures
- Surgical:
 - Decompressive craniectomy
 - Will lower ICP and may facilitate discharge from ICU but does not lead to favorable neurological outcomes

3. Optimizing oxygen delivery/substrate to brain

- This is the concept of driving MAP goals to 80 or 85 where the goal is to keep CPP between 60-70 where $CPP = MAP - ICP$.
 - Currently little evidence to support this recommendation but we do know that if CPP is too low, i.e. less than 50-55, this leads to poor outcome as well as if we overshoot it > 90-95.
 - It becomes even more challenging to really know what a patient's CPP is without measuring ICP. And thus, there should be some caution to driving MAPs up to 80 without some form of monitoring to measure the patient's ICP. There is potential for harm by using fluids and pressors to drive a patient's MAP up blinding. The major factors in that decision would be the patient's neurological exam, comorbidities, type of neurological injury, CT availability and radiographic findings. Needless to say, I would as a learner, review this goal with your fellow/attending prior to making any formal orders.
- Things are a bit different if the patient does have some form of neuroinvasive monitoring. Within the local ICUs that treat TBIs, there are really 2 forms of neuroinvasive monitoring:
 - **EVD = external ventricular device**: placed into the lateral ventricle
 - Able to drain CSF and transduce ICP
 - Very important to briefly understand the EVD:
 - It is typically left OPEN and at a certain level - e.g. 10 cmH₂O. This is the distance in mmHg between the EVD and the transducer. It is zero'ed typically at the patient's tragus. If an EVD is open and set at 10 cmH₂O, theoretically, it should be draining CSF if the patient has an ICP greater than 10
 - When you examine a patient with an EVD, it is important to know that it is working - this is done by looking for drainage at the CSF

collection tubing or if there is minimal drainage, watching for CSF fluctuations in relation to respiratory efforts within the tubing.

- To measure ICP, you must transduce with the EVD CLOSED. The RNs will typically measure the ICP every few hours or as ordered by the MD.
- Normal ICP should be < 20 cmH₂O
- CSF production is about 500ml per day but the actual volume at a given moment is only about 160ml in otherwise healthy brains which means most of CSF is reabsorbed. Thus, CSF drainage can be very important when this reabsorption process is disrupted. An example would be a patient with blood in their ventricles and having issues with obstructive hydrocephalus.
- **“Bolt”**
 - The bolt is literally a metal device that is usually dual lumened carrying a Licox catheter to measure PbtO₂ and another catheter to measure ICP; it is placed in the non-injured frontal lobe.
 - PbtO₂ = partial pressure of the brain tissue oxygen tension where the goal is > 20 mmHg.
 - The concept is providing adequate oxygen to the brain tissue. In patients, with low PbtO₂, strategies to increase this would be:
 - Improving oxygen content: goal PaO₂-80-100, Hb >80-90
 - Minimizing demand - sedation, paralysis, hypothermia
 - There is a paucity of evidence to support routine use of neuroinvasive monitoring such as the Bolt for TBI but this does not mean patients may not benefit from this and we are still waiting for the right study to be done.

4. Airway Management:

Neuroprotective Intubation

- There is a lot of stuff out there online and in the FOAMed world on this. My overall take for this is to keep things as simple as possible. In general, 3 major goals for me in neuroprotective intubation:
 1. Avoid hypoxia
 2. Avoid hypercarbia
 3. Avoid hypotension
- A lot of the “stuff” online talks about minimizing spikes in ICP from sympathetic surges from maneuvering the airway:
 - Using Lidocaine - topically or IV
 - Unless you are an anesthetist, topical lidocaine is something we do not do in our RSIs outside the OR.
 - IV lidocaine at 1.5mg/kg.
 - Using high doses of fentanyl at 3-5mcg/kg
 - The literature says to do 3-5 minutes prior to intubation. These are doses that will often cause apnea in the patient. So now you have an apneic patient you may need to bag prior to your RSI to avoid hypoxia and hypercarbia.

- Overall, yes the literature supports that these interventions will mitigate rises in ICP but there is none to support any patient-centered outcomes. The flip side is we have very good literature to support that episodes of hypotension and hypoxia in TBI patients will double their mortality(17). My take is that if you don't often do these interventions for your airway management, why start trying it now on a patient who is sick with a brain injury?

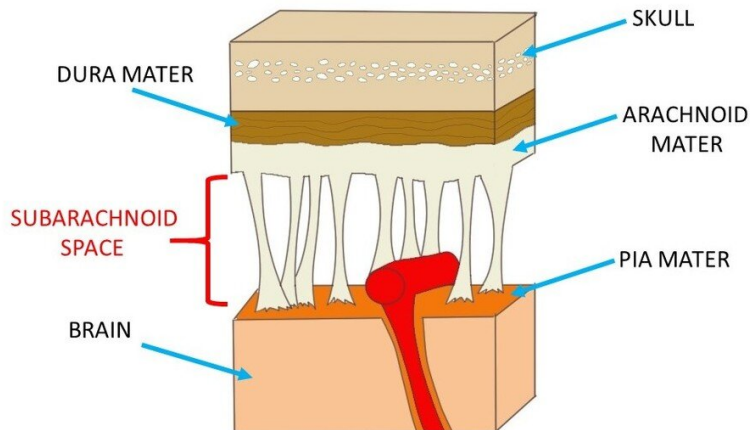
My approach to airway in patients with brain injury:

1. Assess for predictors of anatomical difficulty: LEMONS for laryngoscopy, BONES for BMV and RODS for cricothyrotomy (see airway section for more details PRN)
2. Assess predictors of physiological difficulty: oxygenation status, hemodynamics
3. If confident to be able to BMV and successfully place ETT → proceed with RSI. If not, call for help.
4. RSI:
 - a. Preoxygenate at 100%
 - b. Position - I keep them HOB 30 in sniffing position until induction and minimize head down position. If the patient is collared, have the collar removed after induction and a helper to maintain manual C spine immobilization.
 - c. Equipment: depending on their anatomy, I tend to use the CMAC blade but may use hyperangulated blades with VL such as Glidoscope if anticipating a more anterior airway. DL can be challenging with C Spine precautions due to inability to maneuver the neck as aggressively to obtain a better view. Always styletted tubes. Suction. OPA. BMV. Boogie. ETCO2. LMA as backup.
 - d. Drugs: I generally use ketamine and rocuronium for nearly all my intubations. You can consider succinylcholine for a quicker offset for neurological examination. Old dogma of ketamine and increased ICP has been debunked(20). An alternative induction agent would be etomidate. I tend to avoid propofol as it has a more hypotensive effect. I tend to have norepinephrine infusion and phenylephrine ready as well.
 - i. Specific dosing: in general, the more sick or obtunded, use lower dose of induction. Never short your dose of paralytic if you decide to do RSI. It is less than ideal to have an apneic patient but not fully paralyzed - that is, able to vomit, or gag, or not fully relax at the head and neck to further challenge you securing their airway with an ETT.
 - ii. Ketamine 1mg/kg in general but halved or lower if patient is obtunded or unstable
 - iii. Rocuronium 1.2mg/kg - for most patients, I give 100mg IV. The vials come in 50mg/vial. Some say higher the rocuronium dose, the faster the onset(21). So go big, get them paralyzed as soon as possible to optimize your setting for tube placement. Considering a patient's CO2 rises 3-5mmHg for every minute of apnea, the goal is to get the tube in as soon as possible. Can consider gently bagging the patient, to mitigate any CO2 rises.

- e. Operator: as with everything, #1 objective is patient care however learners need to learn. Patients with increasingly more challenging anatomy and/or physiology, the operator should be increasing in experience and competency.

Subarachnoid Hemorrhage (SAH)

SAH is blood within the subarachnoid space. Recall the linings of brain:



The subarachnoid space is where the blood vessels of the brain lie and where CSF flows. Etiology behind SAH is traumatic vs nontraumatic. Nontraumatic SAH is aneurysmal until proven otherwise.

Aneurysmal SAH (aSAH) classically presents with a thunderclap headache. A patient will present often with the worst headache of his/her life, get a CT head and blood is identified in the subarachnoid space. The amount of blood in subarachnoid space and ventricles can be described in the Modified Fisher Score - a prognosticating tool for risk of vasospasm and delayed cerebral ischemia (DCI).

Modified Fisher Score	CT scan findings	Risk for DCI (%)
0	No SAH or IVH	0
1	Minimal/thin SAH, no IVH	6
2	Minimal/thin SAH, with IVH in both lateral ventricles	15
3	Dense SAH, no IVH	35
4	Dense SAH, with IVH in both ventricles	34

IVH, intraventricular hemorrhage; SAH, subarachnoid hemorrhage.

The next immediate step is to obtain a CTA arch to vertex to identify the vascular abnormality that may have caused the SAH. These steps are often already initiated in the emergency department. Such patients require critical care due to their precarious neurological status that is highly at risk for deterioration (or are already obtunded and intubated), and need meticulous management of blood pressure and close monitoring - needless to say, acute aSAH are not ward patients.

Here is an approach to managing acute aneurysmal SAH that is UNSECURED:

1. Stabilize ABCs
2. Obtain a baseline neurological exam. The Hunt and Hess Grading Scale is the clinical prognosticating tool based on level of consciousness and risk of mortality.

Grade	Characteristics	Mortality Rate (%)
0	Unruptured aneurysm without symptoms	0
1	Asymptomatic or minimal headache and slight nuchal rigidity	1
1a	No acute meningeal or brain reaction but with fixed neurologic deficit	1
2	Moderate to severe headache, nuchal rigidity, no neurologic deficit other than cranial nerve palsy	5
3	Drowsy, confused, or mild focal deficit	19
4	Stupor, moderate to severe hemiparesis, possible early decerebrate rigidity, and vegetative disturbances	42
5	Deep coma, decerebrate rigidity, moribund	77

3. Blood pressure management:
 - a. Get SBP < 140-160. May push even lower if the patient is young and still mentating but caution driving blood pressures too low in patients who do not have a reliable neurological exam or have baseline hypertension. You are trying to balance minimizing any further bleeding from the unsecured aneurysm and maintain cerebral perfusion pressure.
 - b. Agents to do this:
 - i. Labetalol 10-20mg IV q30min PRN or start an infusion if needing repeated doses at 0-10 mg/min
 - ii. Hydralazine 10-20mg IV q30 min PRN
 - iii. Nicardipine 5-15mg/hr IV
 - c. For tight blood pressure monitoring, these patients should get an arterial line
 - d. Ensure perfusion still adequate so MAP > 65
4. Analgesia and antiemetics:
 - a. Pain will increase your blood pressure and vomiting will certainly cause spikes in ICP. I would start with low doses of hydromorphone like 0.2-0.5mg IV q15min PRN and an antiemetic like ondansetron 4-8mg IV q6h PRN or metoclopramide 10mg IV q6h PRN. I avoid dimenhydrinate (Gravol) as it tends to be more sedating and more associated with delirium given its anticholinergic properties.
5. Reverse any coagulopathy:
 - a. Review from GIB section:
 - i. NOAC: Idarucizumab (Praxbind) for dabigatran, all others is PCC (Octaplex)
 - ii. Warfarin: PCC (Octaplex)
 - iii. Antiplatelet: do not give platelets - worse outcome in spontaneous ICH (PATCH trial)
 - iv. PLT < 50: give platelets
 - v. INR > 1.5: give FFP
6. Obtain CTA arch to vertex to identify culprit aneurysm/vascular abnormality; if CTA is unable to identify the culprit vessel; patient is still treated as an aSAH and typically need a formal cerebral angiogram (DSA = digital subtraction angiography) to search for the culprit vessel.
7. Urgent neurosurgery consultation - option is to clip (surgical) or coil (interventional) +/- EVD
8. SCDs for DVTp. Can start chemoprophylaxis if stable CT in 24-48hours after aneurysm secured. This practice is variable depending on the center and severity of illness.

9. Start nimodipine at 60mg q4h NG/PO x 21 days - can spread out the dose if having hypotensive episodes - give 30mg q2h instead. Nimodipine is a calcium channel blocker and was designed to prevent vasospasm but studies have yet to find it to do so but its use regardless has reduced mortality and improved neurological outcome in patients with aSAH(22). Mechanism on how it does so is still unclear. *Level 1 recommendation*
10. Maintain euvolemia - key is to avoid hypotension; a lot of these patients should be kept NPO, so in general I start an NS infusion at maintenance to maintain euvolemia.
11. No role for seizure prophylaxis, no role for TXA

Once the aneurysm is SECURED (i.e., clipping or coiling of the aneurysm), it is important to know whether any residual aneurysms exist that are unsecured. If all is secured then, the concept of allowing the blood pressure to autoregulate on its own. This term is often coined “let it ride”. The brain will tend to start autoregulating its perfusion by driving its own blood pressure up. This is why we usually see hypertension in patients post TBI, post stroke, post ICH, and post SAH. The initial phase, particularly in spontaneous hemorrhages, is to prevent further bleeding and thus lowering blood pressure. Once an aneurysm is secured, we allow the pressure to ride as high as the other organs will tolerate. Let’s now go over the complications of subarachnoid hemorrhages and how to manage:

I break it down to intracranial and extracranial complications:

Intracranial:

1. Rebleeding - most likely to occur in the first 24 hours; management to this is above. Again, blood pressure management and good supportive care.
2. Vasospasm and cerebral ischemia: The timeframe for this is 4-14 days from symptom onset. We used to treat vasospasm with “Triple H therapy” - hypervolemia, hypertension and hemodilution. Then we saw a ton of patients go into ARDS and/or pulmonary edema from all that fluid so triple H therapy is no longer standard of care(23). Now we tend to focus more on hypertension and maintaining euvolemia. Vasospasm is a diagnosis made with a clinical focal neurological change with characteristic radiographic findings, usually seen on CTA. How high do we drive the blood pressure up? To the patient’s neurological exam. It is quite remarkable to see - a patient will have decreased LOC at a pressure of 160/90; and you drive up MAP up to 110 and she becomes awake and obey commands. First-line agents to use would be norepinephrine and then milrinone. Alternative means of treating vasospasm also include some interventional procedures like intra-arterial angioplasty or intra-arterial milrinone or nicardipine. These are refractory and expert opinion cases.
3. Increased ICP - can occur from rebleeding, swelling from cerebral ischemia but more often due to obstructive hydrocephalus. Usually neurosurgery will place an EVD to help mitigate this. Read above in the TBI section for further information on EVDs.
4. Seizures - there is no role of prophylaxis but certainly treat if patient seizes. Consider obtaining an EEG to assess for nonconvulsive status epilepticus in patients who have a worse neurological exam than what their imaging shows.

Extracranial:

1. Cardiopulmonary:
 - a. Arrhythmias - it is believed to result from catecholamine surge that can occur with an acute brain injury
 - b. ST elevations/Cardiomyopathy - Cath labs have been activated for acute STEMIs turning out to have clean coronaries; classically the LV gram reveals apical hypokinesia - this is also known as Takotsubo's cardiomyopathy or stress cardiomyopathy
 - c. Pulmonary edema - can be cardiogenic (i.e. from heart failure) or noncardiogenic (i.e., ARDS)
2. Metabolic:
 - a. Hyperglycemia - do not aggressively treat as hypoglycemia is much worse
 - b. Hyponatremia:
 - i. Two major mechanisms can occur: SIADH vs Cerebral salt wasting. Both will have high urine osm > 300, and urine Na > 40. The key difference is in cerebral salt wasting there is usually higher urine output and hypovolemic state while in SIADH, due to presence of inappropriate ADH, there is lower urine output (i.e. anti-diuresis) and euvolemic/hypervolemic state. Treatment for cerebral salt wasting is fluids and fludrocortisone. SIADH, as you have to caution fluid restricting SAH patients to maintain euvolemia, you usually must offset this hyponatremia with hypertonic saline.
 - c. Fever: blood in the brain can be very inflammatory; the majority of these patients will spike fevers and be merely an inflammatory response. However, these patients often have EVDs in situ and are at risk for infections. Important to use clinical acumen to determine if this is a SIRS response or is the patient truly infectious/septic.

Status Epilepticus

Let's review some key terms:

- Definition of status epilepticus = 5 or more minutes of continuous clinical or electrographic seizure activity OR recurrent seizure activity without recovery (return to baseline) between seizures; (traditionally was 30 or more minutes)

We can further classify status epilepticus into convulsive vs nonconvulsive:

- Convulsions = rhythmic jerking of the extremities
- Nonconvulsive status epilepticus = seizure activity seen on EEG without clinical findings of convulsions

Refractory status epilepticus = patients who continue to seizure despite standard treatment for status epilepticus - typically defined by failure of one adequately dosed benzodiazepine and one antiepileptic drug (AED)

These are sick patients! Mortality at 30 days in patients with convulsive status epilepticus is as high as 25%; 50% for nonconvulsive status epilepticus (24).

Approach to etiology - DIMS is helpful again:

- Drugs - intoxication / withdrawal / noncompliance
- Infectious / Inflammatory - meningitis, encephalitis, CNS abscess, sepsis
- Metabolic - electrolytes, hypoglycemia, liver failure, renal failure
- Structural - abnormal brain - previous stroke, post-arrest, brain injury
- S can also be for sleep deprivation - a common precipitant for epileptics

Workup should include:

- Bloodwork - Renal panel, liver panel, lytes with extended lytes, glucose, AED levels if patient takes AED
- CT head +/- MRI brain
- Lumbar puncture - consider if no other explanation and to look for infectious and inflammatory causes
- Tox panel - consider if no other explanation

Management of status epilepticus:

- Patient is seizing in front of you - the key thing is administration of benzodiazepine. First thing is ascertain whether there is IV access:
 - If IV: give lorazepam 2-4 mg
 - If no IV: next best option is midazolam 5-10mg IM
- After the benzo is given, get patient on monitors, stabilize ABCs
- If still seizing then give 2nd dose of benzo and ask to draw up an AED: options include:
 - Phenytoin 20 mg/kg IV over 20 minutes
 - Levetiracetam 20 mg/kg IV
 - Fosphenytoin 20 mg/kg IV/IM
- If still seizing after 2nd benzo -> patient is likely seizing after 5 minutes now and this is status epilepticus; patient should have airway secured as a lot of the ensuing drugs to suppress seizures will also lead to respiratory depression
- Prior to intubation - examine the patient - very important to look at gaze deviation - may help you localize lesion (seizure patients will have gaze preference away their seizure focus vs stroke patients will look towards their stroke); ascertain any focality - focality = structural cause until proven otherwise

Management of refractory status epilepticus:

At this point, patients are intubated and have already received more than 1 dose of benzodiazepine and 1 AED and unfortunately continue to seize either clinically or electrographically. These patients are at high risk for seizure recurrence and thus management involves aggressive sedation and loading of antiepileptics to achieve burst suppression. In order to assess for non-convulsive seizures, these patients need EEG monitoring, ideally continuous EEG. The stacking of sedatives and AEDs is stepwise and choice depends on presence of any liver or renal dysfunction. I like to break down the sedatives and the AEDs:

Sedatives - given as bolus and/or infusion. Goal is to abort the seizure.

Antiepileptics - given with a loading dose and maintenance dose. Goal is to control seizures, prevent recurrence.

Sedatives:

Benzodiazepines:

- As mentioned above, lorazepam is the first line for abortive therapy and given as bolus.
- If using infusion, we often use midazolam; typically added after propofol. Will last longer than propofol but its the shortest-acting benzodiazepine we have; typically start at 5-10mg/hr and go as high as 50mg/hr

Propofol:

- First line for infusion as easily titratable on and off with quickest half-life. Infusion dosing high up to 100mcg/kg/min so need to monitor for adverse effects such as hypertriglyceridemia, bradycardia, propofol infusion syndrome, etc

Ketamine:

- Typically added as third-line for infusion - start at 1mg/kg/hour, up to 5mg/kg/hour

Antiepileptics:

- First line traditionally has been phenytoin (Dilantin) at 20mg/kg IV - then typically at 100mg IV TID; dosing needs to be adjusted based on levels and patient's albumin status; NB: phenytoin needs to be given through peripheral line and only compatible in saline so access can be an issue for phenytoin; phenytoin loads can be associated with arrhythmias and hypotension and long term use can cause liver dysfunction
- Levetiracetam (Keppra) has been increasingly used as it has significantly less side effects than phenytoin - also 20mg/kg load then typically 500-1000mg PO/IV BID
- Valproate sodium - also 20-30mg/kg IV load and then up to max 60mg/kg/day divided into 6 doses until therapeutic levels are achieved; issues with VPA is hyperammonemia which can cause altered LOC, as well as pancreatitis, thrombocytopenia and hepatotoxicity
- Lacosamide - newer drug, less studied in status epilepticus but increasingly used due to less side effects; start loading at 200mg then 100-200mg IV/PO BID

Barbiturate coma

This is a big decision to start using barbiturates as the commitment is once you load with barbiturates, you commit this patient to days-weeks of a deeply sedated state as barbiturates are heavily sedating and have long half-lives so will take time to wear off! Barbiturate infusions are +++CNS depressants and also makes the neurological exam very unreliable - pupils may no longer react!

- Pentobarbital for infusion - usually 5-15mg/kg then 0.5-5mg/kg/hour
- Phenobarbital for intermittent dosing

Overall these are decisions to make with your attending/fellow.

Novel and special therapies:

- For autoimmune encephalitis:
 - Classically NMDA receptor antibody positive - can be picked up on a Mitogen panel that gets sent to a special lab in Calgary. Classic presentation is female

patient coming in with vague psychiatric complaints and eventually go into a deep coma with nonconvulsive status epilepticus. Look for a pelvic mass for teratomas that are often the source of the NMDA receptor antibodies. Such patients are typically pulsed with steroids and go through PLEX and/or a course of IVIG.

- Other things people may try are ketogenic diet, hypothermia, electroconvulsive therapy and surgical management.

Approach to Pain, Agitation and Delirium in the ICU

Imagine being sick, waking up with lines and tubes connected to you, tied to a bed, having no concept of time and orientation, going in and out of consciousness, with random people talking about you, touching you, and moving you. It becomes intuitive that pain and agitation are normal reactions and furthermore, why delirium is so common in the ICU. It is absolutely imperative for us to assess our patients for pain, agitation and delirium. Unfortunately we don't have much evidence to guide us to how to do so for better patient outcomes and we do know that over-sedation does lead to worse patient outcomes. I think the best approach is to consider what your objective is and use the least evil agent.

Pain:

- The easiest method to assess pain is to just ask our patients how much pain they are experiencing. In awake and alert patients, we often use scales like the Numeric Pain Score - i.e., using a numeric rating out of 10 with 10 being the worst pain possible and 0 as no pain. Unfortunately, patients in the ICU are often confused, sedated, or having an endotracheal tube preventing them from expressing their discomfort and pain.
- Validated scoring tools we use in the ICU include the Behavioral Pain Score or the Critical Care Pain Observation Tool (CPOT). These tools are reported by the nurses in their daily rounds assessment and the components can be looked at through MDCalc or other scoring apps.
- All in all, there is no perfect score but current evidence supports to pick a method and most importantly to assess and treat our patients' pain.

Agents for pain:

There are many types of pain - consider sources of acute pain: surgery, trauma, dissection, bowel obstruction, intracranial hemorrhage. It is important to treat these disease entities with appropriate analgesia:

- Acetaminophen - first step to analgesia in WHO's stepwise approach to analgesia. It is safe with little to none side effects. There is an idiosyncratic reaction that we see only in critical care where acetaminophen use is associated with hypotension. This hypotension however is not associated with any adverse outcome.
- NSAIDs - caution use of NSAIDs in the ICU. A lot of our patients have already developed or at risk of developing acute kidney injuries and/or GI bleeds.

