

Critical Care Board Questions

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Disclosures

- Contributing editor at NEJM for their simulation-based medical education platform

Question 1: Part A

A 45-year-old man with HTN, DM2, and a recent viral URI presents with 24 hours of worsening dyspnea, fever (T_{max} 38.7 °C). He is placed on 40% FiO_2 by facemask.

- BP 99/54
- WBC 19
- ABG: 7.30 / 30 / 67 / 15



Pure metabolic acidosis
Hypoxemia despite 40% FiO_2
Right lower lobe infiltrate



Question 1: Part A

He is admitted to the ICU, placed on broad spectrum antibiotics, given IV fluids, and increased to 60% FiO₂ by facemask.

6 hours later he seems more tired and breathless; he remains lucid.

- ABG: 7.25 / 35 / 87 / 15



Question 1: Part A

What is the most appropriate next intervention?

- (A) Intubate immediately for hypercarbic respiratory failure and begin assist control ventilation
- (B) Decrease the FiO_2 for possibly causing the increased pCO_2
- (C) Begin non-invasive positive pressure ventilation
- (D) Decrease the IVF for possible CHF exacerbation
- (E) Cannulate for Extracorporeal Membrane Oxygenation (ECMO)

Non-Invasive Positive Pressure Ventilation (NIPPV)

- Evidence supports using NIPPV for:
 - **Acute exacerbation of COPD** → less intubation, shorter hospitalization, lower in-hospital mortality (NEJM 1995; Cochrane systematic review 2017)
 - **Cardiogenic pulmonary edema** → less intubation, lower in-hospital mortality (Cochrane systematic review 2019)
 - **Severe acute hypoxemic respiratory failure** → less intubation, decreased 90-day mortality (AJRCCM, 2003), less intubation, lower in-hospital mortality (CCM systematic review 2017)



Non-Invasive Positive Pressure Ventilation (NIPPV)

- Contraindications for NIPPV:
 - Absolute:
 - Cardiac or respiratory arrest
 - Relative
 - Concern for inability to protect airway
 - Unable to fit mask (facial hair, facial fracture)
 - Inability to tolerate mask
 - Copious secretions, recurrent vomiting
 - Recent upper airway or upper GI surgery



Explaining other answers...

(A) Intubate immediately for hypercarbic respiratory failure and begin assist control ventilation



Not necessary as a first step, try less invasive intervention first

(B) Decrease the FiO_2 for possibly causing the increased pCO_2



Only an issue for those with obstructive lung disease

(C) Begin non-invasive positive pressure ventilation



Correct answer!

(D) Decrease the IVF for possible CHF exacerbation



IV fluids are necessary for this patient with probable sepsis, can manage this with NIPPV

(E) Cannulate for Extracorporeal Membrane Oxygenation (ECMO)



Too early in the course of respiratory failure, consider when hypoxemia is refractory