- Opioids:
 - Morphine - avoided in renal failure patients as the metabolite accumulates; has more histamine-mediated side effects than the synthetic opioids.
 - Fentanyl - quickest onset, great for incident pain as boluses; can be used as infusion but has a high volume of distribution so infusions do take time to wear off. Also has serotonergic effects.
 - Hydromorphone (Dilaudid) - my go-to opioid in the ICU as the lowest side effect profile amongst opioids; boluses of 0.2-0.5mg IV q15min PRN and infusions of 0-2 mg/hour
 - Side effects of all opioids: nausea, constipation, confusion, respiratory depression
 - Some principles to consider for opioid use:
 - Use PRN opioids to start - use IV as patients are less likely to absorb PO - patients in shock, ileus, etc as well SC will not be reliable to do edema, fluid shifts.
 - Use PRNs for intermittent pain/incident pain like movements, turns, suctioning, etc
 - Determine how much PRN used and then give regular PO/SC dosing for longer action and to minimize peaks and troughs or an IV infusion
 - typically start at lowest infusion dose possible and then provide a range for nurses to titrate
- Ketamine:
 - Ketamine at low doses is a good opioid-sparing option - using 10-20mg IV boluses q30-60 min should not sedate your patient. Infusions at 0.1-0.3mg/kg/hour
- Lidocaine:
 - Used in perioperative patients by anesthesia; also another opioid-sparing option with mostly evidence in intra-abdominal surgeries - typically used in short-term for up to 24 hours postoperatively (Foo 2021); giving as a loading dose of 1.5mg/kg then an infusion up to 1.5mg/kg/hour
- Gabapentin/Pregabalin
 - Consider if patient at risk or has history of chronic pain

Agitation:

Similar to pain, it is important to assess our patients for agitation. The most commonly used scoring system is the Richmond Agitation Sedation Scale (RASS):

Richmond Agitation Sedation Scale (RASS)

Target RASS	RASS Description
+ 4	Combative, violent, danger to staff
+ 3	Pulls or removes tube(s) or catheters; aggressive
+ 2	Frequent nonpurposeful movement, fights ventilator
+ 1	Anxious, apprehensive, but not aggressive
0	Alert and calm
- 1	awakens 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. 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

There are select circumstances where patients should be fully sedated to a RASS -4 to -5 level - e.g., post-arrest patients that are being cooled, status epilepticus patients in burst suppression, TBI patients with high ICP, moderate-severe ARDS patients, etc. There is a subset that may also require partial sedation to RASS -2 to -3. These patients may need more sedation for safety and patient care. For example, high risk post-op patients like fresh post-CABG, post-spinal fixation, post-transplant, etc, or patients with a significant amount of acute pain - e.g. severe burns, open abdomen, polytrauma patient. But in general, we'd like all our patients to be a RASS of 0, especially patients who are weaning and convalescing.

Agents for Agitation:

Consider the objective of the agent:

To sedate - mostly GABAnergic:

- Propofol:
 - 0-100mcg/kg/min infusion
 - 10-30mg IV boluses
 - Very short half-life; most commonly used sedative in the adult ICU
 - Caution: hypotension, apnea, high infusion doses can be associated with hypertriglyceridemia, pancreatitis, propofol-related infusion syndrome
- Midazolam:
 - 0-10mg/hour infusion
 - 2-5mg IV boluses
 - Caution: hypotension, apnea, and benzos are associated with delirium; much longer half-life than propofol

To calm:

- Alpha-2 agonists:
 - Dexmedetomidine (Precedex) - commonly used to keep agitated patients calm and mildly sedated with much less associated respiratory depression; typically given as an infusion at 0.4-1.4mcg/kg/hour

- Clonidine - much older drug and only can be given oral
- Alpha-2 agonists have anxiolytic properties, as well as analgesic augmentation properties and thus can be opioid sparing. Also helps with autonomic dysfunction in patients with alcohol withdrawal, post-GBS, spinal cord injuries, TBIs
- Caution: bradycardia, hypotension
- Antipsychotics:
 - Haloperidol (Haldol) - first generation high potency antipsychotic - least sedating, helpful for agitated patients with psychotic symptoms - e.g., hallucinations;
 - 1-2mg IV PRN q2h
 - 1.25-5mg SC/PO PRN q2h
 - Caution: EPS, prolonged QT, NMS; IV use has significantly higher rates of side effects so ++caution use
 - Methotrimeprazine (Nozinan) - first generation low potency antipsychotic; more sedating; can be used as a sleep aid
 - Has some anxiolytic and analgesic properties
 - 12.5-50mg PO/NG q4h PRN; or 5-25mg IV/SC q2h PRN
 - Can give stacking evening doses for sleep 25-50mg PO at 2000h, 2200h
 - Caution: hypotension (especially given IV), over-sedation
 - Quetiapine (Seroquel) - second generation antipsychotic; also can be used as a sleep aid
 - 12.5-50mg PO q4h PRN
 - Can give stacking evening doses of sleep 25-50mg PO at 2000h, 2200h
- Benzodiazepines
 - Lorazepam - overall tend to avoid benzos as of all the agents, they are most associated with delirium(25). Population I would use it mostly on is the alcohol withdrawal patients or chronic benzodiazepine use.

*Disclaimer on sleep in the ICU: little to no evidence of whether chemically-induced sleep a) truly induces REM sleep and b) leads to better patient outcome.

Delirium:

1. Step one is to recognize; clinical diagnosis characterized by: acute onset, inattention and fluctuating course; the presence of delirium in the ICU is a major marker of increased morbidity and mortality (26)
2. Treat the underlying cause/precipitant; I like the DIMS approach again:
 - a. Drugs - probably most common; think drug use / intoxication / withdrawal
 - b. Infection - sepsis / UTI / PNA / CNS infection / line infection; Inflammatory states - polytrauma, burns, post-operative, pancreatitis, etc
 - c. Metabolic - Na and Ca derangements, hypoxia, hypercarbia, hepatic encephalopathy, uremia, Wernicke's
 - d. Structural - stroke / ICH / TBI; seizure, sleep deprivation
3. Treatment plan:

- a. Nonpharmacologic:
 - i. Hearing aids, glasses on, windows/curtains open, physio and mobilization during the day
 - ii. Minimize stimulation, lights down, ear plugs during night
 - Things to consider: does this patient need neurovitals q1h still? Do they need a BP cuff to go off every hour?
- b. Pharmacologic:
 - i. Treat pain and agitation (see above)
 - Note on agitation: There is a fidgety patient who can't sit still but is harmless; vs a patient who is pulling out lines/tubes or falling off the bed, i.e., a danger to him/herself; the former may not need treatment vs the latter may
 - ii. Optimize sleep - melatonin may help prevent delirium; adding an additional sleep aid may help reset the patient's circadian rhythm and avoid sundowning at night

Post-Arrest Care:

In Canada, the incidence of Out of Hospital Cardiac arrest is about 55 per 100,000 people. In BC in 2021, the incidence was 138 per 100,000 people (BCEHS Annual Report 2021). Clinical outcomes after OHCA were previously poor with survival to hospital discharge rates around 5% but in recent years, this number has increased to > 10%. Patients who survive to hospital discharge often have good long-term outcomes and thus a lot of efforts have been directed to improving initial survival rates.

Here is my approach to treating post-arrest patients:

1. Ascertain etiology of cardiac arrest and treat it
2. Ascertain extent of injury and provide supportive management

1. Ascertain etiology of cardiac arrest and treat it:

Etiology:

- a. Ischemia requiring reperfusion?
 - Clues - PMHx and substrate for CAD, initial rhythm, ECG findings, echo findings
 - STEMI -> cath lab (AHA Class I recommendation)
 - Shockable rhythm but no STE -> previously would be considered to cath lab but with the trial COACT 2019 - no difference in survival or functional neurological outcome with early cath (within 2h vs after neurological recovery)(27); however if patient has clinical manifestations of persistent significant myocardial ischemia - e.g. cardiogenic shock or persistent ventricular arrhythmias, it would be pertinent to consider pushing for reperfusion.
- b. And go through H's and T's
 - Hypovolemia
 - Hypoxia
 - H+ (acidosis)
 - Hyper/hypoK

- Hypothermia
- Tension PTX
- Tamponade
- Toxins
- Thrombosis - PE, MI

2. Ascertain the extent of injury and provide supportive management:

The primary organ to think about is the brain. Obtaining a good neurological exam helps not only with prognostication but also care. Decision to cool or not cool depends on presence of purposeful movements - i.e. localizing or obeying on exam.

Neuroprotective measures:

To cool or not to cool:

- Initial OHCA cooling studies looked mostly at shockable rhythms and found better neurological outcome (CPC 1-2) and mortality benefit in the patients that were cooled (Hypothermia after Cardiac Arrest Study Group NEJM 2002) (28)
- Later OHCA studies then expanded utility of cooling to the nonshockable population with overall inconclusive evidence to suggest “potential benefit” and lack of harm
- Limited data exists for In-hospital cardiac arrest (IHCA) patients but similar to nonshockable, this is a paucity of evidence to suggest benefit but no evidence of harm
- → Cooling is recommended at AHA Class I recommendation in post-arrest patients; with best level of evidence in the shockable group

How cool?

- Initial studies looked at temperatures of 32-34 deg C
- Later studies, particularly a large study published in NEJM in 2013 (TTM trial) looked in both shockable and nonshockable patients (mostly shockable 80%) and found no difference between T33 to T36 in death or poor neurological outcome (CPC 3-5) (29)
- Interestingly, HYPERION 2019 looked at all cardiac arrest patients (OHCA and IHCA) with nonshockable rhythms, T33 vs T37 and demonstrated improved favorable neurological outcomes (CPC 1 or 2) in the T33 group (30). Major criticism to this study is that the “normothermia or T37 group” were mostly febrile. Furthermore, the majority (>80%) of their patients in both groups had poor neurological outcomes (CPC 5 or higher). And lastly, the fragility index to their primary outcome was 1.
- TTM-2 2021 compared normothermia to hypothermia in OHCA with both shockable and nonshockable patients (mostly shockable at 72%), and found no difference in mortality or poor neurological outcome (mRS 4-6) between T33 vs T37.5 (31)
- → No conclusive evidence to suggest one temperature is better than another but we know fever is bad. AHA and CCS both recommend cooling to a range of T33 to T36.
 - Adverse risks to consider if cooling to “cooler” end:
 - HD stability, arrhythmias and coagulopathy
 - My personal approach and bias would be:
 - Features to consider to cool on cooler side (i.e. T35-36):

- Young, Vf/Vt arrest, limited down time - i.e. a patient you suspect/hope will have a favorable neurological recovery
- Patients to consider a more normothermia or a “less is more” approach in their management (T<37.5):
 - Old, comorbid, nonshockable rhythm, prolonged down-time - i.e. a patient who will unlikely have a favorable neurological recovery no matter what you do

How long to cool?

- AHA and CCS recommend at least 24 hours of “cooling” and 72 hours of temperature management (i.e. no fever)
- Most protocols have cooling phase of 24-28 hours and then gradual rewarming phase the ensuing 24 hours

Supportive care:

- Oxygenation and ventilation:
 - PaO₂ keep 80-100 - hypoxia and hyperoxia are bad
 - Hb > 80
 - PaCO₂ keep 35-45 - hypercapnia leads to cerebral vasodilation = increased ICP; hypocapnia however can lead to vasoconstriction and potentially ischemia
- Sedation:
 - Let the brain rest. Keep CPP high, and ICP low.
 - Use of GABAergic agent like propofol or midazolam, ideally propofol for short-acting properties as once cooling is over, you want to see what kind of neurologically function patient has
- Perfusion:
 - CPP = MAP - ICP
 - Both AHA and CCS recommend normal blood pressure (i.e. MAP > 65) but most protocols have MAP > 80
 - Keep CVP 8-12
 - Treat arrhythmias
- Seizures
 - No need for prophylactic anti-epileptic. Obtain EEG to rule out non-convulsive seizures if persistent decreased LOC in waking phase
- Nutrition and glycemic control
 - No recommendation on specific glucose goals. Aim for normoglycemia and avoid hypoglycemia if anything

Neuroprognostication:

There is a balance to neuroprognostication in post-arrest patients where you are trying to avoid premature withdrawal of life support in patients who will survive and continuing life support in patients who will have poor neurological outcomes. We need to be cautious in our assessments

and do our best to limit biases. We should be very cautious / avoid prognosticating in the first 72 hours.

How do we assess neuroprognostication?

There are 4 types of tests we can perform:

- Clinical exam - e.g., pupillary response, brainstem reflexes, myoclonus, motor exam, etc
- Biochemical markers - for the most part in Canada, not available yet clinically
- Electrophysiological findings - i.e., EEG, SSEP
- Neuroimaging findings - e.g., CT, MRI, NM perfusion scans

What is the goal of a “good” test: a low false positive rate (FPR) as possible; to avoid prognosticating a poor outcome when instead the patient will have a good outcome.

What is a “good” outcome: this will obviously highly depend on the patient’s values, circumstances, etc and thus is very hard to quantify. There are numerous scales to measure “functional status” or “neurological outcome” and one of the more common scales would be the CPC scale or the modified Rankin scale:

Cerebral Performance Categories Scale

CPC Scale

Note: If patient is anesthetized, paralyzed, or intubated, use “as is” clinical condition to calculate scores.
CPC 1. Good cerebral performance: conscious, alert, able to work, might have mild neurologic or psychologic deficit.
CPC 2. Moderate cerebral disability: conscious, sufficient cerebral function for independent activities of daily life. Able to work in sheltered environment.
CPC 3. Severe cerebral disability: conscious, dependent on others for daily support because of impaired brain function. Ranges from ambulatory state to severe dementia or paralysis.
CPC 4. Coma or vegetative state: any degree of coma without the presence of all brain death criteria. Unawareness, even if appears awake (vegetative state) without interaction with environment; may have spontaneous eye opening and sleep/awake cycles. Cerebral unresponsiveness.
CPC 5. Brain death: apnea, areflexia, EEG silence, etc.

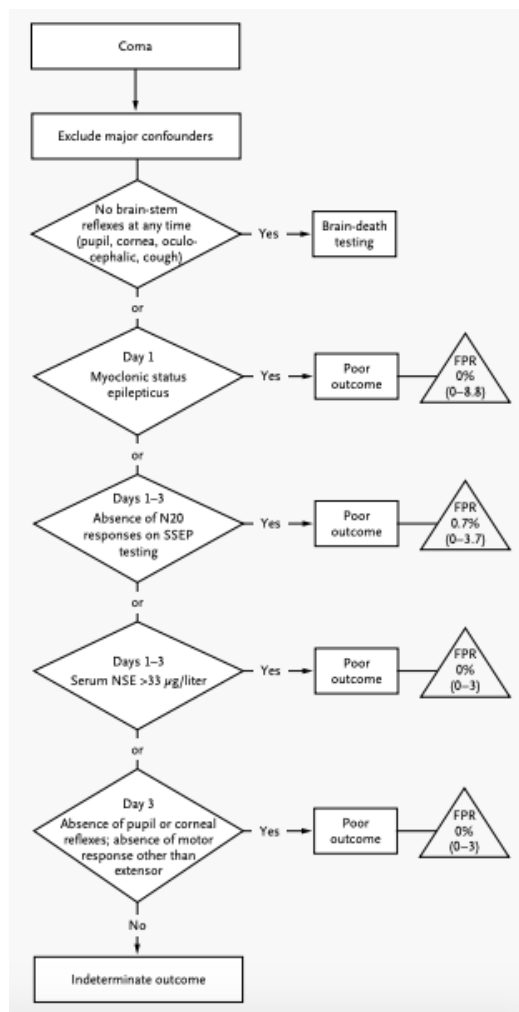
Safar P. Resuscitation after Brain Ischemia, in Grenvik A and Safar P Eds: Brain Failure and Resuscitation, Churchill Livingstone, New York, 1981; 155-184.

- CPC 1 and 2 are considered “good”, while CPC 3-5 “bad”

Modified Rankin Scale (MRS)	
0	No symptoms
1	No significant disability, despite symptoms; able to perform all usual duties and activities
2	Slight disability; unable to perform all previous activities but able to look after own affairs without assistance
3	Moderate disability; requires some help, but able to walk without assistance
4	Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance
5	Severe disability; bedridden, incontinent, and requires constant nursing care and attention
6	Death

In the last 2 decades, there have been a lot of advancements in post-arrest care: specifically we provide better post-arrest care with TTM which is reflective of better survival and neurological outcomes. Prior to that however, most patients who came in post-arrest were assessed using these guidelines in 2006 known as the “Wijck’s Criteria”(32). The Wijck’s criteria encompassed 3 things:

- Neurological exam
- Electrophysiological findings
- Biochemical testing with NSE



Neurological exam:

- Back in the early 2000s, patients who were post-arrest in coma with no major confounders present, if absent brainstem reflexes at any time, were presumed brain dead. Or after Day 3, if absent pupils, corneal or motor response other than extensor were also presumed to have poor outcome.
- Later systematic reviews and meta-analyses have shown that FPR are as high as 5-10% prior to 72 hours (33)

Electrophysiological findings:

- EEG:
 - Myoclonic status epilepticus on day 1 - poor prognosticating factor
- N20 at SSEP = somatosensory evoked potentials measured at 20 msec after electrical stimulation of the median nerve at the somatosensory cortex - if absent at Day 1-3 then poor outcome
- Overall not perfect tests with FPR as high as 5% for myoclonic SE and 3% for absent N20 at SSEP (33)

NSE = neuron specific enolase

- Released by neurons post-arrest/cell death
- Overall not widely available clinically in North America but a level of >33ug/L taken at Day 1-3 was associated with poor outcome
- This test has as high FPR as 12% (33)

Overall there is no perfect test for neuroprognostication and be very cautious doing so in the first 72 hours. Patients should initially be treated with good post-arrest management. As we are doing more neuroimaging, we need to be cautious that neuroimaging findings of hypoxic-induced brain injury has as high FPR as 2% in the first 24 hours. Best to do neuroimaging in Day 3 to 5 to increase sensitivity and specificity.

Brain Death:

Canadian Neurocritical Care guidelines define brain death as “the irreversible loss of the capacity for consciousness combined with the irreversible loss of all brainstem functions, including the capacity to breathe”.

NDD = Neurological determination of death

Clinical criteria for NDD:

- Established etiology capable of causing neurological death in the absence of reversible conditions capable of mimicking neurological death
- Deep unresponsive coma with bilateral absence of motor responses, excluding spinal reflexes
- Absent brainstem reflexes as defined as absent gag, cough, bilateral absence of corneals, pupillary response, vestibulo-ocular reflexes
- Absent respiratory effort based on apnea test

- Absent confounding factors - e.g. unresuscitated shock, hypothermia (T<35), severe metabolic derangements, peripheral nerve/muscle dysfunction/neuromuscular blockade, clinically significant drug intoxications

Diagnosis must be made with 2 physicians with independent licenses

There are situations where it is difficult to meet all of the above criteria - e.g. patient who will not tolerate apnea test - e.g. very hypoxemic, or HD unstable despite full medical therapy. A good example is a patient who is in multi-organ failure from a prolonged post cardiac arrest who neurologically have shown poor prognosticating features after 72 hours - e.g. absent brainstem and motor function, signs of HIBI on CT. Such patients may instead require ancillary tests to help with the diagnosis of brain death - two ancillary tests that we can use are: 4 vessel cerebral angiogram or perfusion scintigraphy. Either will help demonstrate the lack of cerebral perfusion.

Organ Donation:

There are two types of organ donors:

- DCD = donation after circulatory determination of death
- NDD = donation after neurological determination of death

Once someone is NDD aka “brain dead”, they are legally dead but still may have reasonable cardiac function. This usually means the rest of the organs are being perfused which make NDD donors more viable donors. Versus DCD donor, you are not legally dead until the heart stops which sometimes may be a prolonged process and low-flow state making the organs less viable. An example is a patient with a devastating brain injury but still have brainstem function that renders the ability to make a diagnosis of NDD, however family wishes to withdraw life support due to the exceedingly high chance of poor neurological outcome, such patients may still have reasonable cardiopulmonary reserve by which will make their death by circulatory collapse much slower.

Regardless, all patients in the ICU who are at end of life should be considered for organ donation. There is really no major exclusion criteria outside of family and/or patient wishes. In general, the age of 75 years or more are unlikely candidates for donation (exclusion criteria for corneas). **Organ donation should not be raised until the decision to withdraw life support or the diagnosis of NDD has been made.** This can be a highly sensitive topic for patients and their families.

Approach to Respiratory Failure:

Pathophysiology:

What is respiratory failure = inability of the body to ventilate or oxygenate.

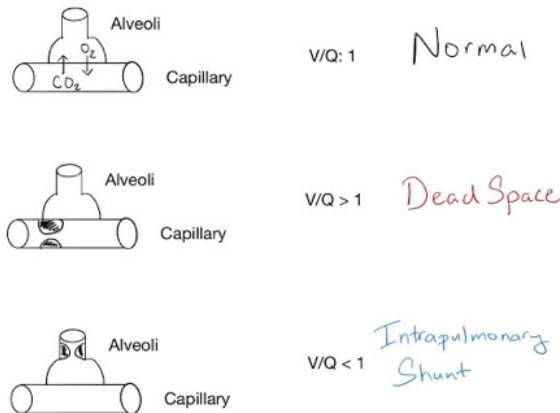
Ventilation, in basic terms, is how the body eliminates carbon dioxide while oxygenation is a more complex process with the end goal of oxygen delivery to tissues.

There are generally 2 types of respiratory failure:

- Type 1 = hypoxemic respiratory failure
- Type 2 = hypercapnic respiratory failure

From a physiological standpoint, there are **6 classic mechanisms by which hypoxemia can develop:**

1. Low inspired P_{iO_2} = if you are on Mt Everest, due to drop in ambient barometric pressure, the inspired partial pressure of oxygen is low despite no change in F_{iO_2}
2. Hypoventilation - if you don't breathe, you won't get oxygen into the blood; the A-a gradient will be normal and this can be best explained by the alveolar gas equation:
 - Let's review the Alveolar gas equation: At sea level, your PAO_2 (partial pressure of oxygen at the alveoli) is:
$$PAO_2 = F_{iO_2} (P_b - P_{H_2O}) - (P_aCO_2 / RQ)$$
$$PAO_2 = 0.21 (760 - 47) - (40 / 0.8)$$
$$PAO_2 = \sim 100 \text{ mmHg}$$
 - A-a gradient = alveolar-arterial gradient = $PAO_2 - PaO_2$
Usually normal can be predicted by $(Age + 10) / 4$; or usually < 20 mmHg. How long for an apneic patient with normal lungs to desaturate?
In healthy lungs, a patient can go up to 10 minutes of apnea before desaturating. For every one minute of apnea, the $PaCO_2$ rises about 3 for every minute -> at 10 minutes the $PaCO_2$ has gone from 40 to 70. Using the alveolar gas exchange equation this equates to a PAO_2 of 60 mmHg which is about O_2 saturation about 92%. This is the whole concept of apneic oxygenation during procedural sedation and intubation because you are increasing the F_{iO_2} to provide a buffer and compensate for the increases in $PaCO_2$.
 - Some causes of hypoventilation:
 - Won't breathe: drugs, CNS lesions (e.g., stroke, TBI, ICH), spinal cord lesions (i.e., high cervical spine injuries)
 - Can't breathe: chest wall disorders (e.g. obesity, burns, flail chest, kyphoscoliosis), neuromuscular disorders (e.g. myasthenia crisis, GBS, muscular dystrophy, ALS), obstructive airways (e.g. COPD, asthma, OSA)
3. V/Q mismatch - each alveolar-capillary unit, you'd ideally want equal ventilation (V) to perfusion (Q); the most extreme ends of that ratio is $V/Q = 0$ aka shunt, where you have perfusion but zero ventilation; and $V/Q = \infty$ aka deadspace, where you have ventilation but zero perfusion; V/Q mismatch is the most common type of hypoxemia and will have an elevated Aa-gradient and will respond to oxygen. More of this to come.



4. Shunt - the most extreme end of V/Q mismatch of no ventilation and only perfusion; that is blood flows to the lungs but unable to exchange with air for gas exchange; you can imagine that increasing FiO_2 would not help shunt and thus increasing FiO_2 will not improve hypoxemia

5. Low venous admixture - this is much more relevant when there is shunt physiology going on. E.g., imagine an area of the lung that is densely consolidated that there is minimal ventilation but blood still flows to that area of that lung. Then you bring deoxygenated mixed venous blood to that area that won't even have gas exchange, this deoxygenated blood never gets oxygenated and returns back to the left ventricle for distribution. The more deoxygenated this blood is, the more venous admixture there will be, exacerbated by the shunt and worsening the hypoxemia. This highlights the importance of treating shock in our hypoxemic patients.

6. Diffusion limitation - the interface between the capillary and alveoli is disrupted limiting diffusion of gas; the treatment would be to treat the underlying process - e.g. pulmonary edema, inflammation, fibrosis, etc

Presentation and Workup for Respiratory failure:

I suppose the first thing to the management of respiratory failure is the prompt recognition of it. Without any blood work or radiographic findings, one should be able to recognize respiratory failure through the **physical exam**.