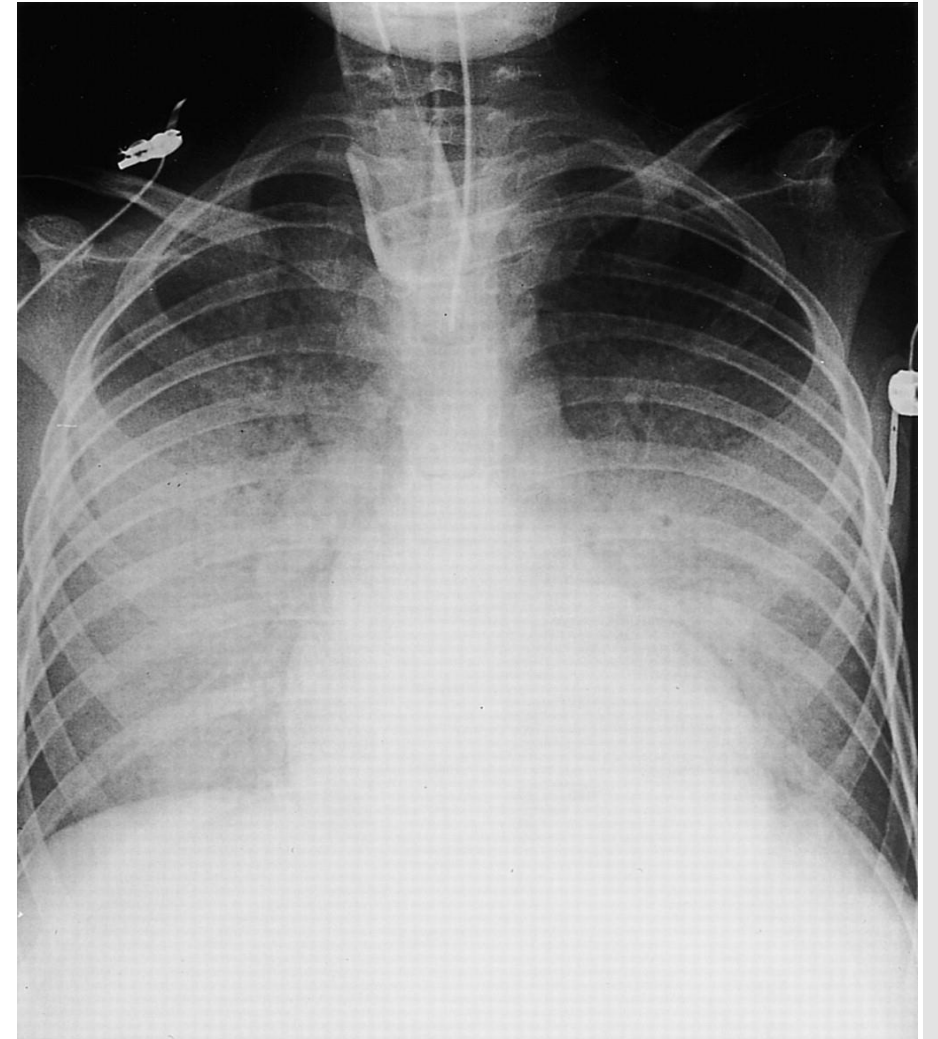
Learning Objectives: Respiratory Failure

- **Non-invasive positive pressure ventilation (NIPPV) can help to avoid intubation in patients with:**
 - acute exacerbation of COPD
 - cardiogenic pulmonary edema
 - severe hypoxemic respiratory failure
- **Contraindications for NIPPV include:**
 - Cardiac or respiratory arrest (absolute)
 - Need for airway protection
 - Inability to fit mask
 - Unstable hemodynamics

Question 1: Part B

Despite NIPPV, the patient deteriorates within hours and is intubated for progressive, refractory hypoxemia. He is diagnosed with ARDS based on the Berlin criteria defined in 2012:

- Acute onset (<7 days)
- $\text{PaO}_2:\text{FiO}_2 < 300$
- Bilateral pulmonary opacities
- Not fully explained by cardiac failure or volume overload