1. Vital Signs - important to note respiratory rate but recognize that tachypnea is a sensitive but not specific finding of respiratory failure. Think about the DKA patient who has a RR of 40 and completely normal respiratory function. Oxygen saturation is obviously helpful but also recognize that "low sats" can be also due to poor peripheral blood flow and the patient may instead be either very cold or in cardiovascular shock.

2. Level of consciousness - ability to protect their airway, manage their secretions
3. Work of breathing - arguably the most important. Stand at the foot of the bed and watch the patient breathe. Have a conversation with them - are they able to converse? How many word-sentences? What is their body position? Tripoding vs upright vs supine texting on their phone? Expose their neck, their abdomen. Is there use of accessory muscles?

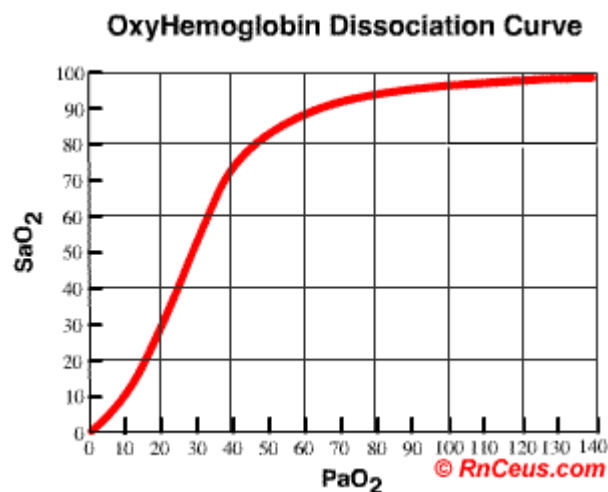
Blood gasses:

Blood Gas Value	Arterial	Venous
pH	7.35-7.4	7.30-7.40
PCO ₂	35-45 mm Hg	42-48 mmHg
HCO ₃	22-28 mEq/L	24-30 mEq/L
PO ₂	80-100 mmHg	35-45 mm Hg

Blood gasses are helpful to obtain in the workup for respiratory failure but indicated infrequently in acute situations. Caution using a single ABG as a solo determinant for intubation. Such decisions should be determined by your clinical assessment. Some uses for ABG include:

1. Is my patient responding to therapy - mechanical ventilation, NIV
2. Determine severity of hypoxemia when oxygen saturation measurements through oximetry may be not reliable - e.g. patient in shock

ABGs are most reliable for pH and PaO₂ but VBGs are a good alternative option for PaCO₂, and HCO₃. Although O₂ saturations are often reliable to assess for hypoxemia, due to the sigmoidal nature of the oxyhemoglobin curve, there is a plateau effect of oxygen saturation. It is not infrequent where we are consulted for HAU admission for “increasing O₂ requirements, now on 70% Optiflow” but the patient has PaO₂ of 200.



We may obtain blood gasses to assess the patient’s ventilatory status or their PaCO₂. Be weary of routinely ordering an ABG without a clear question in mind. A classic example is a patient coming with AECOPD - you manage this with bronchodilators, steroids and antibiotics as

per the GOLD guidelines. Consideration of using NIV modalities such as BiPAP has shown to decrease hospital length of stay and prevent intubation(34). Patients like these will present with either significantly increased WOB or have CO2 levels so high they have altered or decreased LOC. An ABG is not required to make this diagnosis. Sometimes however, I see ABGs being drawn on patients with no WOB, alert and mentating and their CO2 is incidentally high and patients are started on BiPAP to “clear the CO2”. An isolated elevated CO2 does equate to acute hypercapnic respiratory failure. Hypercapnia without acidemia can be normal especially in patients with chronic hypoventilation disorders such as COPD, obesity hypoventilation syndrome, and OSA. A review of blood gasses for respiratory acidosis:

- For every 10 mmHg increase in CO2, a chronic renal compensatory change is an increase in 4 mmol/L of HCO3 - that is a patient with a CO2 of 80 can be normal for him/her if the HCO3 is 40 and especially if the pH is normal.

Furthermore, starting patients on BiPAP who are at their baseline compensatory state can potentially cause harm. Dropping their CO2 and overcorrecting their hypoxemia may not only remove their drive to breathe but may also worsen gas exchange via V/Q mismatch and the Haldane effect.

Another time it would be prudent to obtain an ABG is when the oxygen saturation measurement is not reliable. A great example is a patient in cardiogenic or obstructive shock - they are peripherally cold and shut down. They may appear mottled and even cyanotic but if you measure their PaO2, it may supraphysiologic because they are often given supplemental oxygen at the time of the ABG being drawn due to their “low sats”. These patients may also be tachypneic but not from respiratory failure but from metabolic acidosis from lactic acidosis. They may not yet be hypotensive, especially the younger population due to their ability to compensate and intubating such patients for “respiratory failure” without adequate resuscitation may result in cardiac arrest peri-intubation.

Radiology:

I think it is suffice to say that a Chest XRay is prudent for workup for respiratory failure. LITFL has a great summary review on interpretation for Chest XRay - <https://litfl.com/drsabcde-of-cxr-interpretation>

Bedside POCUS can be helpful as well - the major windows I look for are:

- Lung sliding for pneumothorax
- Costophrenic angles for pleural effusions
- B lines for pulmonary edema
- Cardiac windows for RV, LV function, presence of MR on color

Our UBC POCUS group has a great section on lung windows:

<https://www.ubcimpocus.com/lung>

CT chest:

Can provide a ton of detail, what the burden of disease is, help with your differential diagnosis, obviously it is your go-to test to diagnose pulmonary embolism but consider the following:

- Is your patient stable enough to go to CT? If not, will the CT change your management? If so, consider how to make your patient more stable? Is the patient intubated? Can he tolerate lying flat? If it would not change your management, it is probably best to treat and stabilize the patient first.

Blood work:

The differential can be broad in terms of elucidating the etiology of the patient's respiratory failure. Common things being common it is often infectious, inflammatory or ARDS. A septic workup including blood and sputum cultures are helpful. An infectious workup is important with considerations of TB, fungal, atypical and viral causes which require additional testing on top of the routine C+S. If heart failure is on the differential - ordering BNP can help rule out heart failure but is not overly specific. Caution ordering troponin in critically ill patients - it is often positive and now you have a positive troponin to deal with. Procalcitonin can be helpful in the ICU not so much as ruling in sepsis or an infectious etiology but there is reasonable evidence for it to help guide stopping antibiotics or antibiotic duration (35). In the era of COVID, we have gotten used to ordering inflammatory markers such as ferritin, CRP, LDH, etc but there is a paucity of evidence to demonstrate having an effect on patient outcome (more of this to follow in the COVID section).

Management of respiratory failure:

Once respiratory failure is recognized, there are really 2 things to do:

1. Treat the underlying etiology
2. Supportive management through means of oxygenation and ventilation

Treating the underlying etiology. Not to go too in-depth here but there aren't that many things we can do outside of:

- If there is an infection:
 - You give antibiotics, start broad and narrow based on cultures, serology, risk factors for resistant / opportunistic organisms
- If there is a pleural collection:
 - Air / pus / blood / fluid, you drain it.
- If there is an inflammatory process:
 - You give steroids +/- other anti-inflammatory agents
- If there is pulmonary edema:
 - You diurese and provide positive pressure ventilation
- If there is a pulmonary embolism:
 - Barring contraindications, you anticoagulant +/- you lyse / remove clot.

Supportive management: oxygenation, ventilation and perfusion

Oxygenation:

Supplemental oxygen:

FiO₂ = fraction of inspired oxygen

We really provide two modes of oxygen concentration: room air at 21%; or 100% through any supplemental oxygen source. What the true FiO₂ administered will depend on the flow rate administered and whether the system is open vs closed.

Low-flow modalities:

- Nasal prongs provide 1-6L/min; by estimation with a spontaneous breathing patient with a relatively normal minute ventilation, this type of supplemental oxygen provides roughly 4% increase per L/min. So 1L/min = ~24%, 2L/min = ~28%, 3L/min = ~32%, 4L/min = ~36%, 5L/min = ~40%
- Simple face-mask provides similar increments in FiO₂ per L/min at around 4% and typically is set at 6-10L/min and thus up to 60% FiO₂.
- Nonrebreather at 15L/min can provide up to 90-95% FiO₂ as it is a closed system with the bag as a reservoir and overall limits the amount of entrained air.

High-flow modalities:

- High-flow nasal cannula (HFNC) also known as Optiflow, or High-flow fask mask
- Administered warm, humidified oxygen from 30-60L/min.
- Benefits to high-flow:
 - High flow rates helps with nitrogen washout and limits deadspace breathing
 - Providing warm humidified oxygen is better tolerated, conditions the airways for better secretions mobilization and clearance
 - Theoretical PEEP of about 3-5 cmH₂O depending on tightness of fit with the nasal cannula and if mouth is open vs closed.
 - Improved work of breathing - a patient in respiratory distress with generate higher inspiratory flow rates than one at rest / healthy; these flow rates often exceed rates provided by low flow resulting in entrainment of air, and thus lowered FiO₂; with high-flow, these rates are often much higher than the patient's inspired rate and limits work of breathing and provides more reliable FiO₂.
 - HFNC has reasonable evidence in improved patient outcome in studies like FLORALI in 2015 for patients with acute hypoxemic respiratory failure, as well its extensive use during the COVID pandemic.

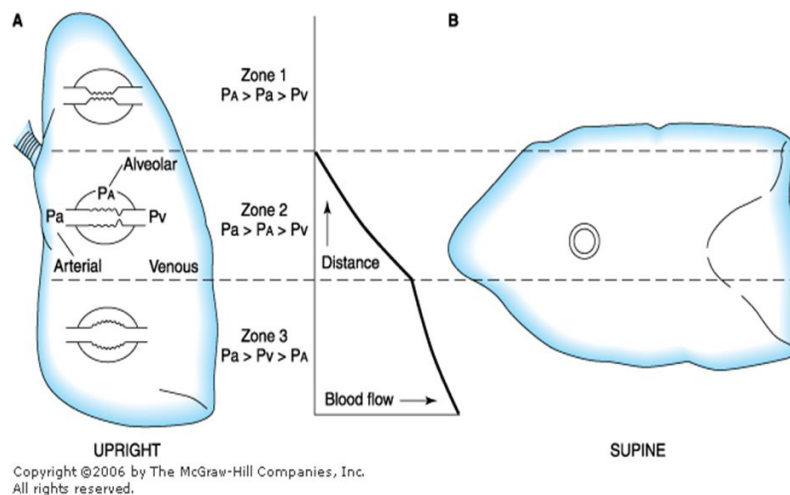
PEEP:

- PEEP improves oxygenation through alveolar recruitment - consider atelectasis, ie., collapsed alveoli are a major source of shunt. Shunting will not respond well to increased FiO₂. A solution is opening up the alveoli and keeping it open with positive end-expiratory pressure aka PEEP.

Positioning:

- West Lung Zones are key to understanding how positioning helps to improve V/Q mismatch. Consider if you have a densely consolidated left lung from pneumonia, you may improve V/Q and oxygenation by positioning the patient right side or good lung down for better perfusion to zone 3 lung.

ZONES OF THE LUNGS



Mechanical ventilation

- Taking full control of a patient's breathing can alleviate most of the work of breathing. The muscles for respiration at rest use only about 5% of the body's oxygen consumption, with increasing stress, this can increase up to 50%. By reducing the oxygen consumption required by the respiratory muscles, there is less demand required by the cardiopulmonary system to meet. Recall tissue hypoxia occurs when oxygen delivery < oxygen consumption.

Ventilation

The term ventilation is often used to describe CO₂ clearance. To improve a patient's ventilation, consider the equation for minute ventilation:

- **MV = Respiration rate x tidal volume**

A normal minute ventilation is generally about 5-8L/min in a resting healthy individual.

Respiratory rate: not too slow, not too fast:

- "Won't breathe" disorders may have low RR, and/or low tidal volumes due to poor effort/atelectasis. The most classic example for a reversible hypoventilation condition would be opioid overdose, with naloxone and bagging the patient in the interim.
- Consider a patient who is anxious and has underlying lung disease, they may have high RR but ineffective ventilation due to poor tidal volumes. Recall about 150ml of each tidal volume is dead space ventilation - i.e. ventilation that does not take part in gas exchange. Increasing RR and decreasing tidal volume will actually decrease your alveolar ventilation.
- A disease entity to which tachypnea can be very dangerous is severe COPD - patients with very poor FEV₁, e.g. <50% predicted, their ability to exhale is compromised,

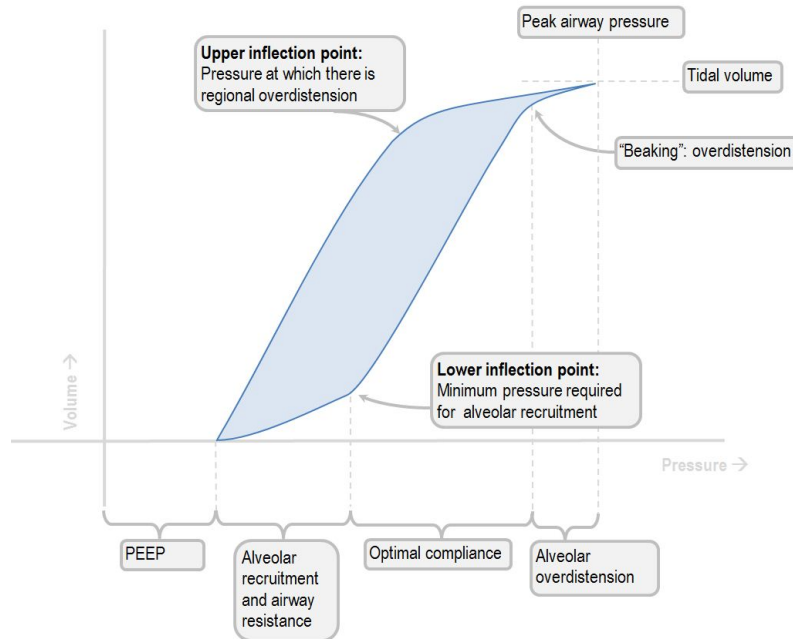
increasing RR, will decrease their expiratory time and can lead to breath-stacking, hyperinflation resulting in hypercapnic respiratory failure.

- Concept of I:E ratio:
 - In a normal spontaneously breathing patient, the I:E ratio is 1:2. That is you spend twice as long expiring than inspiring air.
 - In patients with obstructive airway disease, and thus higher resistance to airflow, their ability to expire is limited and need higher I:E ratios of 1:3 and 1:4 during an exacerbation of their disease.

Tidal volumes:

- This is generally the “can’t breathe disorders” - e.g. interstitial lung disease with poor compliance, i.e. stiff lungs
 - Compliance = change in volume / change in pressure
 - Normal spontaneous breathing patients have compliance of 100-400ml/cmH₂O; mechanically ventilated patients with normal lungs generally have compliance of 50-100ml/cmH₂O
- Methods to improve compliance and tidal volumes:
 - PEEP - concept of lung recruitment (see picture below); goal is to find optimal PEEP where the alveoli are open at a position that are not overdistended (prone to ventilator-induced lung injury or VILI) or underdistended (prone to atelectrauma - opening and closing stress of collapsed alveoli). The optimal PEEP is usually found at the lower inflection point where the lung compliance is at its highest (steepest section of the volume-pressure curve).
 - Position - sitting patient up, proning - better lung recruitment
 - More wakeful state in spontaneous breathing patients - improving delirium, minimizing sedation
 - Diuresis - wet lungs are stiff lungs
 - Draining pleural space - large pleural effusions result in compressive atelectasis
 - Steroids for inflamed stiff lungs
 - Driving pressure - may increase tidal volumes but at injurious pressures if compliance is poor - more of this to follow in mechanical ventilation section

-



ARDS = Acute Respiratory Distress Syndrome

ARDS is an acute, diffuse inflammatory form of lung injury that is associated with a variety of etiologies. Key part is that it is a syndrome, not a diagnosis. Common causes of ARDS include sepsis, trauma, burns, pancreatitis, COVID, aspiration, inhalational injury, transfusion (TRALI), infection, etc.

There are many ways to define ARDS but most often we use the Berlin Definition:

1. Acute - onset within 1 week of insult
2. Respiratory Distress:
 - a. Bilateral opacities on radiography
 - b. Hypoxemia - $\text{PaO}_2 / \text{FiO}_2$ ratio of $< 300\text{mmHg}$ on at least a PEEP of $5\text{ cmH}_2\text{O}$
3. Syndrome not due to volume overload or cardiac failure

Classify ARDS based on severity:

- Mild is P/F ratio of 200-300
- Moderate 100-200
- Severe < 100

ARDS has high mortality - up to 45-50% with severe disease.

Management of ARDS

- primarily supportive and treat the underlying cause

As we have gained more experience and knowledge with mechanical ventilation and acute lung injury, we have over the past 2 decades changed how to ventilate patients. The biggest landmark paper published in NEJM in 2002 by the ARDSnet group(36) taught us the concept of lung protective ventilation to prevent what we now call ventilator induced lung injury (VILI)

- Using lower tidal volumes at 6ml/kg and lower RR to prevent volutrauma
- Using PEEP to optimize lung recruitment and minimize atelectrauma
- Minimize plateau pressures to < 30 cmH₂O or driving pressure < 15 cmH₂O to minimize barotrauma

Low tidal volume ventilation will ultimately result in hypercapnia and thus a lot of lung protective strategies are based on the concept of “permissive hypercapnia”. We generally will lower pH of 7.25-7.35 and higher CO₂ levels. Hypercapnia alone is not necessarily harmful unless the patient becomes increasingly acidemic and thus we generally have pH goals rather than CO₂ goals. Hypercapnia however is dangerous for head injured patients due to the cerebral autoregulation curve is heavily dependent on CO₂ as CO₂ is a potent cerebral vasodilator; thus post-arrest, TBI or other head injured patients are not typically managed with permissive hypercapnia as higher CO₂ levels can increase ICP due to the vasodilatory effects. Barring head injury, the lung protective strategies of low tidal volume ventilation and higher PEEP are often used but are generally not well-tolerated by patients. Our innate respiratory drive is heavily influenced by pH and CO₂, and low pH, high CO₂ will stimulate the respiratory system to increase ventilation. Our lungs will want to be ventilated at higher minute ventilations, this can result in ventilator asynchrony, agitation, delirium and self-induced lung injury (SILI). Thus, ARDS patients who are being ventilated by lung protective strategies require heavy sedation +/- paralysis to mitigate that. RASS goals of -4 to -5 are generally necessary. Sedation with propofol +/- an opioid like fentanyl or hydromorphone infusions are often used.

Oxygenation can be difficult in patients with ARDS as the lungs can become quite stiff from the inflammatory response leading to pulmonary edema. As this is noncardiogenic, diuresis and positive pressure alone will not alone reverse the insult.

Guidelines now provide us a good step-ladder approach to managing ARDS:

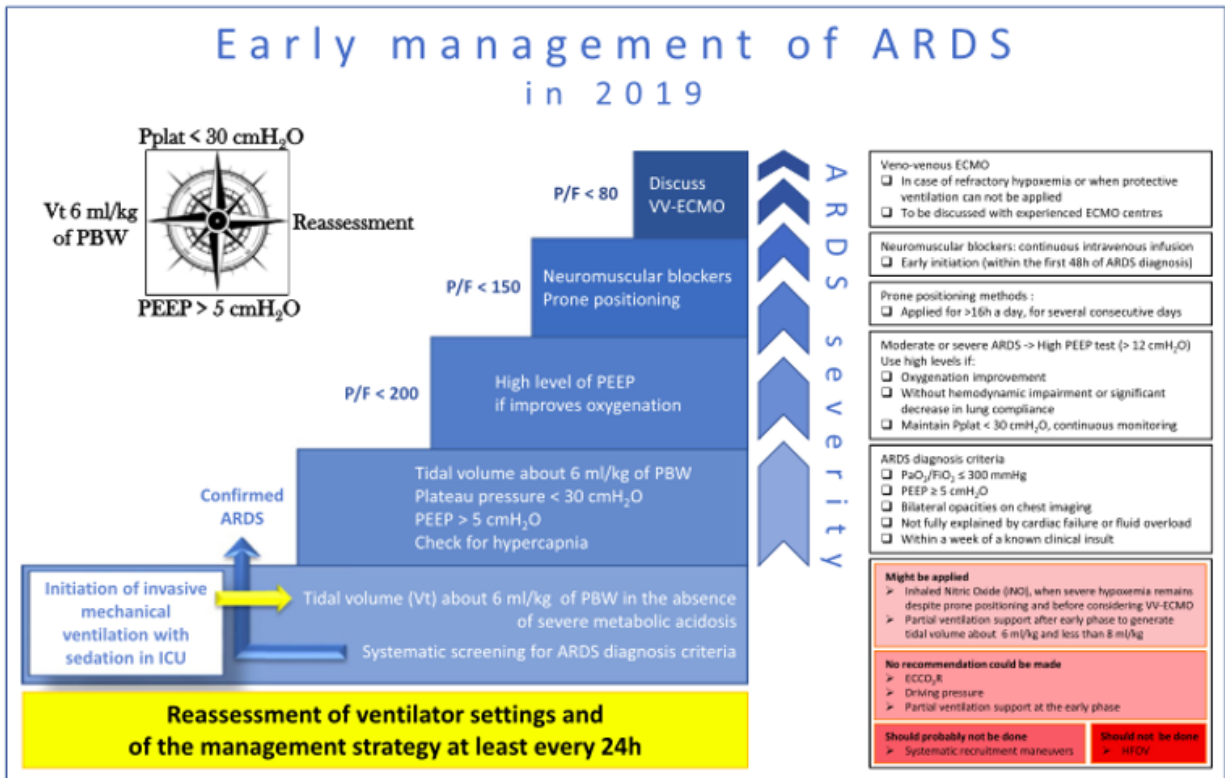


Fig. 1 Therapeutic algorithm regarding early ARDS management (EXPERT OPINION)

1. Lung protective ventilation, PEEP, and sedation **mortality benefit**
2. Paralysis with neuromuscular blockade - we often use Rocuronium boluses of 0.5-1mg/kg IV PRN q1h or cisatracurium (Nimbex) infusions generally at 0.3-0.6mg/kg/hour for train of four of 2 or less. Cisatracurium infusions are often preferred and has better evidence with *mortality benefit* in early ARDS (ACURASYS 2010)(37)
3. Proning: 3 benefits to proning: **mortality benefit** (PROSEVA 2013)(38)
 - a. Better lung recruitment
 - b. Better V/Q mismatch
 - c. Better secretion clearance
4. Corticosteroids - in patients with moderate to severe ARDS, there is likely a mortality benefit as well as less days ventilated in administering steroids early (within 4 days) of ARDS presentation. Can either use 1mg/kg methylprednisolone IV daily (39) for 14 days followed by a taper till day 28 or Dexamethasone 20mg IV daily x 5 then 10mg IV daily x 4 (DEXA-ARDS 2020)(40)
5. Inhaled pulmonary vasodilators - options are inhaled nitric oxide - generally start at 20ppm (range 0-40) or inhaled Flolan or epoprostenol. These therapies will improve oxygenation but have not shown to improve patient outcomes like mortality, days in ICU, etc compared to the therapies listed above.
6. vvECMO - end of the line. ECMO is a great option for bridge to recovery or bridge towards transplantation but patient selection must be very careful. In general: young, single system issue, minimal other comorbidities, and early in disease course (before 7 days).