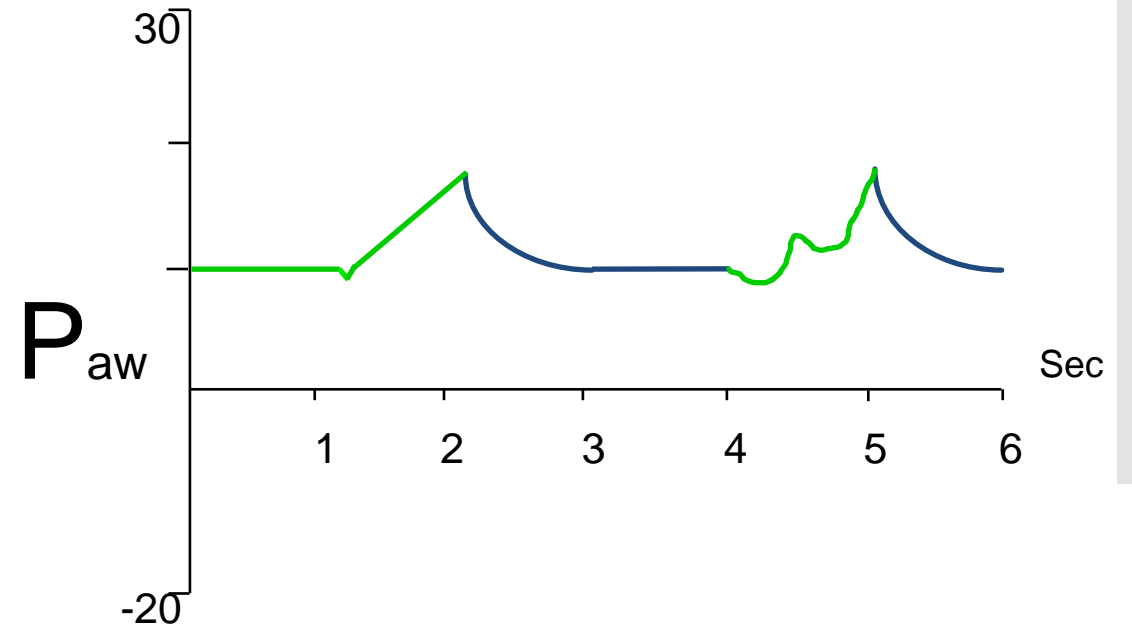


Question 1: Part B

You are called to evaluate the patient for agitation. His current vent settings are:

- Assist control ventilation
- Tidal volume 450cc (6cc/kg IBW)
- PEEP 10 cm H₂O
- RR 14 bpm
- FiO₂ 60%

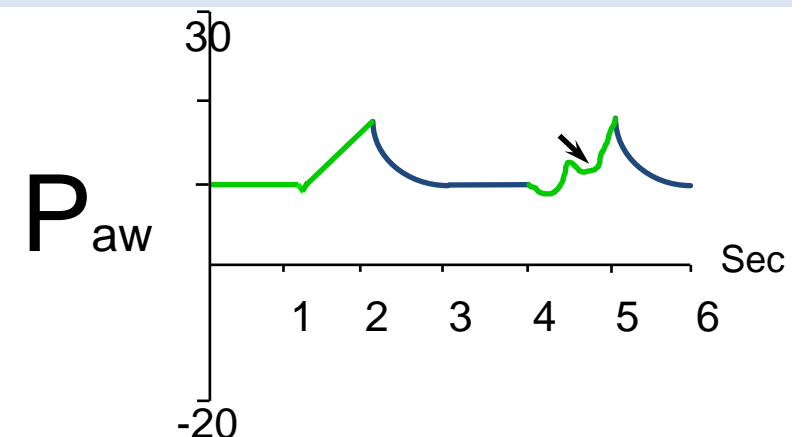
His pressure/time waveform is displayed here:



Question 1: Part B

What is occurring at the arrow and what is the best way to address it?

- (A) Ventilator malfunction. Bag the patient and change the machine.
- (B) Patient-ventilator dyssynchrony. Sedate the patient more heavily.
- (C) Air hunger. Increase the tidal volume.
- (D) Air hunger. Increase the inspiratory flow.
- (E) Auto-PEEP. Increase the set PEEP to match the auto-PEEP and lessen his work of breathing.



Air hunger

- Patient wants more flow than is being delivered and so she/he initiates a negative pressure breath that causes downward scooping of the pressure curve during inspiration.



- Increasing the flow rate will resolve this type of patient-ventilator dyssynchrony.

Explaining other answers...

(A) Ventilator malfunction. Bag the patient and change the machine.



There is no indication of vent malfunction.

(B) Patient-ventilator dyssynchrony. Sedate the patient more heavily.



This is a form of dyssynchrony, but best to explore other solutions before increasing sedation.

(C) Air hunger. Increase the tidal volume.