COVID-19

Coronavirus Disease 2019 is caused by SARS-CoV-2 = Severe Acute Respiratory Syndrome Coronavirus-2

- Coronaviruses are +RNA viruses, known pathogens to humans and animals
- Obviously led to a major pandemic in 2020-present.
- Transmission primarily droplet-contact but still recommended to practice airborne especially in aerosolizing procedures
- Symptoms can be very broad as the ACE-2 receptor is found ubiquitously throughout the body - lungs, heart, GI tract, vasculature, kidneys, bladder
 - In general, ILI symptoms like fever, cough, SOB, URTI symptoms, n/v/d
- As disease progresses, around day 7-8, severe disease and complications can arise:
 - ARDS
 - Cardiac - arrhythmias, cardiomyopathy, myopericarditis
 - Thromboembolic - stroke, PE, DVT
 - Neurologic - encephalopathy
 - Inflammatory - cytokine storm, Kawasaki's/multisystem inflammatory syndrome (MIS)
 - Secondary bacterial infections - pneumonia, bacteremia
- Risk factors for severe illness: AGE (>65 years), obesity, diabetes, CAD, smoking, chronic lung disease

Workup:

- COVID-19 testing - NP swab generally done, can have tracheal aspirate as well
- Sputum cultures (if intubated) to help guide antimicrobials
- CXR, ECG
- Low threshold to get CT chest 1) to rule out PE 2) to ascertain parenchymal disease burden 3) assess for barotrauma such as pneumothorax, pneumomediastinum
- Blood work:

Laboratory features associated with severe COVID-19^[1-6]

Abnormality	Possible threshold
Elevations in:	
▪ D-dimer	>1000 ng/mL (normal range: <500 ng/mL)
▪ CRP	>100 mg/L (normal range: <8.0 mg/L)
▪ LDH	>245 units/L (normal range: 110 to 210 units/L)
▪ Troponin	>2× the upper limit of normal (normal range for troponin T high sensitivity: females 0 to 9 ng/L; males 0 to 14 ng/L)
▪ Ferritin	>500 mcg/L (normal range: females 10 to 200 mcg/L; males 30 to 300 mcg/L)
▪ CPK	>2× the upper limit of normal (normal range: 40 to 150 units/L)
Decrease in:	
▪ Absolute lymphocyte count	<800/microL (normal range for age ≥21 years: 1800 to 7700/microL)

- Bedside POCUS or formal echo if any signs of shock to look for RV/LV function
- Consider procalcitonin to help stop antibiotics if no other signs of bacterial infection

Management:

1. Primarily supportive
 - a. High flow oxygen therapy
 - b. Mechanical ventilation with lung protective strategies for patients with ARDS from COVID
2. Steroids - RECOVERY trial 2020. Dexamethasone at 6mg daily for 10 days or until hospital discharge has mortality benefit in anyone requiring supplemental oxygen(41). In ICU, we have extrapolated our steroid use in ARDS to use higher dosing of steroids in managing COVID patients on mechanical ventilation with moderate to severe ARDS - i.e. 1-2mg/kg daily of methylprednisolone for 14 days then taper or dexamethasone at 20mg IV daily x 5 then 10mg IV daily x 5. The use of higher steroids than the 6mg is not evidence based. There is however some evidence to use 12 mg instead of 6mg(42).
3. IL-6 pathway inhibitors (tocilizumab, sarilumab) - REMAP-CAP trial also showed mortality benefit in patients requiring critical care defined by high flow oxygen therapy, vasopressors or mechanical ventilation within 24 hours to presentation to critical care (43) - we have been using the dose of tocilizumab at 6mg/kg IV or 400mg IV x 1 dose; with shortages of tocilizumab; we have also used baricitinib for up to 14 days as an alternative
 - a. Relative contraindications include:
 - i. Immunosuppression - however during the pandemic, most patients on biologics for immunosuppression have received toci as the general consensus from rheumatology, oncology and transplant medicine is the benefit likely outweighs the harm
 - ii. Neutropenia - ANC < 1
 - iii. Thrombocytopenia - PLT < 50
 - iv. Transaminitis - ALT or AST 5x above upper limit of normal
 - v. Active serious bacterial infection
 - vi. Hospitalized with COVID for > 14 days
 - vii. Already received tocilizumab or equivalent as long-term therapy or in index hospital visit
4. Not following not currently recommended by our BCCDC guidelines:
 - a. Hydroxychloroquine
 - b. Remdesvir - not recommended in patients requiring critical care; very borderline benefit in patients hospitalized on low flow oxygen
 - c. Lopinavir/ritonavir
 - d. Interferon
 - e. Ivermectin

VTE prophylaxis:

Very contentious topic. No real consensus on what to do. Obviously if a patient has reason to anticoagulate - i.e., known VTE, previous VTE, mechanical valve, AFib, etc, you anticoagulate. Mixed literature - we know COVID is a pro-thrombotic disease but we also have found that full

anticoagulation in critically ill patients can lead to bleeding. What we do not know is how to mitigate the VTE risk prophylactically without the bleeding?

In general - hospitalized patients with COVID on oxygen should receive standard VTE prophylaxis at usual dosing, e.g. enoxaparin at 40mg SC daily. This is the current guidelines for WHO and NIH guidelines.

What we have integrated in the Lower mainland practice is what is being derived from newer evidence from this multiplatform RCT:

that if patients get admitted with COVID on oxygen but without organ support (ie, high flow, NIV, MV, pressor support), full anticoagulation is started empirically.

*“If used, anticoagulation for COVID-19 should start within 72 hours of admission and be continued for 14 days or until hospital discharge. Therapeutic anticoagulation was superior to standard of care for composite 21-day organ support free survival in the ATTACC/ACTIV-4a/REMAP-CAP trials. Benefits appear to be driven by reducing progression to high-flow oxygen, non-invasive ventilation, or vasopressors. There was insufficient certainty on whether therapeutic anticoagulation improves mortality or intubation. Therapeutic anticoagulation reduces thrombotic events (1.4% vs 2.7%) but may increase major bleeding (1.9% vs 0.9%). *High risk features for bleeding include: age 75 or greater, eGFR less than 30 mL/min, any coagulopathy, platelet count less than 50 x 10⁹/L, use of dual antiplatelet therapy, recent history of serious GI bleed or recent intracranial condition (stroke, neurosurgery, aneurysm, cancer), epidural or spinal catheter.” - BCCDC guidelines*

However if a patient comes directly to critical care, VTE prophylaxis dosing is recommended. As the aforementioned trial shows that critically ill patients did not show benefit and potentially harm. In practice we still tend to use the higher dose of 0.5mg/kg of SC enoxaparin BID. This is with minimal to no evidence to demonstrate benefit.

What is unclear is what to do on hospitalized patients who were not on organ support and now need organ support, whether to continue therapeutic anticoagulation. This will be a patient-to-patient decision depending on their bleeding vs thrombosis risk.

Good summary of our BCCDC guidelines are: <http://www.bccdc.ca/Health-Professionals-Site/Documents/Antimicrobial-Immunomodulatory-Therapy-adults.pdf>

Overview of Mechanical Ventilation:

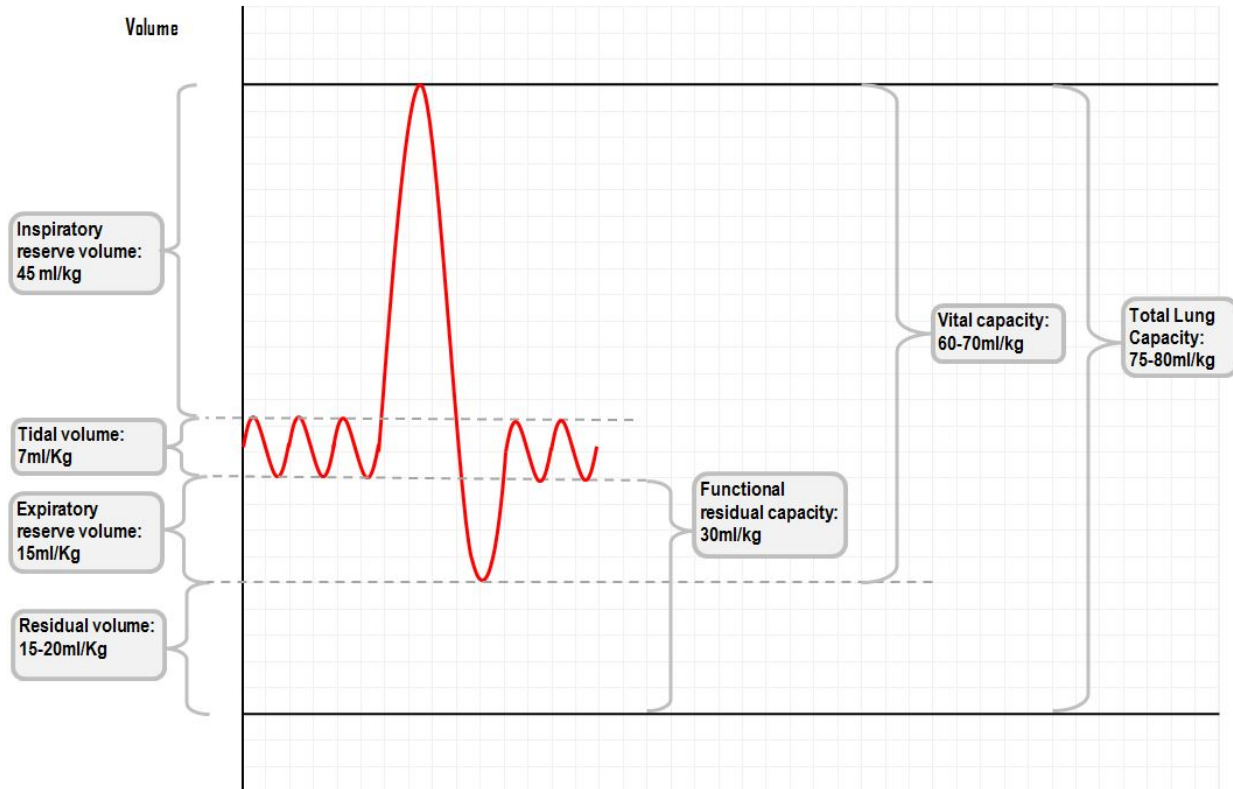
Before we go over mechanical ventilation, let's briefly review the physiology of normal spontaneous ventilation.

When we breathe, our respiratory muscles, i.e., primarily the diaphragm, contracts and lowers to expand our thoracic cavity. This generates negative pressure by which atmospheric air will flow

from high to low pressure gradient during inspiration. The passive recoil of our lungs and relaxation of our diaphragm will move air outwards during expiration.

- Review of Ohm's law = Flow = change in pressure / resistance ($Q = P / R$)

At rest, these volumes of inspiration and expiration are called tidal volumes. See below for definition and roughly normal values of lung volumes:

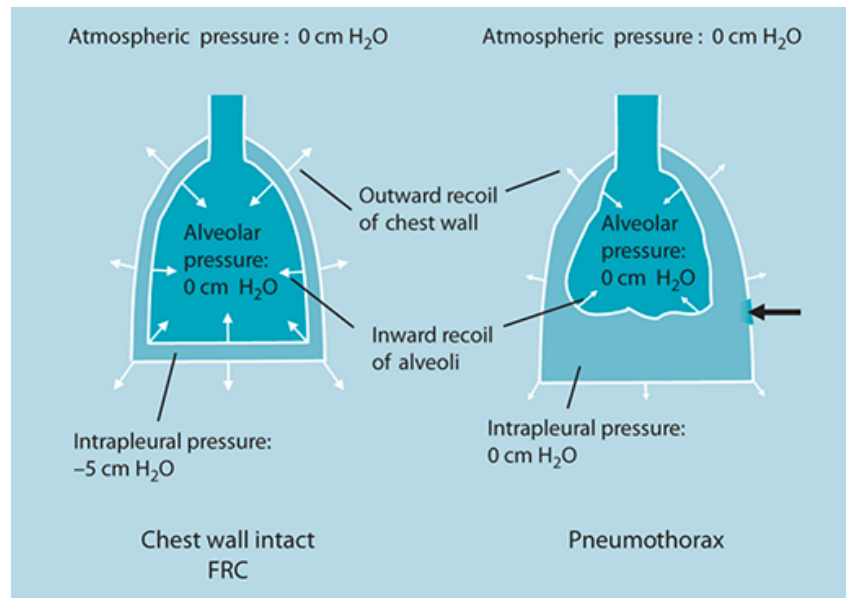


Functional Residual Capacity (FRC) is an important concept to cover. At rest, the end of expiration is determined by the natural inwards recoil of our lungs and the outwards expansion of our chest wall; the pressures where these two opposing forces equalize determines our FRC. At FRC, our lung compliance is at its highest and airway resistance as its lowest (essential zero due to equalizing pressures). The remaining lung volume at the end of expiration, i.e., FRC, provides a reservoir of air to continue to participate in gas exchange. This is exceedingly important during intubation where we paralyze patients and during apnea, the time to desaturation is heavily dependent on FRC.

Conditions that will decrease FRC:

- Age / size of person - small people (e.g., babies) = small lungs
- Large abdomens - obesity, pregnancy, distended abdomen from intraabdominal sepsis, bowel obstruction, post-op
- Stiff lungs - i.e., poor compliance; e.g., pulmonary edema, ILD, consolidation
- Pleural effusions
- Pneumothorax

- Chest wall disease - obesity, burns, kyphoscoliosis



Source: Michael G. Levitzky: *Pulmonary Physiology*, 9e
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Mechanical ventilation:

Two types:

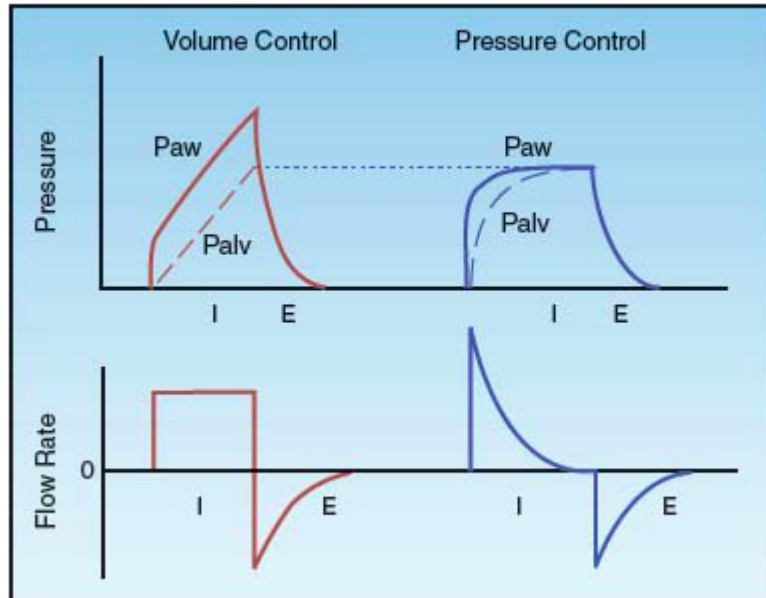
- Noninvasive - high flow therapy, BiPAP, CPAP
- Invasive

Invasive MV:

2 modes:

- Controlled
 - Volume control (VC), also can be referred to assist control or AC
 - Pressure control (PC)
- Spontaneous
 - Pressure support ventilation (PSV)
 - Proportional assist ventilation (PAV)
 - Neurally adjusted ventilatory assist (NAVA)

We will cover VC, PC and PSV as they are for the most part, the main modes of ventilation we use in the ICU.



Volume control:

- Set a tidal volume - for example, 6ml/kg in a 70kg male = 420ml
- Set a T_i - time of over which the inspired volume is delivered
- Set a RR
- Set a F_{iO_2}
- Set a PEEP
- Set a trigger type and sensitivity:
 - Volume control - if you set a RR of 12 and TV of 420; the ventilator will deliver 12 breaths at 420ml over a fixed timed cycling. The controlled breaths are triggered and cycled via time. However if the patient decides they want to breathe, the sensitivity to which the ventilator senses this spontaneous breath is often set to a certain pressure or flow a patient must meet for the ventilator to deliver the breath. Every breath - whether it is controlled by the ventilator or the patient, the ventilator will always deliver the set volume.
 - You can imagine that if a patient has a high respiratory drive to breathe - e.g. acidemia, sepsis, burns, pain, anxiety - their triggered breaths may start to interfere with the timed ventilator breaths and thus this often leads to ventilator asynchrony
 - PROS to VC:
 - Guaranteed volume - key for ARDS ventilation at targeting 6-8ml/kg
 - Controlling the volume will have tight control on ventilation and thus CO_2 with the condition that the rate is also in control - this will depend on the patient respiratory drive vs sedation +/- paralysis
 - CONS to VC:

- Small volumes are not comfortable and thus can lead to ventilator asynchrony, patient discomfort/agitation thus requiring more sedation +/- paralysis
- Volume control the inspiratory flow rate is constant (see above the waveform is square) which is not physiologic - also can lead to patient discomfort/agitation
- With poor compliance, the volumes delivered may require high amounts of driving pressure which can be injurious to the lungs. More on driving pressure later.

Pressure control:

- Set a inspiratory pressure or pressure control
- Set a Ti
- Set a RR
- Set a FiO₂
- Set a PEEP
- Set a trigger type and sensitivity:
 - With pressure control, you set a fixed RR and each breath will have a set pressure. The generated volume will depend on the compliance of the patient's lungs. The controlled breaths are triggered and cycled via time. Similar to volume control, if that patient decides to breathe, the assisted breath can be triggered by pressure or flow. But because the volume is not controlled, this may allow the patient to influence the tidal volumes and inspiratory flows better. This is often more tolerated and there is less incidence of ventilator asynchrony.
- PROS to PCV:
 - Guaranteed pressure - able to essentially control the patient's driving pressure
 - More tolerated, less incidence of ventilator asynchrony
- CONS to PCV:
 - Unable to tightly control tidal volumes

Pressure support:

- Set a inspiratory pressure or pressure support
- Set a trigger type and sensitivity
- Set a PEEP
- Set a FiO₂
- PROs to PSV:
 - The mode to use in awake patients who are weaning not only from the ventilator, but weaning from their overall disease burden
 - Ideally we want to use PSV as soon as possible to avoid diaphragmatic atrophy which can occur within 48 hours of being on a ventilator!
- CONs to PSV:

- May lead to hypoventilation if the patient is not maintaining an adequate RR. There are backup rates but generally set at a low rate to encourage spontaneous breaths.
- In patients who have high respiratory drive but poor lung mechanics (i.e., severe COVID or severe ARDS patients), these patients may be sucking in high volumes or high pressures and can lead to SILI or self-induced lung injury. And thus such patients generally should be ventilated via lung protective settings until they improve from a disease burden standpoint - will be indicated by better gas exchange (e.g., lower FiO₂ requirements, improving lactate), and better lung mechanics (e.g., better lung volumes, lung compliance).

Key ventilator parameters to know:

1. FiO₂ - seems intuitive but very important. The overall trend is important to know - e.g., if the patient was on 40% and now is on 80% FiO₂, that is not good. PaO₂/FiO₂ ratio would also be helpful to know as well. You would want to work through the causes of hypoxemic respiratory failure and find out why the patient is requiring more oxygen support. It is important to never forget that oxygen is a drug. Oxygen is vital to our existence but too much of it can be harmful. Oxygen toxicity creates radical oxygen species and can be damaging to the lungs. We generally get concerned with oxygen toxicity when FiO₂ is persistently 70% or higher.
2. PEEP = positive end-expiratory pressure. PEEP can be considered as the positive pressure aimed to stent the alveoli open. With the alveoli open, there is better ventilation and perfusion (V/Q) matching. When alveoli are closed (i.e. atelectasis), or filled with fluid (i.e. pulmonary edema) or pus (i.e. pneumonia), there is a lot of shunt physiology occurring where increases in FiO₂ will not improve oxygenation. These disease entities often need more PEEP to improve oxygenation. However, too much PEEP can result in overdistension in some alveoli, which then can compress and further collapse neighboring alveoli - this particularly occurs in heterogeneous / focal diseases like pneumonia. FiO₂ and PEEP are numbers that tell you the level of oxygenation support the patient is on. There are a few ways to optimize PEEP, one of which is using the ARDSnet table or a PEEP ladder to help titrate your PEEP (see below).

ARDSnet FiO2/PEEP Titration

Goal O2 Sat 88 - 95% (PaO2 55 - 80mmHg)

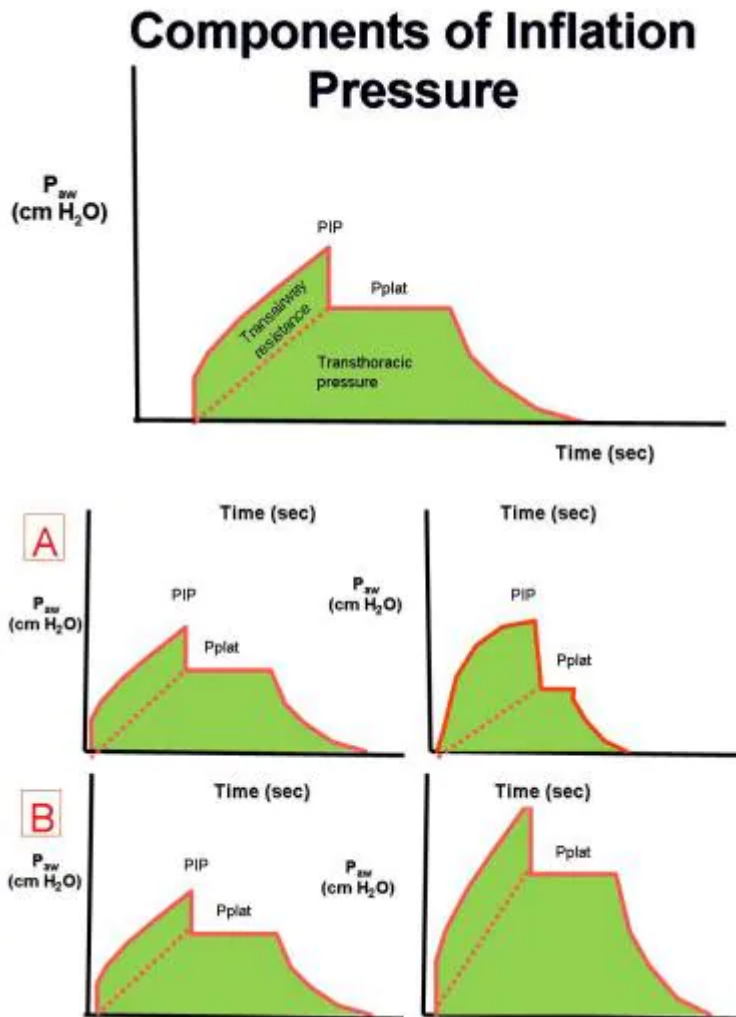
Wait 5 - 10 min Before Step Up or Down
(Titrate FiO2/PEEP at Same Time)

FiO2	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7
PEEP	5	5	8	8	10	10	10	12
FiO2	0.7	0.8	0.9	0.9	0.9	1.0		
PEEP	14	14	14	16	18	18-24		



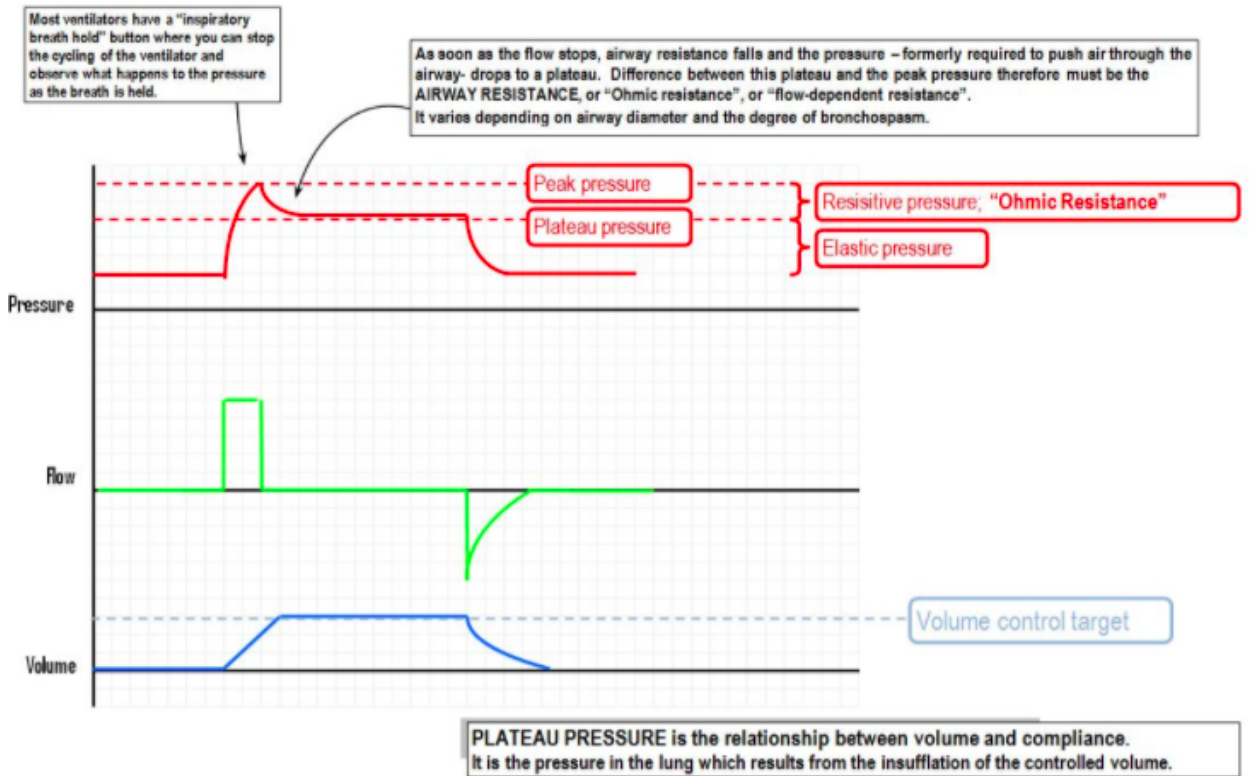
- Tidal volume - in the era of lung protective ventilation strategies we tend to by default ventilate patients at 6-8ml/kg (ideally 6ml/kg) for tidal volumes. This is particularly for patients in a control mode. Patients who are spontaneously breathing, it is much more difficult to control their tidal volumes as we set a pressure support to help achieve tidal volumes that would be sufficient enough. Patients who do not generate sufficient volumes with pressure support are not often ventilated in that mode as obviously their lung compliance is not yet ready. NB: the weight set for tidal volumes is ideal body weight and thus you will see the RTs measure the patient's height to help estimate their ideal body weight
- Peak inspiratory pressure - in a volume control mode, the ventilator is programmed to get a set tidal volume. For the volume to be delivered, the pressure required will depend on 2 things: the lung and chest wall compliance, and the resistance to airflow. The highest pressure at any state is the peak inspiratory pressure. The ventilator is often set to alarm with peak pressures of > 40cmH2O. Peak pressures are sensitive to patient effort and you will note high peak pressures especially in time of patient-ventilator asynchrony. When the RT comes to you to tell you there are high peak pressures, the first step is to remove the patient from the equation by sedating +/- paralyzing the patient. Then you can ascertain what is the etiology of the high peak pressures - is it driven by airway resistance or poor lung compliance. If high peak pressure but low plateau pressure (see below as diagram A), this is an airway resistance issue - treat bronchospasm with bronchodilators, what is the size of ETT, decrease respiratory rate to increase inspiratory / expiratory time; while if high peak pressure and high plateau pressure, this is concerning for stiff lungs or poor/low lung compliance (see below as diagram B).

5. Plateau pressure - is the pressure to keep the alveoli distended at the end of inspiration. This is measured in volume control mode with an inspiratory hold with no patient effort. Plateau pressures ideally should be $< 30\text{cmH}_2\text{O}$ as pressures higher than that are associated with barotrauma and acute lung injury (ARDSnet). High plateau pressure = high pressures required to distend the alveoli. This means poor or low lung compliance or stiff lungs. Causes include pulmonary edema, pleural effusions, atelectasis, ARDS, pneumonia, aspiration



6. Driving pressure = plateau pressure - PEEP. Also known as the delta pressure. Goal is to keep driving pressure $< 15\text{cmH}_2\text{O}$. Newer concept in ARDS ventilation with increasing evidence of better survival (44).
7. Compliance - How is compliance measured? Compliance is change in volume over change in pressure. Less pressure, more volumes = better lung compliance. There is static compliance with absence of airflow, and dynamic compliance which is with presence of airflow. With the presence of airflow, dynamic compliance also incorporates airway resistance. Static compliance can be measured with the plateau pressure -

PEEP. Dynamic compliance uses the peak inspiratory pressure - the PEEP. Normal lung compliance in a healthy patient spontaneously breathing is usually > 100ml/cmH₂O, vs on a ventilator > 50ml/cmH₂O.



Weaning from the ventilator:

These days the RTs really manage the ventilator in near auto-pilot mode. With PPO and admission order sets, doing ICU orders is almost made for dummies. We can tick off a box if we want "conventional ventilation" vs "ALI (acute lung injury) or ARDS ventilation". Conventional ventilation is the usual mode and is the way we ventilate patients without ARDS - i.e., our septic shock, decreased LOC, polytrauma, open abdomen patient. In such patients, they are still ventilated using "lung protective" parameters such as limiting plateau pressures to <30cmH₂O, keeping tidal volumes < 6-8ml/kg, etc. But these patients usually don't have bad lung pathology and thus makes ventilation easier. They tend to follow a "weaning pathway 1" which is essentially an auto-pilot, RT and protocol driven pathway where we wean the patient off the ventilator as quickly as possible in a stepwise fashion.

How do we determine if the patient is ready to be weaned?

- Are they in shock?
 - End organ perfusion parameters - lactate, UO, mixed venous
 - Deescalating / minimal vasopressor or inotropic support
- How is their gas exchange?
 - pH > 7.25, p/F ratio > 150

- Stability in disease course?
 - Active issues - e.g. seizing, bleeding, uncontrolled sepsis

Once we agree the patient can be weaned:

- We align this by backing off on sedation, ideally RASS goal 0
- The RT will then swap the patient to a spontaneous mode of ventilation, most commonly pressure support ventilation (PSV), and incrementally decrease the pressure support to achieve sustainable and efficient ventilation. This is determined by the patient's tidal volumes, RR, vital signs, work of breathing/appearance, and blood gas.
- Once the patient is on de-escalating and/or minimal ventilatory support - e.g. PSV 10/8 or less (pressure support of 10 and PEEP of 8 or less), the RT will then do a spontaneous breathing trial (SBT) to see if the patient is potentially able to be liberated off the ventilator. I use this term because some of our patients are trach'ed and instead of extubation, we place them on high flow oxygen instead - this term is called "T-piece". T-piece is just extra tubing to limit the amount of resistance the patient must breathe through now without positive pressure.
- An SBT with most intuitions in BC is PSV 5/5 or pressure support of 5 and PEEP of 5. It is done to ascertain readiness for extubation or liberation off the ventilator. The RT switches the patient to this mode and monitors their tidal volumes, RR, vital signs and work of breathing. The patient passes their SBT when they are comfortable, with minimal WOB, stable vital signs, sufficient tidal volumes and low RR. The term "F/Vt" is often used and is RR / tidal volume in liters. A number < 105 is considered good (often referred to as Tobin's index or Rapid Shallow breathing index), and is indicative that the patient's breathing is efficient and is a good predictor for successful extubation.

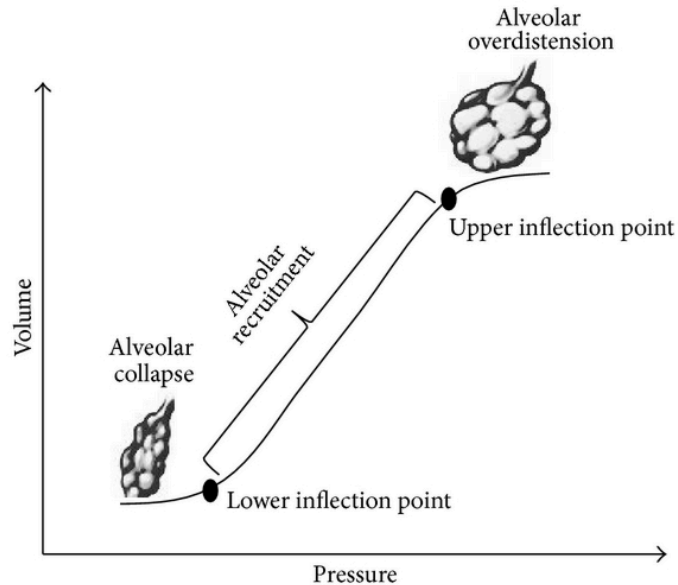
Difficult weaning:

- There will be a number of patients who follow a more protracted course in the ICU. These are patients may be frail or medically comorbid to begin with, which reminds us to be thoughtful on who we put on ventilators; or these can also be patients with severe burden of disease resulting in a deconditioned state with neuromuscular weakness, delirium and/or poor cardiopulmonary reserve that makes it difficult for them to be liberated from the ventilator.
- These patients are often trach'ed as we anticipate a prolonged course - typically by day 10 of mechanical ventilation we start thinking of the need to make this decision to perform tracheostomies in anticipation for a difficult wean trajectory. Early tracheostomy (< day 10) has trends towards decreased rates of VAP, higher ventilator-free days, more likelihood of discharge from ICU, and better patient comfort.
- A difficult weaning protocol is often designed individually for the patient - the concept is to rest the patient on a well-supported mode (usually a control mode); with periods of "exercise" to rehabilitate the patient while on the ventilator. For example, patients will be rested on VC and have 1 hr of CPAP 5 trial or PSV 5/5. If this is well-tolerated, the next day would be 2 hours, then 2 x 2 hours, etc. You work your way up incrementally to 12 hours then 24 hours. Some patients may not even tolerate PSV or CPAP, and may need a separate weaning pathway using alternative modes of ventilation such as NAVA or PAV. In brief, NAVA is neural-adjusted ventilatory assist where the ventilatory support is

triggered by the electrical diaphragmatic activity of the patient. It has shown to help with patient-ventilator dyssynchrony during difficult weaning. PAV is proportionally assisted ventilation where each breath and support given by the ventilator is set proportionally based on the patient's effort - that is more effort more support. NAVA and PAV are newer modes of ventilation that are not as frequently-used in our local ICUs but are potential avenues for difficult weaning patients.

Troubleshooting the ventilator:

- The RT may page you to help with managing the patient and the ventilator. Here are some common reasons:
 - **High peak pressure alarms:** as previously mentioned, peak airway pressure is usually due to high airway resistance or patient-ventilator dyssynchrony. First thing to consider is dyssynchrony, assess the patient, are they agitated/awake, do they need more sedation. If they are adequately sedated but still asynchronous, do they need paralysis? If dyssynchrony is not the issue, consider sorting out why high airway resistance:
 - Check all tubes - plastic lumens: any obstruction, kinks
 - Patient airway lumens - suctioning the patient
 - Chest X-Ray - any collapse due to mucus plugging
 - Bronchospasm - bronchodilators: e.g., salbutamol, ipratropium, magnesium
 - **High plateau pressures** - this is typically indicative of poor lung compliance. True plateau pressures should be measured with zero patient effort so if in doubt, sedate and paralyze the patient to remove them from the equation.
 - Chest Xray or lung US - any signs of large effusions, pneumothorax, pulmonary edema - intervene as needed
 - Obtain an ABG - how much room is there to come down on the tidal volumes?
 - Sedate, paralyze the patient.
 - Try to ascertain the ideal amount of PEEP - is the patient potentially underrecruited and increasing PEEP may improve lung compliance (see graph below)? Other options to determine optimal PEEP: PEEP ladder, bedside PEEP study, esophageal balloon

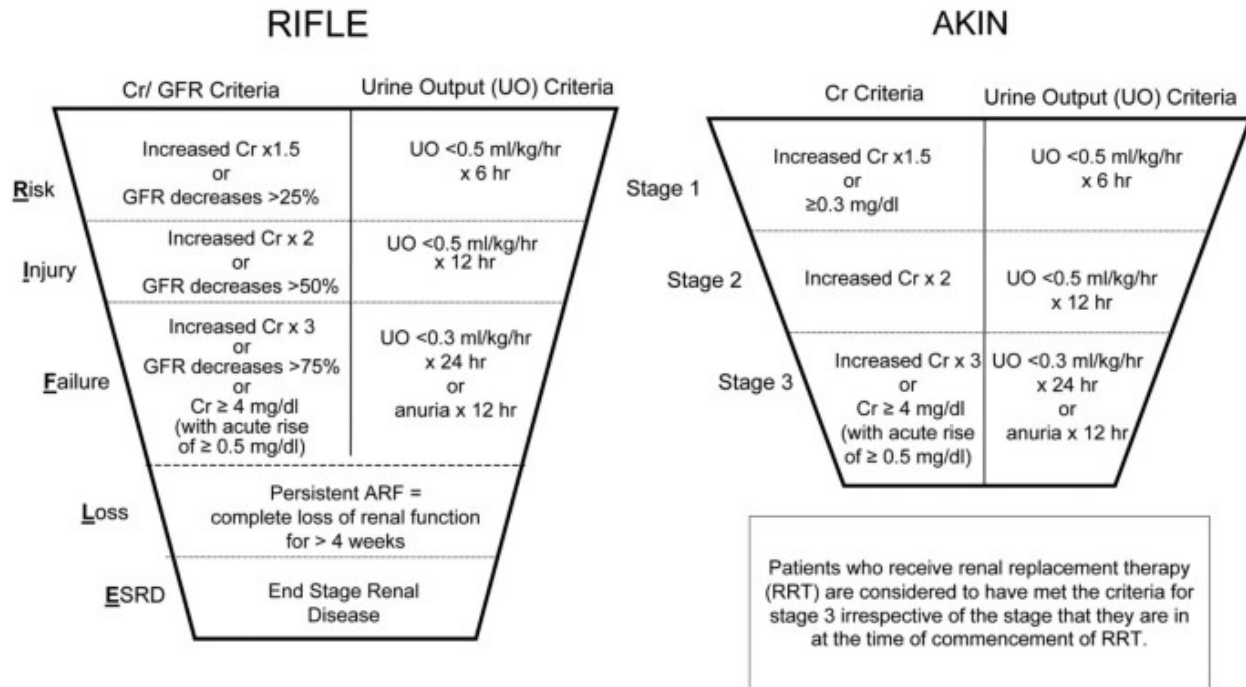


- **A desaturating patient:** Textbooks and resources often use the DOPES mnemonic:
 - Displacement and disconnect - check the tubing from the patient to the machine. Especially in peds, ETTs can be dislodged above the glottis due to their short tracheas. Disconnect the patient from the ventilator and bag the patient.
 - Obstruction - kinks, plugs within the plastic and patient lumens
 - Pneumothorax - barotrauma is much less common now due to lung protective ventilation but lung US or CXR to look for PTX
 - Equipment - check the ventilator, oxygen source
 - Suction/Sedate - deep suction and sedate +/- paralyze the patient
- Consider that there are only a few things that will acutely drop a patient's saturations removing patient-ventilator dyssynchrony and equipment issues from the equation:
 - Pneumothorax
 - PE
 - Airway obstruction - often mucus plug/bleeding/secretions within the airways

Approach to Acute Kidney Injury:

AKI = acute (< 7 days) and sustained (> 24 h) decline in renal function

How does one classify AKI? Can use the Rife criteria or AKIN criteria:



AKI is very common, in fact about 1/2 of our patients will have an AKI in the first week of their ICU admission. The etiologies are nevertheless the same so the same approach as you would on the ward or in the ED:

Pre-renal vs renal vs post-renal

From a workup and management perspective:

- History: drug exposures, episodes of hypotension, GI/GU losses, history of GU instrumentation, comorbidities - liver disease, heart failure, chronic kidney disease; recent contrast exposure
- Exam: volume status, rash (for drug-related AIN), mental status
- Investigations:
 - Degree of AKI - trend in Cr, U/O
 - Complications of AKI - electrolytes, metabolic acidosis
 - Urine lytes, Urine microscopy
 - Renal ultrasound

Pre-renal and ATN are the most common causes for AKI. Thus, fluids and treating shock would be a good start with management. If in shock - should get a foley to measure output.

As our patients are sick, the question is often - does this patient need dialysis? A simple approach would be the same AEIOU acronym learned in medical school:

- Acidosis - shock
- Electrolyte disturbance - most particularly K and phosphate - ECG changes, cardiac arrhythmias, weakness

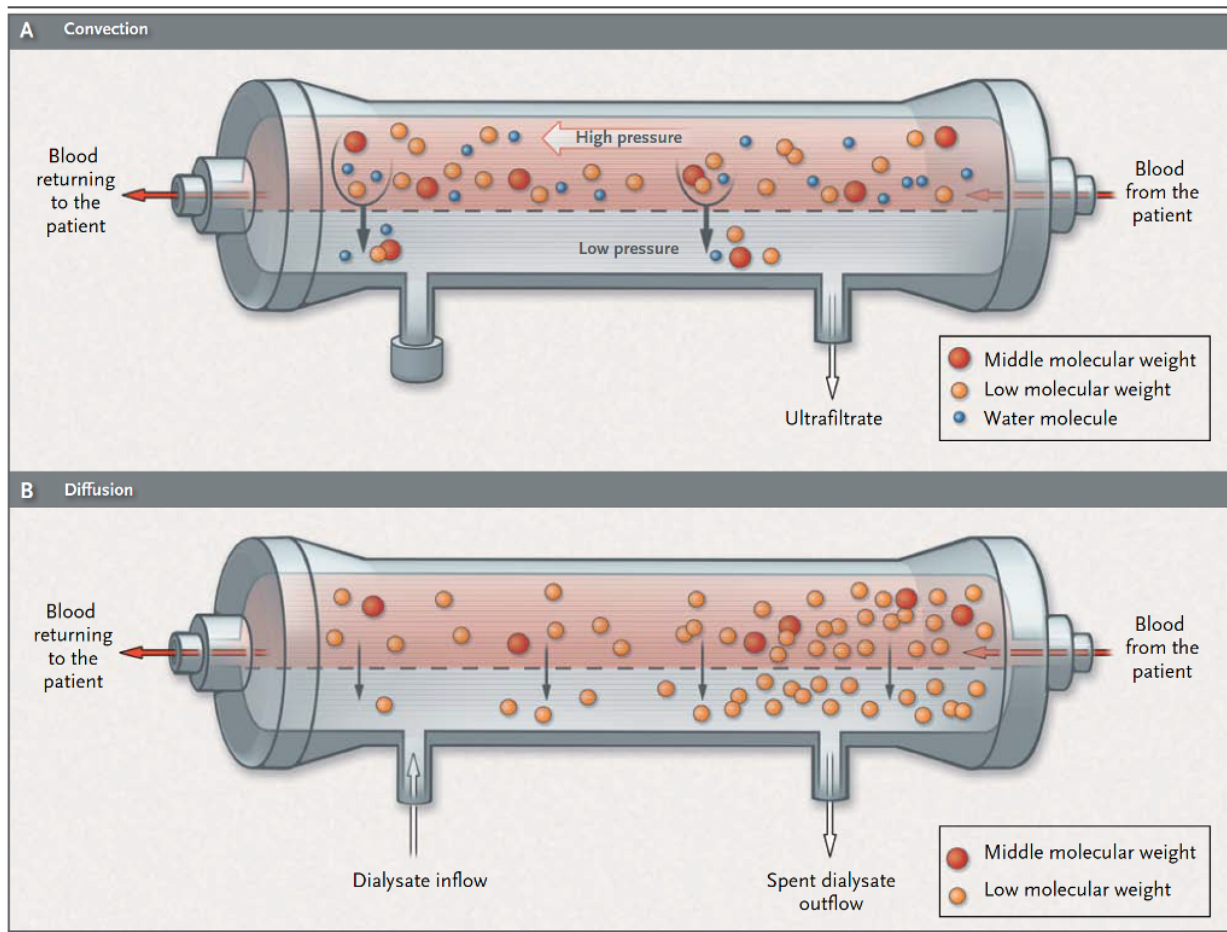
- Intoxication - e.g., salicylates, toxic alcohols, lithium, metformin, etc
- Overload - is there respiratory failure due to overload?
- Uremia - altered mental status

Renal Replacement Therapy:

- In most simplest forms there is 2 types: continuous renal replacement therapy (CRRT) and intermittent hemodialysis (IHD)

Dialysis or renal replacement therapy in the most simplest form removes solutes and/or fluid from the body in the way our kidneys are built to do.

3 basic mechanisms to achieve this:



Diffusion:

- Using dialysate to provide a concentration gradient to remove small molecules like creatine and urea

Convection

- Pushing fluid across a membrane to remove larger middle molecules via concept of solvent drag - e.g. myoglobin, cytokines and other inflammatory mediators
- Thought to be helpful in inflammatory mediated diseases like sepsis but so far no compelling evidence to prove is beneficial
- Requires replacement fluid which can be given pre-filter or post-filter

Filtration

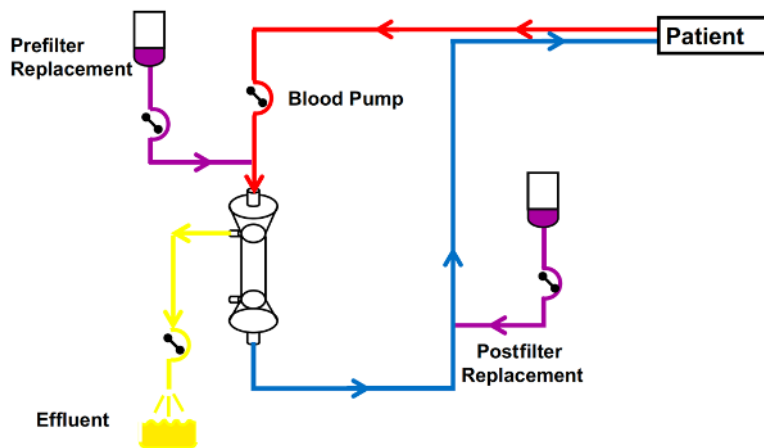
- Removing fluid
- Also known as “ultrafiltration”

IHD - works mostly with diffusion and filtration

CRRT can be provided in a variation of these modes:

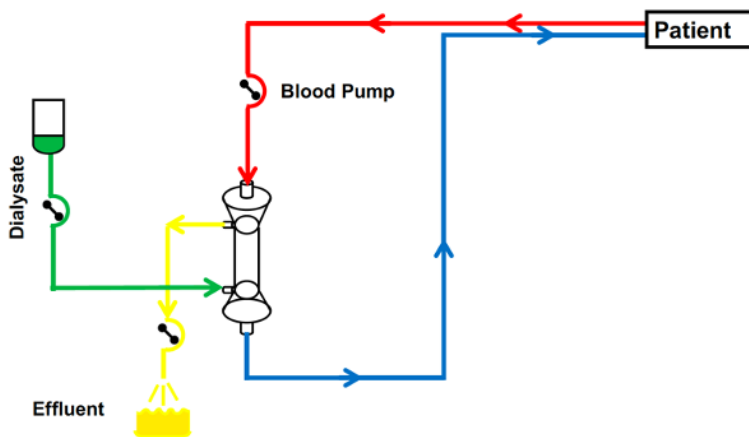
- CVVH = continuous venovenous hemofiltration
 - Mostly convection and filtration

CVVH

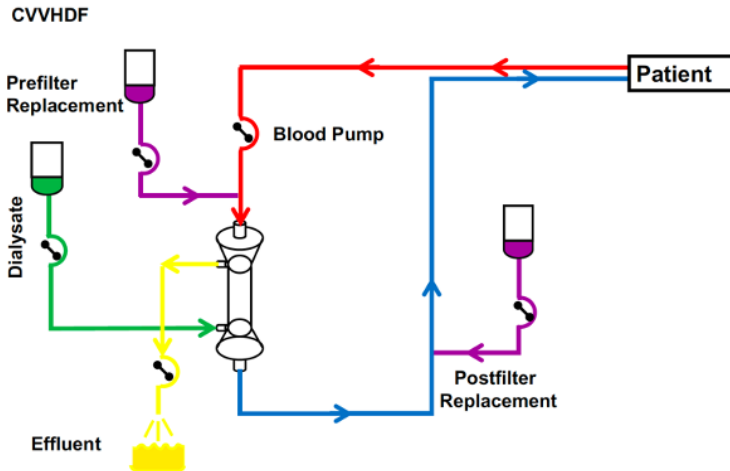


- CVVHD = continuous venovenous hemodialysis
 - Mostly diffusion and filtration

CVVHD



- CVVHDF = continuous venovenous hemodialysis filtration
 - Uses diffusion, filtration and convection
 - Most centres will use CVVHDF



CRRT is a slower, continuous form of dialysis and is more hemodynamically gentle than IHD. In the ICU, as most of our patients are in shock / on vasopressor therapy, they tend to be dialyzed by CRRT.

Having said that, there is no compelling evidence that use of CRRT over IHD has any clinical relevant difference in mortality or need for long-term dialysis (45).