This is air hunger but more likely flow than volume problem, and with ARDS should maintain lung protective ventilation with low V_t

(D) Air hunger. Increase the inspiratory flow.



Correct answer!

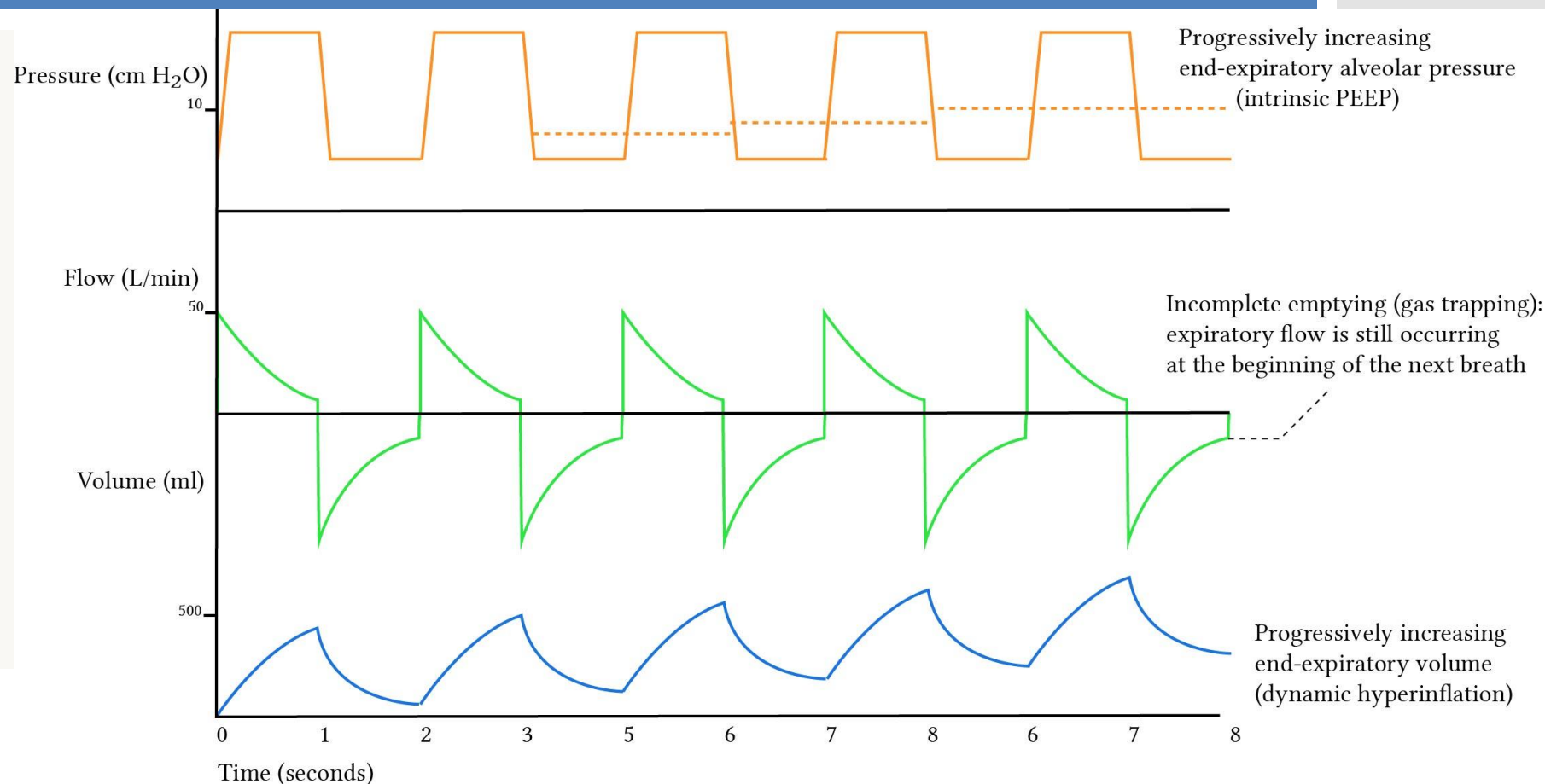
(E) Auto-PEEP. Increase the set PEEP to match the auto-PEEP and lessen his work of breathing.