	Pros	Cons
CRRT	<ul style="list-style-type: none"> Minimal less effects on hemodynamics Able to remove larger amounts of fluid (over a longer period of time) Can use convective forces to remove middle molecules (e.g. cytokines, myoglobin) 	<ul style="list-style-type: none"> Needs to be run in the ICU Citrate runs will have citrate-related side effects Tend to require anticoagulated runs More expensive Slower clearance and less effective Continuous runs; unable to mobilize patients Requires HD line
IHD	<ul style="list-style-type: none"> Does not need anticoagulation Can be run anywhere in the hospital Cheaper Faster and more effective at removing smaller solutes (e.g. hyperkalemia, toxic alcohols) Can use HD line or fistula 	<ul style="list-style-type: none"> Much more associated with hypotension Not well-tolerated in patients in shock Bigger fluid and solute shifts

How to prescribe CRRT:

- As mentioned we tend to use CVVHDF
- Before anything, the patient will need vascular access. Dialysis line insertion is the same as central line placements; the catheters are just larger (12-13 Fr vs CVC lines are 7-8 Fr)

- Best place to place an HD line is in the right internal jugular. It is a straight shot down to the right atrium. In most patients, a 15-16 cm to the R IJ will work.
- Second best place would be a R femoral line, third would be L femoral line. 20 cm.
- Tend to not place subclavian HD lines due to it being a less compressive site if there was any line misadventures and also associated with more subclavian vein stenosis which can compromise future viability of long term access issues
- After line placement, instill citrate within the line to prevent any clot formation with the line. The amount of citrate needed will be clearly displayed on the catheter (usually 1-3ml)
- Prescription of CRRT:
 - Most centers will have a PPO to make life easy for us:
 - First, decide on whether anticoagulation will be used:
 - We tend to anticoagulate at least the priming solution with heparin, minimal to none of this gets to the patient, the only patient you would consider to use zero anticoagulation would be a patient with an intracranial or spinal bleed.
 - We rarely fully anticoagulate patients these days to run CRRT. The advantage of anticoagulated runs is to prolong filter life, i.e. cost. Options are heparin vs citrate.
 - Some centres run citrate - citrate runs work well but there are side effects associated with citrate use.
 - Monitor citrate toxicity - calcium gap (total calcium / ionized calcium) > 2.5 - indicates citrate toxicity
 - Citrate binds to calcium, total calcium will increase and ionized calcium will decrease as citrate accumulates
 - The liver metabolizes citrate -> in liver failure, accumulation of citrate leads to metabolic acidosis
 - Citrate is metabolized into a base and leads to metabolic alkalosis
 - Electrolyte disturbances: hypocalcemia, hypernatremia, hypomagnesemia
 - At VGH, we tend to just heparinize the priming solution and run unanticoagulated CRRT.
 - If the filter tends to clot - I would recommend heparinizing the circuit.
 - Second, prescribing the "dose"
 - Studies found that the best dose would be 20-25ml/kg/hr
 - Studies found higher doses at 40ml/kg/hr (RENAL Trial 2009) did not show a mortality benefit (46)
 - How to distribute the dose:
 - We tend to use a 1:1 ratio between the dialysate dose and the replacement rate
 - The replacement rate is the split between pre-filter and post-filter.
 - The higher proportion pre-filter - prolongs filter life

- The higher proportion post-filter - provides additional concentration gradient, will increase post-filter proportion in hyperkalemia patients; usually default is 200ml
- Example: 70kg patient, 25 x 70 = 1750ml/hour -> round to 1800ml.
- 900 dialysate dose, 900 replacement dose; 700 pre-filter.
- Third decision is if you want to ultrafiltrate
 - What is your volume goal:
 - No fluid removal
 - Euvolemia, i.e. net zero
 - Fluid removal - target goal per hour vs per 24 hour.

Approach to Nutrition in the ICU:

Nutrition is important. We obviously don't have the capacity to feed our patients a daily delicious Mediterranean diet but we should do our best to treat and prevent malnutrition. About 75% of our patients are malnourished in the ICU where about 1/3 of these patients were already malnourished entering the ICU but most (2/3) become malnourished in the ICU admission. Why does this occur? ICU patients are hypermetabolic in their critical illness - higher energy expenditure, proinflammatory states, immobilization = increased muscle breakdown and muscle loss

How to feed our patients:

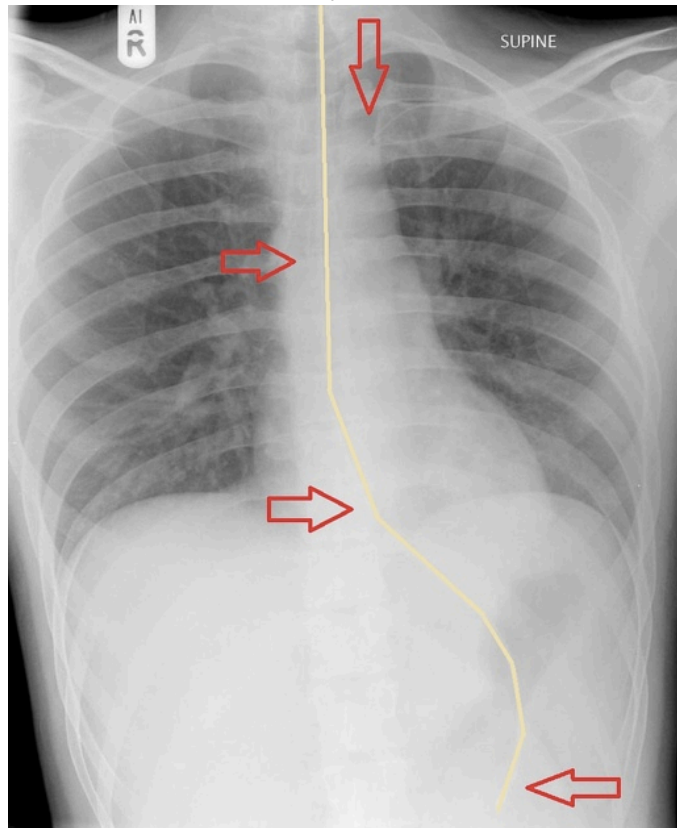
- Enteral vs parenteral

Enteral feeding:

- Use the gut!
 - Benefits of first pass metabolism at the liver, maintenance of GI structure and function
 - Very few contraindications to enteral nutrition exist:
 - Bowel obstruction
 - Bowel discontinuity
 - Ischemic bowel
 - Anastomotic leaks
 - Severe shock
 - Severe GI Bleeding
- Very few patients are eating by mouth in the ICU so the first thing is to obtain gastric access - this is often inserted by the nursing team. If one anticipates a longer need for mechanical ventilation, then inserting an orogastric tube (NGT) is associated with less risk for sinusitis. We often swap to a nasogastric tube (OGT) if anticipating extubation and need for immediate and reliable enteral access in patients who have been intubated for >24-48h. Otherwise, such patients can have a bedside swallowing assessment and if passed can just eat.

- **How to confirm OGT or NGT on abdo XRay:**

- 1) You want the tube BELOW the diaphragm.
- 2) Salem sumps are large bore gastric tubes and can feed and suction the stomach; on XRay, the radiopaque line is a thin line. While a feeding tube or “Entriflex” is smaller and can only feed. On XRay, the radiopaque line is thicker and has a weighted end at the end.
- 3) For Salem sumps, you want the proximal port, which is also 10cm from the distal end of the tube, and also indicated by a break along the radio-opaque line, to be at least 3 cm from the gastro-esophageal (GE) junction. This can be estimated where the L hemidiaphragm transects the midline.
- 4) For the Entriflex, you want the weighted port to be at least 3cm below the GE junction. There is no proximal port. Sometimes we may ask for the nasoduodenal tube (NDT) or post-pyloric tube where this tube is advanced deeper into the duodenum for patients who are having gastroparesis/high gastric residuals. This is confirmed by the distal end crossing midline and pointing downwards (i.e., in at least the second portion of the duodenum).



Prescribing enteral feeds:

- Here is a wonderful cheat-sheet created by our amazing dietician team at Vancouver General Hospital:

DETERMINING ENERGY REQUIREMENTS: CALORIE CALCULATOR

HOW TO USE: Determine goal feed rate based on patient weight. Standard formula is Isosource 1.0HP. Only choose Resource 2.0 or Novasource Renal if a fluid restriction is required and/or patient is receiving IHD. CRRT patients should receive Isosource 1.0HP. Use refeeding goal rate for malnourished patients.

PATIENT WEIGHT	GOAL CALORIES (25kcal/kg)	GOAL FEEDING RATE Isosource 1.0HP (mL/hr)	GOAL FEEDING RATE Resource 2.0 or Novasource Renal (mL/hr)	REFEEDING GOAL RATE (20kcal/kg) Isosource 1.0HP (mL/hr)
Less than 40kg	1000	40	20	30
41-50kg	1125	45	25	35
51-60kg	1375	55	30	40
61-70kg	1625	65	35	50
71-80kg	1875	80	40	55
Greater than 81kg	2000	85	45	65

MALNUTRITION AND REFEEDING SYNDROME: To prevent significant electrolyte and fluid shifts associated with refeeding syndrome, recommend initial goal feeding rate provide 20kcal/kg for patients suspected to be malnourished. Advance to goal (25kcal/kg) when electrolytes have been within normal limits for 24h.
SEVERELY MALNOURISHED PATIENTS: Initiate feeds at 25mL/hr and only advance to the refeeding goal rate (20kcal/kg) once electrolytes are repleted.

RISK FACTORS FOR MALNUTRITION
 Substance abuse
 NPO/suboptimal intake ≥ 5-7 days
 ≥ 10% weight loss over past 6 months
 Physical signs of malnutrition

ENTERAL NUTRITION FORMULARY

FORMULA	ISOSOURCE 1.0HP	RESOURCE 2	NOVASOURCE RENAL	ISOSOURCE 1.2	PEPTAMEN INTENSE
kcal/mL	1.0	2.0	2.0	1.2	1.0
% of calories from protein	25%	17%	18%	18%	37%
COMMENTS	-Standard feed for ICU admission -High protein -Appropriate for CRRT	-Fluid restricted -Quite low protein	-For stable IHD patients -Fluid restricted -Contains low levels of K and PO ₄ -Quite low protein	-For stable ward patients -Quite low protein	-Very high protein -Use during Propofol infusion to provide adequate protein without overfeeding calories

Originally developed by J. Greenwood, RD. Critical Care Program: VCHA – VA. Update Mar 2019

Parenteral feeding:

- This form of feeding is through the venous system. There are many types but TPN or total parenteral nutrition is the most common form and is done through a central line. There is peripheral PN but it is short term and only when central access is contraindicated.
- If one anticipates a patient will not have optimal enteral feeds within 3-5 days then TPN should be started, especially in patients who are already malnourished. Such patients will either receive all of their nutrition parenterally or supplemented with the enteral feeds
- Parenteral feeds do not come without risk. They are more associated with:
 - CLABSI (central line associated bloodstream infections)
 - Fungal infections
 - PNALD (parenteral nutrition associated liver disease) - cholestatic liver injury that can progress to cirrhosis
 - GI atrophy due to lack of stimulation
 - Bone disease
 - Metabolic complications:
 - Glycemic control
 - Electrolyte disturbances

- Hypertriglyceridemia
- How to prescribe TPN:
 - First obtain central access (see under ICU procedures), ideally feed through PICC or neck line
 - Normalize electrolytes. TPN should not be the means of replacing electrolytes.
 - Goal calories per day for ICU patients is about ~25-30kcal/kg; if malnourished, start at 20kcal/kg
 - General breakdown to be 20% of calories from protein, 30% from fat and 50% from carbs
 - Most simplest is to start standard solutions where you prescribe the kcal/day goal and the dietician can help during the weekdays to fine tune the other details
 - ASPEN has great resource on PTN dosing: <https://www.nutritioncare.org/clinicalguidelines/>

TABLE 1. MACRONUTRIENTS

Disease/Clinical Condition	Protein/Amino Acids (g/kg/d)	Total Energy (kcal/kg/d)	PN Component		
			Dextrose (mg/kg/min)	ILE* (g/kg/d)	Fluid (mL/kg/d)
Stable	0.8-1.5	20-30	4-5	1	30-40
Critically ill, trauma, sepsis	1.2-2.5	20-30	<4	<1	Minimal to provide adequate macronutrients
Different Amino Acid Requirements than Above	Protein Amino Acids (g/kg/d)	Total Energy (kcal/kg/d)			
Traumatic brain injury	1.5-2.5				
Burns	1.5-2				
Open abdomen	Additional 15-30 g/L exudate				
Acute kidney injury	0.8-2.0				
Continuous renal replacement therapy	Additional 0.2 g/kg/d not to exceed 2.5 g/kg/d				
Chronic kidney failure with maintenance hemodialysis	1.2				
Hepatic failure	1.2-2 (based on "dry" weight and tolerance)				
Obese	2-2.5 (based on IBW)	22-25 (based on IBW)			

IBW = ideal body weight

*Soybean oil-based emulsion. For indications and dosing of other lipid injectable emulsions (ILE), see manufacturer's product literature.

TABLE 2. ELECTROLYTE AND MINERAL

Nutrient	Standard Daily Requirement	Factors That Increase Needs
Calcium*	10-15 mEq	High protein intake
Magnesium	8-20 mEq	GI losses, medications, refeeding
Phosphorus*	20-40 mmol	High dextrose intake, refeeding
Sodium	1-2 mEq/kg*	Diarrhea, vomiting, NG suction, GI losses
Potassium	1-2 mEq/kg*	Diarrhea, vomiting, NG suction, GI losses, medications, refeeding
Acetate	As needed to maintain acid-base balance	Renal insufficiency, metabolic acidosis, GI losses of bicarbonate
Chloride	As needed to maintain acid-base balance	Metabolic alkalosis, volume depletion

TABLE 3. DAILY REQUIREMENTS FOR ADULT PARENTERAL VITAMINS*

Vitamin	Standard Daily Requirement
Thiamin (B ₁)	6 mg
Riboflavin (B ₂)	3.6 mg
Niacin (B ₃)	40 mg
Folic acid	600 mcg
Pantothenic acid	15 mg
Pyridoxine (B ₆)	6 mg
Cyanocobalamin (B ₁₂)	5 mcg
Biotin	60 mcg
Ascorbic acid	200 mg
Vitamin A	990 mcg
Vitamin D	5 mcg
Vitamin E	10 mg
Vitamin K	150 mcg

* Prescribe full daily dose unless patient able to ingest and/or absorb orally/enterally. Full dose of most multivitamin products available in the US provides the above requirements.

TABLE 4. DAILY REQUIREMENTS FOR ADULT PARENTERAL TRACE ELEMENTS*

Trace Element	Standard Daily Requirement
Chromium	≤10 mcg
Copper	0.3-0.5 mg
Manganese	55 mcg
Selenium	60-100 mcg
Zinc	3-5 mg

* Prescribe full daily dose unless patient able to ingest or absorb orally/enterally. Note: These requirements are different than the multi-trace element products currently available in the US.

Refeeding syndrome:

- common in the ICU and potentially life-threatening so here's a quick review:
 - Refeeding occurs when malnourished patients are abruptly fed -> reintroduction of carbs especially leads to the cellular uptake of glucose and electrolytes -> hypokalemia, hypophosphatemia, hypomagnesemia, thiamine deficiency, fluid and sodium retention
 - Risk factors:
 - Alcoholism, drug abuse
 - Reduced nutritional intake for at least 5 days
 - Weight loss
 - GI compromise/malabsorption - e.g. Crohn's, CF

Gastric residuals:

The traditional concern with high gastric residuals (HGR) was the risk of vomiting and aspiration however the evidence behind HGR and aspiration is poor. In fact some centers have abandoned checking them at all. Unfortunately this movement is still new and as you know, culture is difficult to break in medicine.

Here are some tips on how to troubleshoot high gastric residuals:

- 1) How much - > 250ml is concerned "high"
- 2) Examine the patients - is there concern for mechanical obstruction? Palpate the abdomen, presence of bowel movements, flatus, etc
- 3) If no concerns of mechanical obstruction - gastroparesis is common - start metoclopramide at 10 mg IV q6h (NB: will need to adjust dose if renal impairment) x 4 doses; next prokinetic would be erythromycin at 250mg IV q12h x 2 doses
- 4) If still high residuals - obtain flat plate to assess for obvious obstruction but more commonly if you see gas throughout and some dilated loops, this is ileus and prokinetics will unlikely work.
- 5) In such case of ileus, treat causes for ileus (drugs, electrolytes, immobilization, etc) and try to NDT

Common Procedures in the ICU:

Procedures can be "fun" but come with risk to the patient as well as the operator. Please do your part by educating yourself as much as possible prior to performing a procedure and ALWAYS ask for help if you are ever not familiar/comfortable.

Great resources and videos exist. I like the NEJM website for videos:

<https://www.nejm.org/doi/full/10.1056/nejmvcm044149> - arterial line

<https://www.nejm.org/doi/full/10.1056/nejmvcm055053> - central line

<https://www.nejm.org/doi/full/10.1056/nejmvcm071974> - chest tube placement

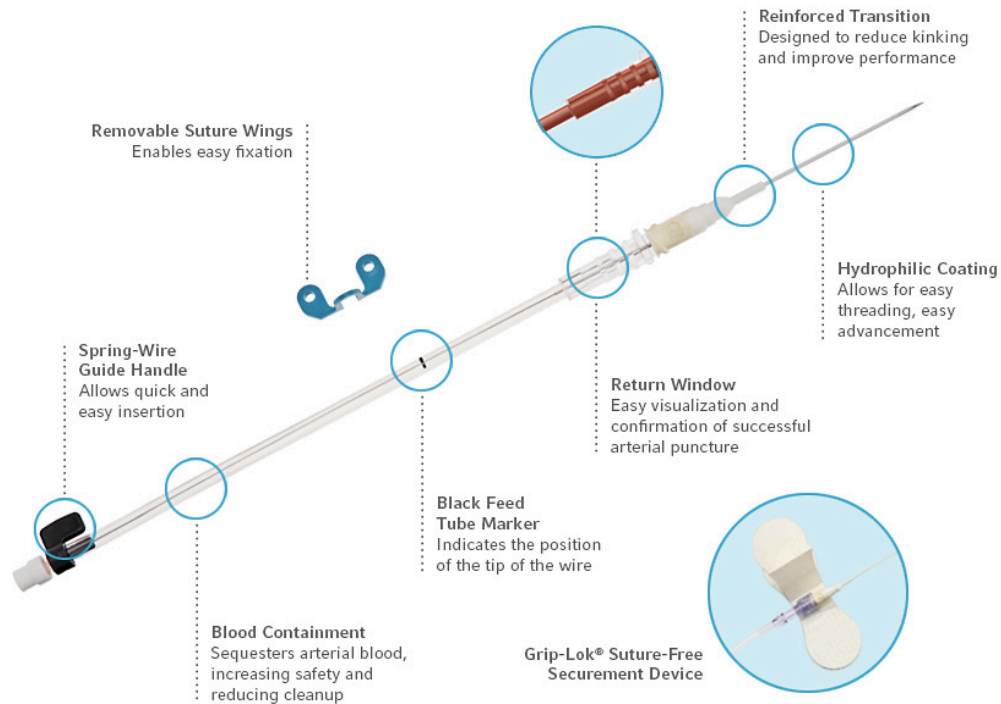
<https://www.nejm.org/doi/full/10.1056/nejmvcm053812> - thoracentesis

Arterial line access:

- Sites: radial (1st choice), femoral, brachial
- Radial and femoral sites can be performed blindly but +++ preference is to use ultrasound to limit attempts unless experienced with palpation method. More attempts = more bleeding = more risk of arterial injuries (e.g. hematomas, pseudoaneurysms)
- Indications:
 - Blood draws - can do them for diseases like severe DKA that require frequent blood draws.
 - Hemodynamic monitoring - in general, patients persistently on vasopressors should have an arterial line
 - ARDS / severe respiratory failure - for frequent ABGs

Radial artery:

- Most centers have Arrow kits where there is a catheter with a needle and wire as a unit (see below)
- Best to perform an Allen's test prior to cannulation to ensure there is adequate collateral flow to the hand. Most people are ulnar dominant or have adequate collateral flow and thus cannulating the radial artery should not compromise perfusion to the hand.



- **Tips:**
 - Cannulate the artery more proximal when using ultrasound; the artery straightens, travels medially and deeper proximal towards the arm
 - Cannulation by palpation is easier more distally as the artery is more superficial and more palpable
 - Once you achieve flash, drop your angle slightly, thread the wire through and pass the catheter gently to cannulate
- Important to suture the line and please perform this procedure in a sterile fashion. ICU arterial lines can be used for potential weeks vs hours in the OR.

Femoral artery:

- Some centers have their own kits but easiest is to use a single lumen CVC kit. Cannulate the artery in the same fashion you would cannulate a femoral vein. **LIMIT** pokes as this increases the risk of a formation of a pseudoaneurysm or retroperitoneal bleed.
- Do NOT dilate the artery as you would for a central line. Otherwise the procedure is the same.

Brachial artery:

- Please do not attempt this site blind. Please use ultrasound. There are many vital structures within the antecubital fossa including the median nerve.

- Unless the patient is very thin, Arrow kits will not work for the brachial artery as the catheter is not long enough. You can often obtain a brachial arterial kit in the OR.
- This site is the least preferred site in the ICU as it requires the patient to keep their arm extended as the cannulation is often right at the antecubital fossa. Furthermore, the brachial artery is the single artery for perfusion to the rest of the arm and has higher rates of distal ischemia.

Central Line Placement:

Site:

- Internal jugular (1st choice), femoral, subclavian
- There is a review for central line complications in the ICU (NEJM 2015) that found that subclavian lines are associated with the lowest rates of infection but there are higher rates of pneumothoraces (47). The major caveat to this article is that the physicians performing the subclavian lines had performed hundreds. Nearly all residents coming through the ICU have not. I would advocate residents to use ultrasound and safely place internal jugular and femoral central lines. Subclavian lines are traditionally placed blindly and can be facilitated with ultrasound but in general are trickier lines to place and the more inexperienced the more association with hematoma and pneumothoraces. Subclavian site is more difficult to compress due to the existence of the clavicle.