No indication of auto-PEEP on waveform, would not occur during inspiration.

Auto PEEP

- When flow does not return to zero by the end of expiration, gas trapping may occur and lead to dynamic hyperinflation.



Learning Objectives: Ventilator Dyssynchrony

- Think about **air hunger** when the pressure tracing scoops downward during the delivered breath:
 - Address this by increasing inspiratory flow
 - Do not reflexively increase sedation
- Think about **auto PEEP** when the flow tracing does not return to baseline at the end of expiration:
 - This can cause increased work of breathing and dyssynchrony, predispose to barotrauma, and impact hemodynamics

Question 1: Part C

After 6 days, the patient is improving. He no longer has fever. He is hemodynamically stable. He just had a CT chest that demonstrated improvement in bilateral opacities. His current ventilator settings are:

- Assist control ventilation
- Tidal volume 450 cc (6cc/kg IBW)
- PEEP 6
- RR 10 bpm
- FiO₂ 40%

You are called because his vent is alarming for high pressures. The respiratory therapist tells you that the peak inspiratory pressure has acutely increased from 22 to 34 and the plateau pressure has increased from 15 to 28.

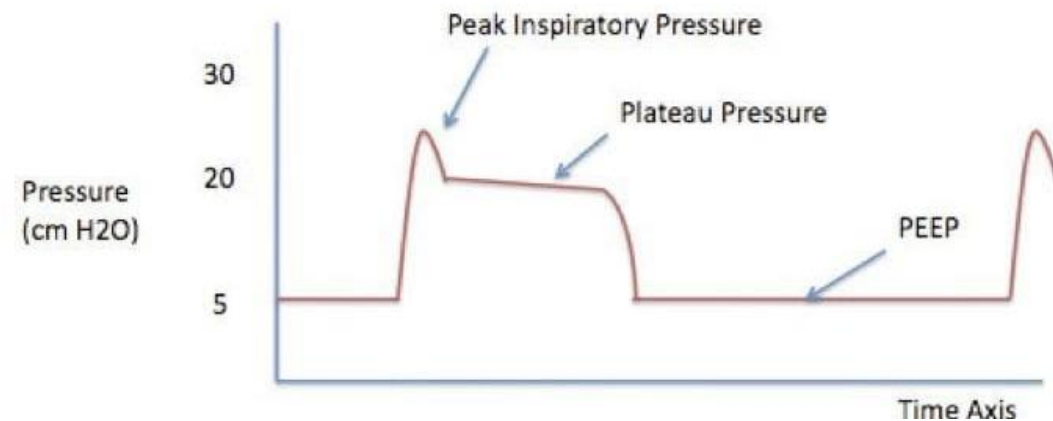
Question 1: Part C

Which of the following is most likely cause of the high pressure alarm?

- (A) His endotracheal tube migrated into his right mainstem bronchus.
- (B) His endotracheal tube is kinked.
- (C) He has a mucus plug in a main airway.
- (D) He has developed an acute pulmonary embolism.
- (E) This is part of the natural history of ARDS.

Elevated Airway Pressures

- Peak Airway Pressure = Airway Resistance Pressure + Plateau Pressure
 - Airway Resistance Pressure = Flow x Airway resistance
 - Plateau Pressure = Tidal volume / Compliance
*measured when flow = 0 (inspiratory hold)