Various types of central lines and indications:

- Cordis (7, 8.5Fr) catheters: *note French or Fr size is #/3 = mm width
 - o massive transfusion
 - o TVP placement (7Fr) - transvenous pacing; 8.5Fr for PA catheter
- Triple lumen (7Fr) catheters:
 - o Transduce CVP
 - o Draw blood
 - o Administer hyperosmolar / irritating / vasoactive drugs – e.g. CaCl, hypertonic saline, 10% dextrose infusions, chemo, vasopressors
 - o Reliable vascular access
 - o TPN
- Dialysis (e.g. Niagara) 12.5 Fr
 - o For renal replacement therapy, plasma exchange (PLEX)
- Pulmonary artery (PA) Catheter aka Swan-Ganz
 - o For hemodynamic monitoring usually in the setting of severe mixed shock – less down now due to availability of cardiac ultrasound

Internal Jugular vein:

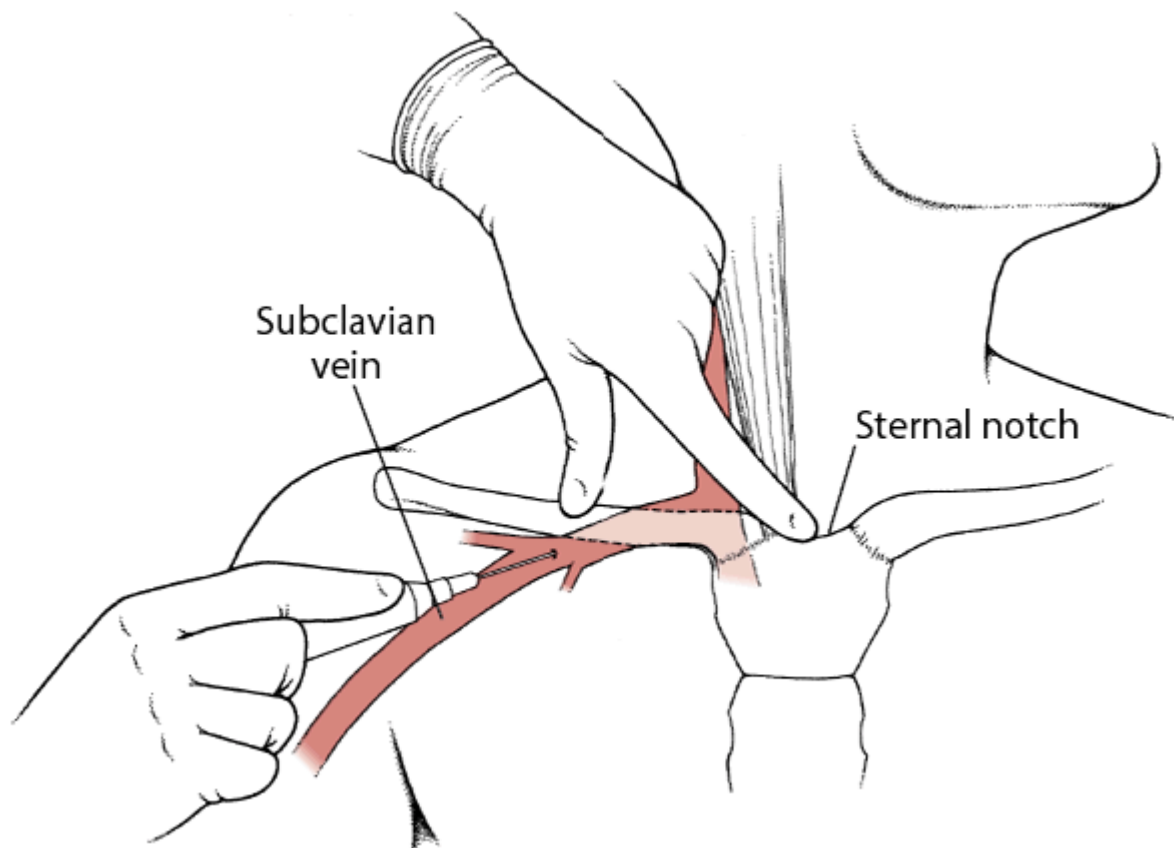
- Use a 16cm for the right IJ; 20cm for the left IJ
- supine/trendelenburg with head rotated away from placement
- Landmarks: between the two bellies of the sternocleidomastoid muscles, traditionally if blind is to aim the needle towards the ipsilateral nipple
- Ultrasound: identify the carotid artery (medial), and the lung

- with aspiration of venous blood, advance wire, dilate, thread catheter, wire out, aspirate and flush catheter, secure device with sutures and dressing

Femoral vein:

- Use a 20 cm for either side; 16cm is OK too
- Supine with ipsilateral leg slightly abducted and externally rotated
- Landmarks: Palpate the artery at the inguinal crease; NAVY - vein is medial to the artery, aim towards the umbilicus
- Ultrasound: identify the femoral artery and the vein is medial to it
- with aspiration of venous blood, advance wire, dilate, thread catheter, wire out, aspirate and flush catheter, secure device with sutures and dressing

Subclavian vein (infraclavicular approach):



- Use a 20cm catheter for either side
- Position:
 - o supine/Trendelenburg
 - o head neutral / rotated away from placement side
 - o arm adducted
 - o troubleshooting: roll/bump under ipsilateral shoulder or caudal arm traction -> get humeral head out of the way
- landmarks: deltopectoral groove (part of clavicle that curves back) or 1cm lateral and inferior to midclavicular line, sternal notch

- advance with needle aspiration technique, bevel aimed caudally, keep needle horizontal and parallel to avoid lung
- advance needle towards sternal notch
- maximize 3 attempts, if unable to cannulate, ensure flush needle of clots, try with needle tip more superior and deeper
- with aspiration of venous blood, advance wire, dilate, thread catheter, wire out, aspirate and flush catheter, secure device with sutures and dressing

Confirmation of CVC:

- o Transduce a venous waveform
- o Venous blood gas - pay more attention to PO2
- o Chest XRay – tip should be in sinoatrial junction (for IJ and subclavians)
 - Roughly at the right mainstem bronchus / level of carina

Complications:

- Puncturing artery
- Hematoma
- Retroperitoneal hematoma (for femoral lines)
- Catheter-related thrombosis
- Pseudoaneurysm
- Pneumothorax (1.5-3.1%) (for neck lines)
- Hemothorax (for neck lines)
- Infection – local vs systemic
- Air embolism (for neck lines)
- Dysrhythmia - PVCs to VT if wire/catheter in RV (for neck lines)
- Wire lost
- Allergy – most catheters are impregnated with sulfa
- Malposition
- Chylothorax (Left subclavian only)
- Brachial plexus injury (for subclavian only)

Tube Thoracostomy

- Seldinger vs open
 - In general seldinger or pigtail insertion is more suitable for pleural effusions or large pneumothoraces
 - For traumatic hemothoraces, traditionally better to place large bore chest tube via open method but there is increasing trauma literature that states traumatic hemothoraces can be drained with pigtails
 - Small to moderate pneumothoraces are best drained especially if patient is on positive pressure ventilation - open method is better as the window for needle insertion is often difficult to identify and open method is safer.

Indications:

- Diagnostic – new pleural effusion NYD

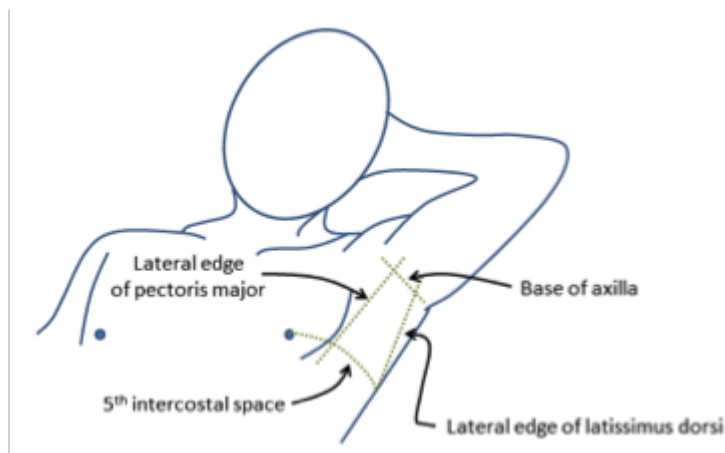
- Therapeutic:
 - to improve oxygenation and ventilation
 - symptomatic
 - tension HTX or tension PTX – to improve hemodynamics
 - drain fluid – blood and pus always need to be drained; serous fluid if recurrent from CHF/renal failure/malignancy/liver failure – do not always need to get drained as they tend to just reaccumulate
 - drain air:
 - traumatic PTX – drain if:
 - also contains blood/fluid
 - can observe if small
 - spontaneous PTX – drain if:
 - small + significant symptomatic (usually will be large)
 - small + growing despite medical therapy (i.e. oxygen)
 - large: > 3cm from apex or >2cm from hilum
 - recurrent + will need inpatient workup and management
 - requiring air transport
 - bilateral
 - requiring positive pressure ventilation

Contraindications:

- NO absolute
- Relative:
 - Overlying cellulitis
 - Coagulopathy
 - Pleural effusion not safely amenable to drainage – e.g. too small, loculated

Chest tube size selection:

- Air only: 8-14Fr (pigtail)
- Serous fluid: 8-14Fr (pigtail)
- Blood: open method 24-36Fr
- Pus: 24-32Fr (but can put 12-16Fr - can get these larger pigtails from IR)



Seldinger Technique:

- Position:
 - o Sitting up leaning onto table = best for thoracocentesis via posterior approach
however not realistic in acutely ill patients or if the tube is to stay in a bedbound patient
 - o Semirecumbent in otherwise all other patients
- Steps:
 - o Equipment: I usually grab single lumen CVC kit plus the catheter set, pleur-vac, 3 way stopcock, lidocaine, sterile prep, PPE
 - o Position patient
 - o For fluid, identify best pocket, mark skin
 - o For air, use the triangle of safety
 - o Sterile prep
 - o Anesthesia: anxiolysis with midazolam, analgesia with fentanyl, +++ local with 1-2% lidocaine with epi (generally don't need dissociative ketamine)
 - o 18G long needle connected 10ml syringe – keep needle perpendicular to skin, go over rib to avoid NV bundle
 - o Aspiration of fluid / air, disconnect syringe and thread wire
 - o Seldinger method for catheter placement; to avoid kinking of wire, catheter should be placed with rigid introducer
 - o Connect tubing to pleur-vac, usually to suction (may want to drain slower if chronic effusion)
 - o Get post-procedural CXR to confirm placement
 - o Clamp at 1.5L for pleural effusion to avoid re-expansion pulmonary edema

Complications:

- Pneumothorax (up to 11%)
- Hemothorax
- Liver/spleen/diaphragmatic injury
- Empyema/Infection
- Tumour seeding
- Re-expansion pulmonary edema
- Pain and cough more common but benign

Open Technique:

- Equipment: Needle and syringe for lido with epi, sterile prep, jelonet/polysporin, dressing tape, gauze, Chest tube tray, chest tube, pleur-vac, 0 silk suture, tape, PPE
- Position patient
- Go for triangle of safety
- Sterile prep
- Anesthesia: anxiolysis with Midazolam, analgesia with Fentanyl, +++ local with 1-2% lidocaine with epi (generally don't need dissociative ketamine)
- Prep tube with Kellys proximally and distally, estimate length at which to advance to tube
- Vertical incision
- Blunt dissection manually with your finger and/or with Kellys

- Enter pleural space with Kellys – go over the rib to avoid NV bundle
- Once in pleural space – gush of air/blood -> open Kellys to open up space created
- Use finger to sweep and bluntly dissect any adhered lung
- Advance tube into pleural space – for PTX – aim for apex, for HTX aim for bases -> misting of air /blood drainage helps confirm entry to pleural cavity
- Secure tube with suture with 0 silk – purse string/horizontal mattress, sandialing
- Unclamp distal Kelly from tube and connect to pleur-vac
- Polysporin dressing + gauze + Tape
- CXR to confirm placement

How to check for air leak:

- If bubbling = air leak
 - o If stops with clamping -> patient source; if continues to leak -> system source
- If increasing / persistent / large air leak – concern for bronchopleural fistula



Airway:

- Back to basics. ABCs start with A and B. There is no B without A.
- There is much more to airway besides intubating a patient.

There are many ways to provide an airway to patients. In spontaneously breathing, awake patient you may not need to provide an airway but in a decreased LOC patient you can provide an airway via:

- Nasopharyngeal airway (NPA)
 - How to size: to use the width of the patient's nostril to the size of the NPA catheter and tip of nose to angle of jaw
 - In general, well-tolerated as it avoids triggering the gag reflex as an oropharyngeal airway (OPA) would
 - Caution in coagulopathic patients as it can cause epistaxis, making your airway problem much more challenging...
- Oropharyngeal (OPA)
 - How to size: estimate by angle of jaw to the corner of the mouth
 - Caution in using as can stimulate gag and induce vomiting in patient who is already decreased LOC

- Often used as temporary airway to facilitate bag mask ventilation
- Airway maneuvers to improve airway patency:
 - Jaw thrust
 - Head tilt

Bag Mask Ventilation (BMV):

This is a very important skill to provide. This is basic life support. Outside of anesthesiologists and the operating room, we lose this skill as our RTs often provide this support. In a code or in a crashing patient who has lost their airway or not effectively oxygenating and/or ventilating, we may need to bag the patient until a definitive airway is secured.

Ways to optimize BMV:

- 2 person technique - 1 person to focus on jaw thrust and mask seal, 1 person focus on bagging
- Use OPA to displace soft tissue/tongue
- Jaw thrust and mask seal - using fingers to lift jaw, and thenar eminence and thumbs to provide mask seal:



- When bagging, look for chest rise, ventilate 1 breath every 3-5 seconds, make sure to give time for expiration. In critical situations, we tend to bag big volumes and quickly and can easily breathstack the patient by overbagging as well as overinflating the stomach increasing the risk of aspiration

Predictors of difficult BMV:

MOANS:

- Mask seal (bearded patients, male, high mallampati)
- Obstruction/obesity
- Age > 55
- No teeth
- Stiffness - burns, obstructive lung disease

Indications to intubate a patient:

- Failure to protect airway
 - Decreased LOC, usually set at an arbitrary of GCS < 9 but more important to consider is the loss of airway protective reflexes - e.g. gag, cough, swallowing; as well as the trajectory and course of illness of the patient. For example, a drunk person with a GCS of 3 but spontaneously breathing with preserved cough and gag may not necessarily need to be intubated, versus a found down, obstructing airway patient.
 - In the ICU, we often have to intubate patients for “bronchopulmonary toileting”, and our airway are made of tubes and can be analogous to plumbing - unable to handle secretions, such tubing becomes obstructed, leading to desaturation and hypoventilation
- Failure to oxygenate
 - Traditionally set of PaO₂ < 70 mmHg despite supplemental oxygenation
 - Failure to improve after non-invasive ventilation
 - Traditionally RR > 40 but I think of this more of severe shock and/ or severe work of breathing; for example a patient with severe metabolic acidosis but adequately compensating, i.e. a patient in DKA who is not in shock or have underlying lung disease/injury, does not need intubation and in fact, intubation may potentially harm the patient as we often unable to match the human body’s ability to ventilate.
- Failure to ventilate
 - Traditionally set of PaCO₂ > 55 mmHg
 - Failure to improve after non-invasive ventilation
 - Neurological/neuromuscular disease entities, mostly derived from pediatric GBS literature use 20/30/40 rule - Vital capacity < 20ml/kg; Maximal inspiratory pressure of < 30cmH₂O and maximal expiratory pressure of < 40 cmH₂O
- Anticipated clinical course
 - Good example is polytrauma patient who will need OR - intubating early and take control, allow for sedation for multiple procedures - e.g. vascular access, chest tubes, splinting, etc

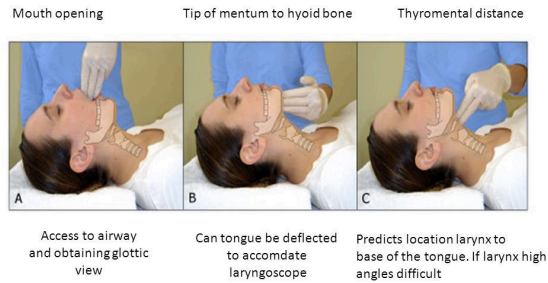
Predictors of difficult airway:

LEMON:

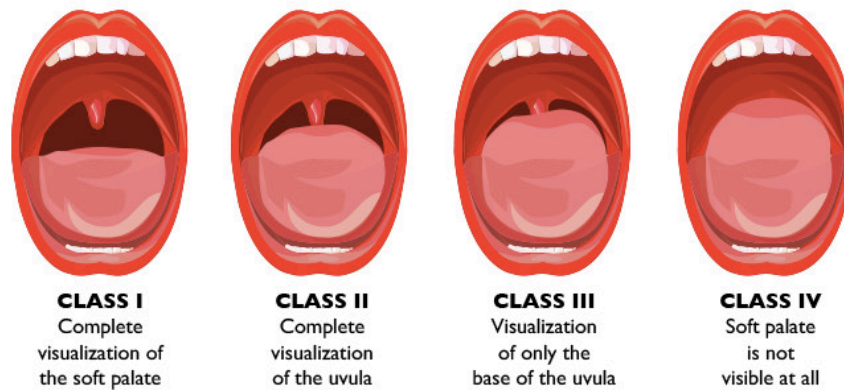
- Look externally - gestalt, facial trauma/bleeding
- Evaluate - 3-3-2 - 3 fingers for mouth opening, 3 fingers for hyo-mental distance, 2 fingers for thyro-hyoid distance

- Mallampati: 3 or higher; honestly hard to measure in our patients in ICU, a lot of them are too sick to perform this; but in general, you are looking for mouth opening and size of tongue
- Obstruction and obesity
- Neck mobility - hx of c spine fixation, c spine instability - trauma, RA, Trisomy 21

Assessment for Difficult Intubation: Evaluate: 3-3-2 Rule



The Mallampati Score

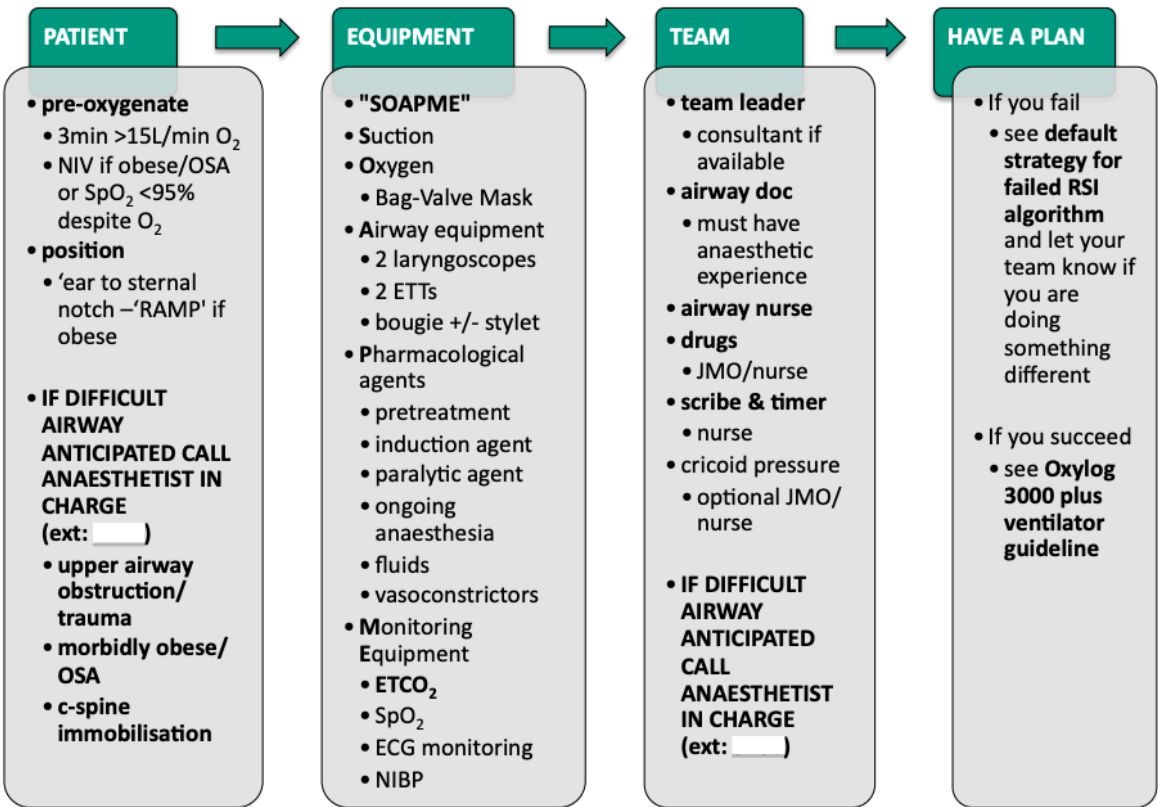


Preparation prior to intubation:

- Equipment! Use a checklist (see below)
- Preoxygenation - NRB, BiPAP, HFNC are good options
- Apneic oxygenation ideally with NP
- Position the patient! Pillows/towels/blankets to position the patient into sniffing position - tragus over sternum, head slightly extended; obese patients ramped up head up to displace soft tissue of neck, chest and abdomen



RAPID SEQUENCE INDUCTION CHECKLIST



modified from www.safetyintubation.com

Medications for intubation:

In the ICU, for the most part, we perform some form of Rapid Sequence Intubation (RSI).

Key concepts for RSI are following:

- Preoxygenation is VERY IMPORTANT. Apply 100% FiO2 for at least 3 minutes - either through NRB, HFNC or BiPAP. Maximize your preoxygenation to avoid hypoxemia peri-intubation.
- The assumption that patients are not fasted and at risk for aspiration. For the most part, avoid bagging the patient and traditionally apply cricoid pressure but these two rules are no longer emphasized

- Drugs are administered in a rapid sequence - induction and then paralytic.
- Avoid RSI without help of anesthesia if patient has predictors of difficult airway
- Patients in the ICU are often sick/unstable - have norepinephrine infusion ready and in-line to the patient. If the patient has a normal BP, they will become hypotensive upon induction and positive pressure ventilation. Have norepinephrine started or have phenylephrine given with induction or ready to push - 100-200mcg IV bolus.

Induction agents:

- We largely use ketamine in the ICU due to the properties being more hemodynamically friendly (compared to propofol, midazolam)
 - Dose: 0.7-1mg/kg IV; use lower dose if more altered/unstable patient
 - Historically associated with increased ICP but this has been debunked.
- Etomidate is also hemodynamically friendly
 - Dose: 0.3mg/kg IV; can also half dose if more altered/unstable
 - Associated with adrenal insufficiency but no real data to suggest clinical significance

Paralytic agents:

- Rocuronium
 - Largely used in ICU/ER
 - Dose: 1.2mg/kg IV
- Succinylcholine:
 - 1-2 mg/kg IV
 - Contraindicated in:
 - Hyperkalemia
 - Hx of malignant hyperthermia
 - Recent denervation (> 5 days) - stroke, spinal cord injury
 - Neuromuscular disease/myopathies
 - Intraabdominal sepsis > 5 days
 - Burns > 10%
 - Crush injury
 - ^^ All these disease states result in receptor upregulation at postsynaptic membrane and can lead to massive K efflux with administration of succinylcholine

Post-intubation care:

- CONFIRM ETT - ETCO2 and CXR for placement
- Optimize hemodynamics - norepinephrine, central line placement PRN
- Post-intubation sedation - start with propofol 0-80mcg/kg/min
- Ask RN to place gastric tube - ask early especially with patient has been working hard for a while or any bagging as performed - the stomach is often filled of air and at risk for a massive emesis

Direct/Mac Laryngoscopy (DL) technique:

- Size of blade: 3 for women/smaller patients, 4 for men/taller patients
- Size of tube: 7-7.5 for women/smaller patients, 7.5-8 for men/taller patients
- Check your light ALWAYS

- Use the laryngoscope with your left hand, advance the blade along the soft palate, careful not to cut the palate as the blade is relatively sharp, lift and sweep the tongue left, identify the epiglottis, advance the blade into the vallecula and lift to provide a view of the glottis (i.e. vocal cords)
- Your view of the glottis can be described as the Cormack-Lehane grading:



Grade 1 View

Grade 2 View

Grade 3 View

Grade 4 View

- Take your STYLETED tube (the ICU is generally not a place for unstyletted tubes) - advance the tip through the cords, then ask the helper/RT to withdraw the stylet 2-3cm, advance more until the cuff is beyond the cords, then withdraw the stylet 2-3cm or fully out, and advance the tube until the cords are between the 2 black lines of the ETT. In generally this will provide adequate distance but can do 3x the ETT size as a general estimate



Video laryngoscopy (VL) technique:

- Many different models:
 - Glidescope: traditionally designed with a hyperangulated blade built to limit need to lift and to improve glottic views in patients with anterior airways; now there are Mac blades available as well
 - C-Mac: a Mac blade with a video at the tip of the blade, also comes with hyperangulated blade
 - McGrath: portable version of Mac blade with video; also comes with hyperangulated blade
 - King Vision: portable version of hyperangulated blade
- Video laryngoscopy has shown to be superior in providing a better glottic view however the evidence behind improving 1st pass success is not as robust. In general, video is most helpful for learners as it provides a view for everyone to see and allows the

supervisor to help troubleshoot the learner. It also requires less lifting and displacement skills as one needs for DL.

- As one often will get a full glottic view or “grade 1 view” with VL, the challenge is often passing the tube. The more anterior the airway, the more challenging this can be.

Some tips:

- Pull the blade back to make your view less ideal but gives you more space to maneuver the tube
- Rotate the tube 90 deg clockwise, so you coming along the side
- Can try using a bougie to get into the airway first and railway the ETT over after

Rescue airways:

- There will be situations, hopefully not too often, where you are unable to intubate. These situations should be anticipated and avoided at all costs. Rescue airways are devices placed supraglottically until a definitive airway can be placed. If you are using a rescue airway, anesthesia/help should be already on their way/paged. Examples include:

- LMA (laryngeal mask airway)
 - Size 3 for women, 4 for men/larger people
 - How to place - lubricate the tip and insert. Inflate the cuff slightly to optimize seal
- Igel
 - Largely replacing the LM
 - Does not need to inflate cuff
 - Size 4 for a 50-90 kg person. Literally insert.

Predictors to difficult supraglottic airway:

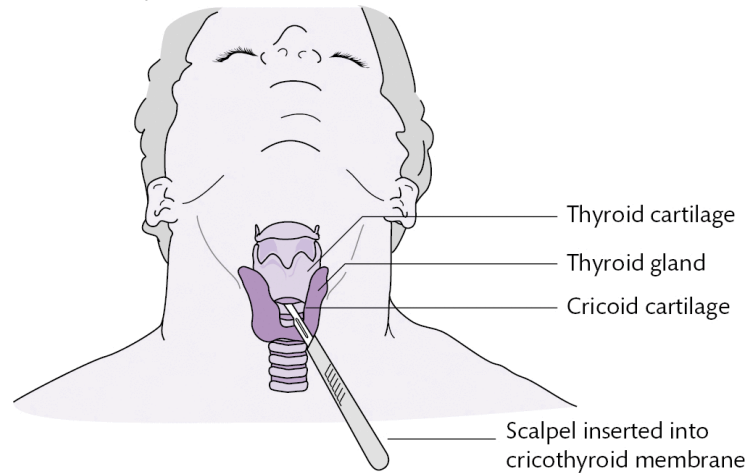
- RODS
 - Restricted mouth opening
 - Obstruction / obesity
 - Distorted anatomy
 - Stiffness - lungs

Surgical airway:

- This is a scenario where all of the above is failing.
- Easiest way to perform emergent surgical airway is via open technique, scalpel + boogie.
- Technique:
 - Palpate the thyroid cartilage, i.e. “Adam’s apple” in men. There should be a dip and then another firm structure should then be the cricoid cartilage. This is the structure you push posterior when one would provide cricoid pressure traditionally in a non-fasted RSI scenario (though we don’t tend to do so anymore as there is no evidence it prevents aspiration and often does not actually occlude the esophagus and just interferes with the view.
 - The soft dip between the thyroid cartilage and cricoid cartilage is the cricothyroid membrane. Make a vertical incision and use your finger to bluntly dissect to the membrane. Then make a horizontal incision through the membrane and then a

vertical incision. Place your finger through the incision and place a bougie into the airway until you feel resistance. Feeling resistance confirms entry into the trachea and onto the carina (vs esophagus you would not feel resistance).

- Railway a #6 ETT over, inflate the cuff, ventilate and secure the airway. ENT should be consulted as upon stabilization, the patient should be taken to the OR for a definitive airway - either converted back into oral ETT or tracheostomy (often the latter).



Predictors of difficult surgical airway:

- SMART
 - Surgery - recent surgery to neck area
 - Mass - mass to the area
 - Access/Anatomy - e.g. scarring, edema, obesity, SC emphysema
 - Radiation - previous radiation to neck area
 - Trauma

Methods to confirm airway:

Reliable:

- ETCO₂ / capnography
- Direct visualization
- Ultrasound

Not reliable:

- Auscultation of chest / abdomen
- Misting of the tube
- Chest XRay
- O₂ saturation

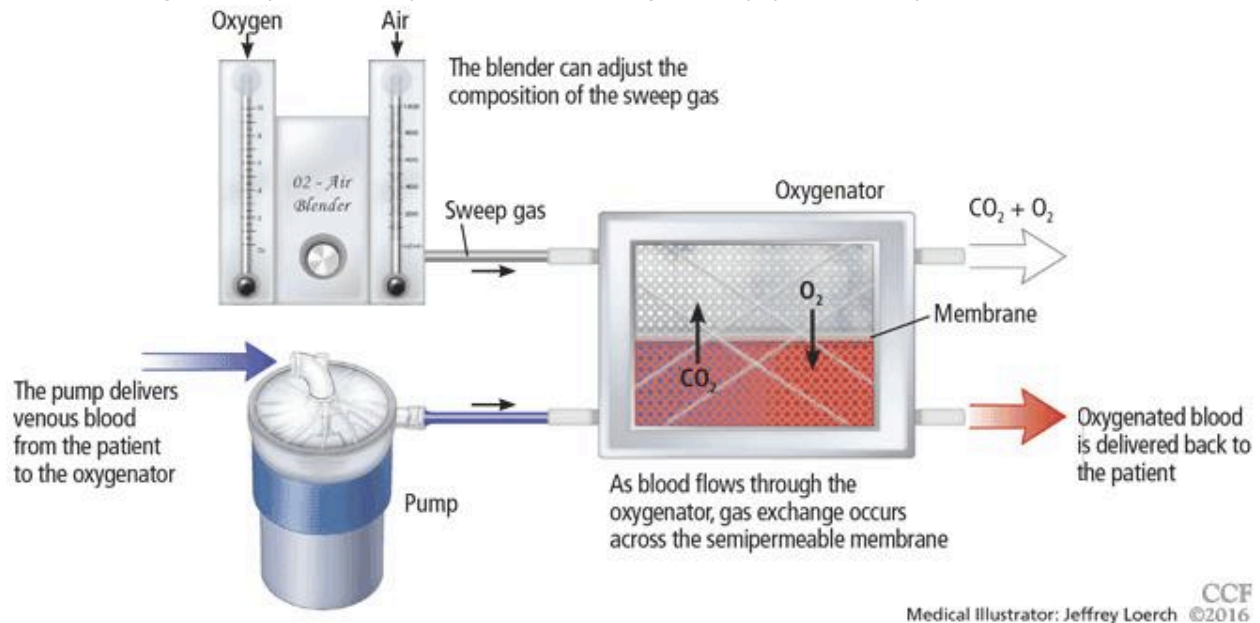
An Introduction to ECMO

Resources:

- LIFTL, Deranged Physiology have great pages on ECMO
- ELSO website: <https://www.else.org/ecmo-resources/elseo-ecmo-guidelines.aspx>
- An excellent intro video by Dr. Thiara (VGH ICU) <https://vimeo.com/511319172>

What is ECMO:

- Extracorporeal membrane oxygenation
- Set up involves an access cannula that drains venous blood, connected to tubing that takes the blood through a centrifugal pump which then pumps blood through an oxygenator that oxygenates blood and removes CO₂ and then pumps it back either into a large vein (VV-ECMO) or back into a large artery (VA-ECMO)



ECMO is a method of life support that acts as a bridge to recovery, longer term support device (e.g. LVAD for cardiogenic shock), or transplant.

2 types:

- **Veno-arterial ECMO (VA-ECMO)**
 - Provides circulatory support
 - **Indications:**
 - Refractory severe cardiogenic shock due to (not an exhaustive list):
 - Acute coronary syndrome
 - Arrhythmia
 - Drug toxicity
 - Myocarditis
 - Pulmonary embolism
 - Trauma
 - Post cardiac surgery - unable to wean off cardiopulmonary bypass
 - Chronic cardiomyopathy
- **Veno-venous ECMO (VV-ECMO)**
 - Provides respiratory support
 - **Indications:**
 - Refractory hypoxemic and/or hypercapnic respiratory failure** due to (not an exhaustive list):

- Obstructive lung disease - e.g. Asthma, COPD
- Infectious - e.g. bacterial pneumonia, COVID-19
- Aspiration
- Trauma
- ILD
- Pulmonary hemorrhage
- Smoke inhalation

**Respiratory failure refractory to medical management is often defined by the EOLIA criteria (2018). EOLIA was a landmark trial in 2018 looking at use of vv-ECMO in severe ARDS and though it did not show a 60 day mortality benefit, there was some trend towards benefit in its secondary analyses (48). Another landmark ECMO trial would be CESAR trial in 2009 which also did not demonstrate benefit to ECMO but did demonstrate benefit with referral to ECMO centers. (49)

Thus such patients *should be considered at least a referral / consultation* to an ECMO center for respiratory failure:

Severe ARDS according to usual Berlin criteria and 1 of the 3:

- P/F ratio < 50 with FiO₂ > 80% despite optimization of medical care (i.e. iNO, recruitment, paralysis, proning etc)
- P/F ratio < 80 with FiO₂ > 80% for 6 hours despite optimization of medical care (i.e. iNO, recruitment, paralysis, proning etc)
- pH < 7.25 with PaCO₂ > 60 for 6 hours resulting from mechanical ventilation and to keep Pplat < 32 cmH₂O

Exclusion criteria would include:

- Mechanical ventilation for more than 7 days
- Poor neurological status
- Severely elevated BMI (>45)
- Malignancy with life expectancy < 5 years

Contraindications: would be scenarios where there is no exit strategy for the patient, example:

- Disseminated/untreatable malignancy
- Known severe brain injury
- unwitnessed/prolonged cardiac arrest
- Severe multiorgan failure - e.g. cirrhosis, renal failure
- Age - most cutoffs at 60-65 years
- Compliance - lack of social support

Other contraindications would stem more from ineffectiveness of the support:

- VA specific:
 - Aortic dissection
 - Severe aortic regurgitation
 - Severe peripheral vascular disease
- VV specific:
 - Severe cardiogenic shock
 - Severe pulmonary hypertension

Note on ECPR = Extracorporeal cardiopulmonary resuscitation:

- A means of cardiopulmonary resuscitation via VA-ECMO in a cardiac arrest setting
- Indications to consider:
 - Young (< 60 years of age) with minimal comorbidities
 - Cardiac cause of arrest:
 - I.e., acute ischemia, arrhythmia
 - Manifested by: VT/VF arrest, preceding chest pain / ischemic event, ST elevations on ECG
 - Within 20 minutes of arrest

Complications:**Bleeding:**

- Most common (10-30%)
- Due to systemic anticoagulation, circuit-related coagulopathy
- Monitor coagulopathy with daily INR, PTT, fibrinogen, PLT and D-dimer

Thrombosis

- More clinically significant in VA-ECMO as arterial clots are much more catastrophic than venous clots and thus VA-ECMO typically requires full anticoagulation
- At VGH, we tend to use anti-Xa or heparin levels to monitor our systemic anticoagulation
 - using unfractionated heparin as first-line to target levels of 0.3-0.5 for VV-ECMO runs and 0.4-0.7 for VA-ECMO runs. PTT is otherwise used for UFH titration, but PTT measurements are more prone to inaccuracy especially in patients who are pro-inflammatory.

Infection

- Large plastic tubing is requiring for ECMO and thus are potential nidus for infection
- Note patients on ECMO often have their temperature controlled by the circuit - i.e. often cooled and will be difficult to measure fever
- Have low threshold to culture and start antibiotics

Neurological sequelae

- Ischemic strokes, macro and microvascular
- Hemorrhagic strokes
- Thus, the goal is to ideally have patients awake for neurological assessments once patient stable enough to lighten sedation

Hemolysis

- Shear stress sustained by the RBCs with flow through the circuit and oxygenator
- Monitor by plasma-free hemoglobin, and other markers of hemolysis: CBC, LDH, haptoglobin

Configuration:**VA-ECMO:**

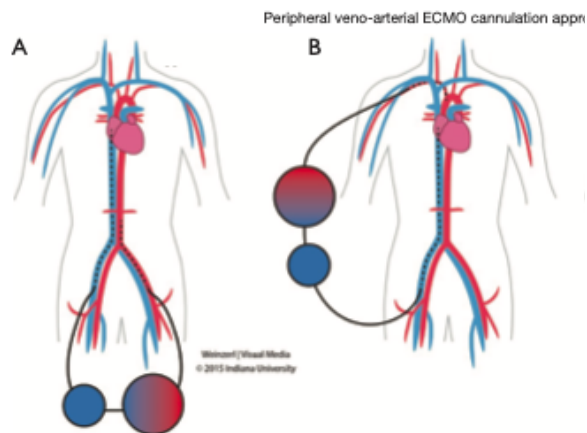


Figure 3 Peripheral veno-arterial ECMO cannulation approach: femoral vein (for drains) used for perfusion. ECMO, Extra Corporeal Membrane Oxygenation.

VV-ECMO:

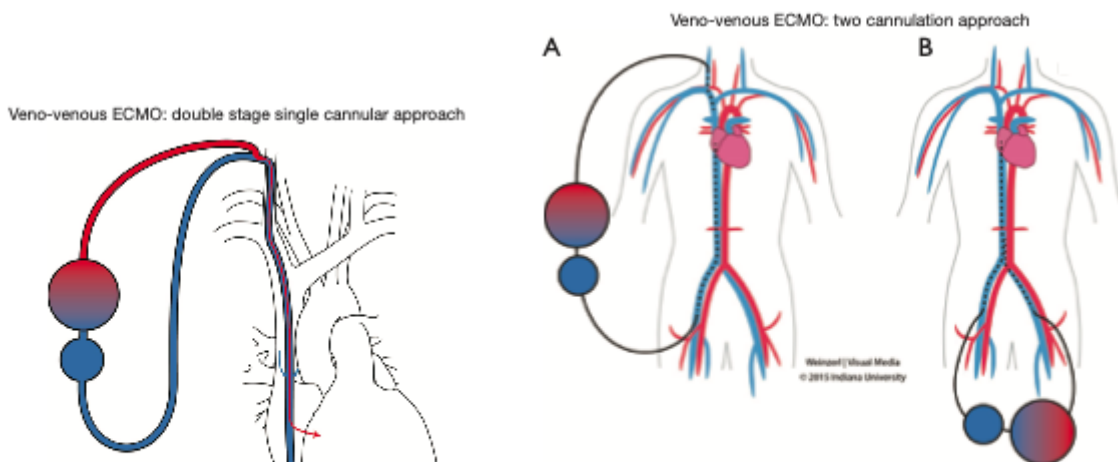


Figure 2 Veno-venous ECMO: two cannulation approach (A) femoral vein (for drainage) and right internal jugular for infusion, (B) both femoral veins are used for drainage and perfusion. ECMO, Extra Corporeal Membrane Oxygenation.

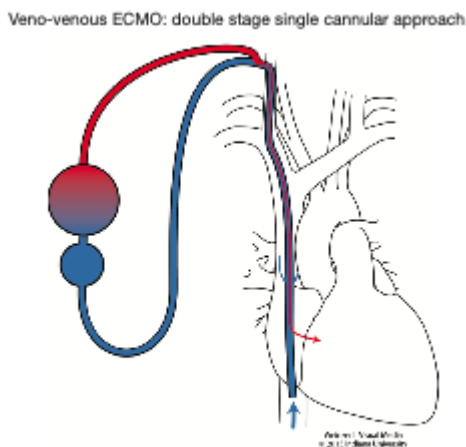


Figure 1 Single cannula approach.

Single cannula approach has benefits that include facilitating mobilization and have lower rates of recirculation but can be finicky for optimizing position.

Routine Care on ECMO:

There are a few things unique to patients on ECMO:

Hemodynamics in VA-ECMO:

- For patients in severe refractory cardiogenic shock from LV failure, the set-up for VA-ECMO is draining blood from the vena cava and returning oxygenated blood into the femoral artery. This return of blood at a range of 3.5-5L/min leads to increased LV afterload in an already failing LV. VA-ECMO does not provide “rest” to the LV like VV-

ECMO does for the lungs or VA-ECMO does for the RV. VA-ECMO however acts to provide end organ perfusion. The practice of using MAP as a surrogate for perfusion is de-emphasized. Instead, it is imperative to maintain pulsatility to ensure adequate perfusion to the cerebral and coronary circulation.

- Use right upper extremity arterial line as this is the most reliable marker for perfusion to the cerebral and coronary circulation
- Maintain pulsatility of at least 10 mmHg - ECMO circuit provides continuous flow and should not have pulsatility; pulsatility can only be generated by native cardiac output. Achieve this through inotropic and vasopressor support and volume.
- Serial echos to ensure opening of the aortic valve and monitoring for overdistension of the LV
- Monitor lactate, urine output, cap refill, mixed venous

Oxygenation in VV-ECMO:

- For patients in severe refractory hypoxemic respiratory failure, the goal of ECMO is to provide oxygenation and ventilation and allow the lungs to rest or provide a bridge to transplant.
- We often tolerate lower oxygen saturations with O₂ sat as low as 80-85% instead so long as the patient has adequate perfusion (i.e. normal lactate, adequate urine output, normal cap refill, etc). Remind ourselves that oxygen delivery = oxygen content and cardiac output.
- How to maintain adequate perfusion:
 - Optimize supply - the circuit is doing the bulk of the oxygenation vs the ventilator, help the circuit out by optimizing oxygen content - keeping Hb > 80-90 typically, maintain adequate cardiac output
 - Minimize demand - sedation, paralysis, cooling

Ventilator management: “Rest the lungs”

- Especially for VV-ECMO where we use ECMO for respiratory support, the goal is to rest the lungs with as least injurious ventilator settings as possible while still maintaining some degree of ventilation to avoid severe derecruitment. There are no clear guidelines as to what those settings should be but in general, minimize FiO₂, low tidal volumes, low rates and low driving pressures. We tend to use “10, 10, 10” settings locally so pressure control of 10 cmH₂O, RR of 10 and PEEP of 10.

Sedation:

- Once the patient is hemodynamically stable and have decreasing dependent on the degree of extracorporeal support, we ideally try to keep patients as awake as possible to a) minimize deconditioning and b) allow for neurological assessments

Drugs and infusions:

- The ECMO circuit tends to adsorb a ton of intravenous drugs, in general the more lipophilic the drug, the more it gets adsorbed. Furthermore, with the increase in fluid shifts the volume of distribution for drugs increases significantly. Sedatives like

midazolam and fentanyl often take forever to be eliminated from the patient. Thus once clinically appropriate, we start getting patients on enteral medications and get them off infusions.

- This ECMO sink effect has other implications for drugs like antibiotics which often need drug adjustments.

Procedures:

- Line placement or any other procedures should be done by experienced operators only due to risk of bleeding and air embolism.
- Attempts should be limited for a number of reasons: usually few sites left as ECMO cannulas already occupying sites, patients are often anticoagulated/coagulopathic
- Air embolism is avoided by diligent care to keep the catheter closed off to air during procedure and having the perfusionist turn down the flows from needle introduction to catheterization complete.

Circuit-related numbers to be aware of:

- Delta P - the pressure gradient across the oxygenator; normal should be <50 or in a <10:1 ratio with the flow rates; big increase in delta P is concerning for circuit integrity
- Post-membrane gasses:
 - PO₂ > 200 (at sea level PaO₂ with 100% FiO₂ should around 400-500mg) - decreasing post membrane PO₂ = concerning for circuit integrity
 - PCO₂ > 40 = concerning of circuit integrity
- Sweep
 - Essentially the ventilation side of ECMO
 - Recall a normal minute ventilation in a healthy patient is about 4-6L/min
- Flow
 - The oxygenation side of ECMO
 - Usually set at 3.5-5L/min

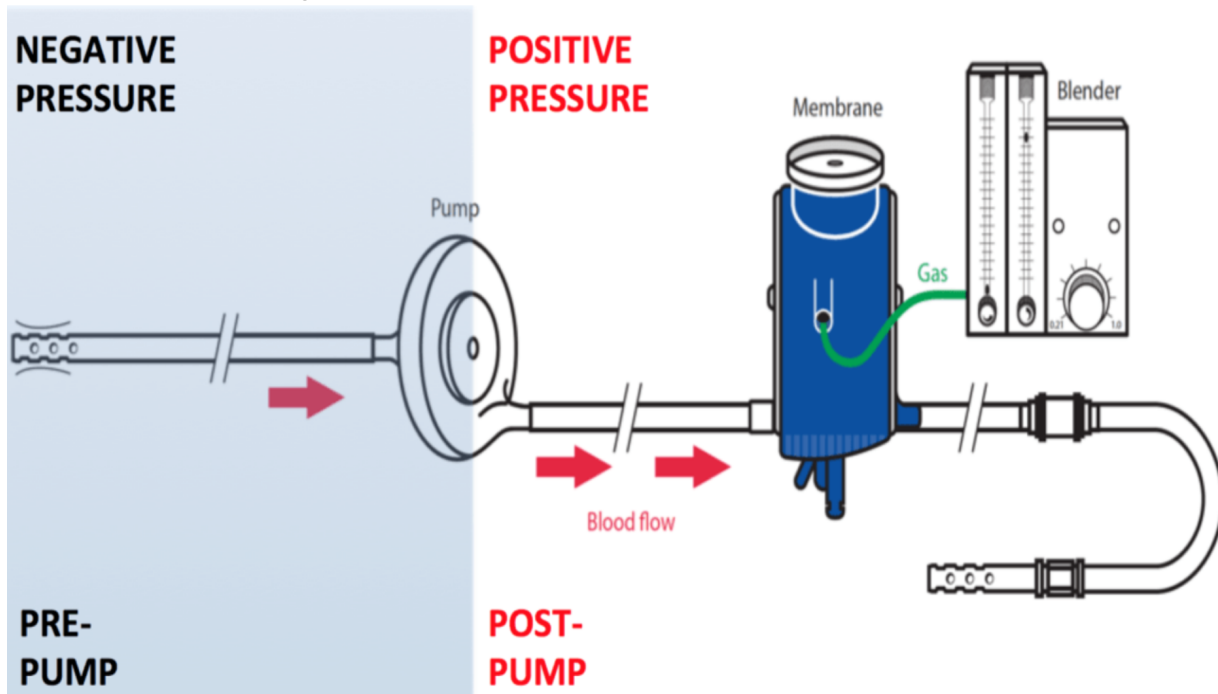
Troubleshooting ECMO:

Here are some common or serious issues that can arise with ECMO:

“Chatter” or flow limitations in the access pump:

- Differential diagnosis to this problem can be broken down into circuit vs patient:
 - Circuit:
 - Cannula position - any migration of cannula?
 - Kinks/obstruction to the cannulas - follow the cannula from the patient to the circuit. Look for kinks, clots.
 - Patient
 - Is the patient agitated/coughing? - fluctuations in intra abdominal and intrathoracic pressures will affect venous pressures and flow. Does this patient need some sedation to mitigate this?
 - Hypovolemia - the perfusionist/nursing team often have already tried fluid boluses with persistent chatter but at times may need more fluid ordered from the physicians. 1-2 bottles 100ml of albumin 25% is often used.

- Manifestations of “chatter”
 - Physical wiggling of the access cannulas - occurs as the vein is collapsing around the access cannulas due to negative venous pressures being generated
 - Without adequate flow of the circuit, this will need to hypoxia and/or hemodynamic instability
 - The diagram below can help conceptualize these pressures:



Recirculation in VV-ECMO:

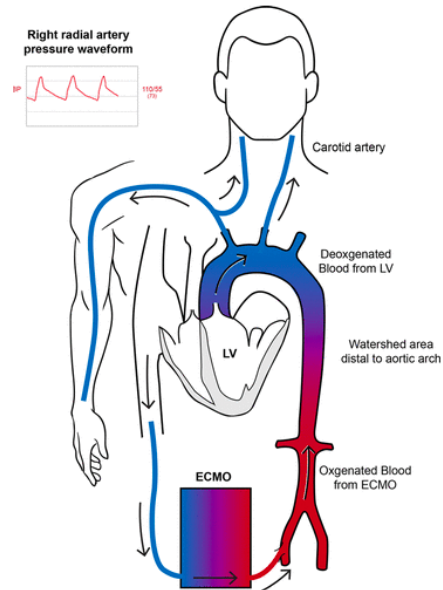
- This occurs when blood returning to the patient from the circuit gets directly drained back into the circuit and the patient does not receive the oxygenated blood.
- This will be manifested by hypoxemia and hypoxia in the patient; and the same colouration and saturation of blood between the return and access cannulas
- Causes:
 - Position of the cannulas - in two cannula system often with the cannulas too close to each other
 - Impediment of venous return from the patient - high intrathoracic or intraabdominal pressures - flow will always go in the path of least resistance
 - Circuit flow, cannulas pressures - larger cannulas = more flow for less pressure

Limb ischemia in VA-ECMO

- The return cannula in the femoral artery pushes blood in a retrograde fashion back up to the heart. This intuitively can result in distal limb ischemia. Some centers routinely place distal limb perfusion catheters. At VGH, we tend to observe closely and ask Vascular surgery to assist if signs of hypoperfusion - i.e. loss or diminishing pedal pulses

Harlequin syndrome or North-South syndrome in VA-ECMO:

- Occurs in setting of VA-ECMO where the native cardiac output is pumping hypoxemic blood due to inability of the lungs to oxygenate due to poor pulmonary function - e.g. pulmonary edema, aspiration, pneumonia
- Importance to measure your ABGs and PaO₂ at the right arm arterial line; keeping your O₂ sat probe on the right hand or head
- Management:
 - Treat the lung disease - optimize ventilator, diuresis, antibiotics, steroids PRN
 - May need VAV configuration to improve oxygenation.



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