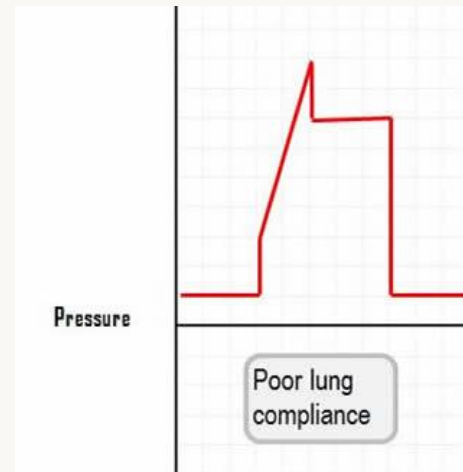


Elevated Airway Pressure

High peak + high plateau

→ Poor compliance

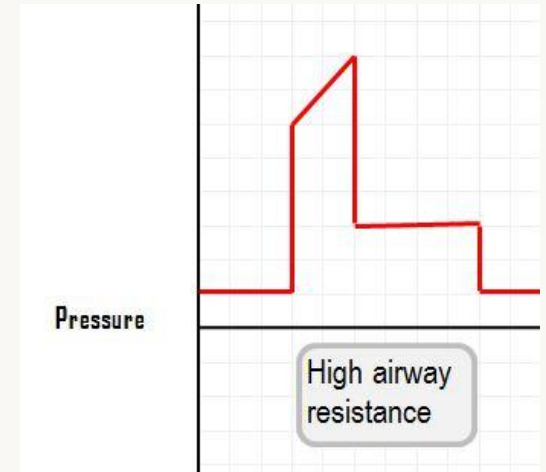
- Mainstem intubation
- CHF
- Pulmonary fibrosis
- Pneumothorax
- Abdominal compartment syndrome
- Circumferential burn of thorax



High peak + normal plateau

→ Poor resistance

- Bronchospasm
- Mucous plug
- Kinked endotracheal tube



Explaining other answers...

(A) His endotracheal tube migrated into his right mainstem bronchus.

→ Correct answer!

(B) His endotracheal tube is kinked.

→ This would cause increased resistance; plateau pressure would be normal.

(C) He has a mucus plug in a main airway.

→ This would cause increased resistance; plateau pressure would be normal.

(D) He has developed an acute pulmonary embolism.

→ This would not have significant immediate effect on peak pressure or plateau pressure.

(E) This is part of the natural history of ARDS.

→ The natural history of ARDS does not include a sudden worsening of compliance, in fact over time compliance usually improves slowly.

Learning Objectives: Elevated Peak Airway Pressures

- When the vent alarms for elevated peak airway pressures, **use the plateau pressure to determine whether the issue is airway resistance or lung compliance**
 - If the plateau pressure is normal, think about causes of increased airway resistance
 - If the plateau pressure is elevated, think about causes of decreased lung compliance

Question 2: Part A

A 64-year-old woman with a history of HTN, HLD and diverticulosis, presents to the ED with abdominal pain, altered mental status, and hypotension.

- **Vitals**

- BP 90/60
- HR 110
- RR 16
- SpO2 94% on 4L
- Temp 101.2 F
- Weight 70 kg

- **Exam**

- Ill-appearing
- Drowsy and difficult to arouse
- Extremities are mottled
- Diffuse involuntary guarding of abdomen

Question 2: Part A

- CT scan demonstrates a perforated sigmoid colon. She is sent to the OR 2 hours after arrival to the ED for laparotomy. She has a grossly contaminated abdomen however the surgeons are able to repair the perforation and clean the peritoneal cavity.
- She is transferred to the ICU for post-operative management.
- In the OR, she received 4L of LR. She was given one dose of ceftriaxone and metronidazole at the start of the case (2 hours after arrival to the ED). At the time of transfer she is hemodynamically stable.

Question 2: Part A

Which of the following is true regarding antibiotics in this case?

- (A) Antibiotics must be continued for a total of 14 days.
- (B) Her chance of dying in the hospital is the same as it would have been if she had received antibiotics in the ED, since both were in the first 6 hours after presentation.
- (C) Antibiotics may be stopped after a total of 4 days.
- (D) Her mortality will improve by continuing antibiotics until 2 days after resolution of fever, leukocytosis, and ileus.
- (E) The ceftriaxone should be discontinued, and metronidazole monotherapy should be continued for a total of 5 days.

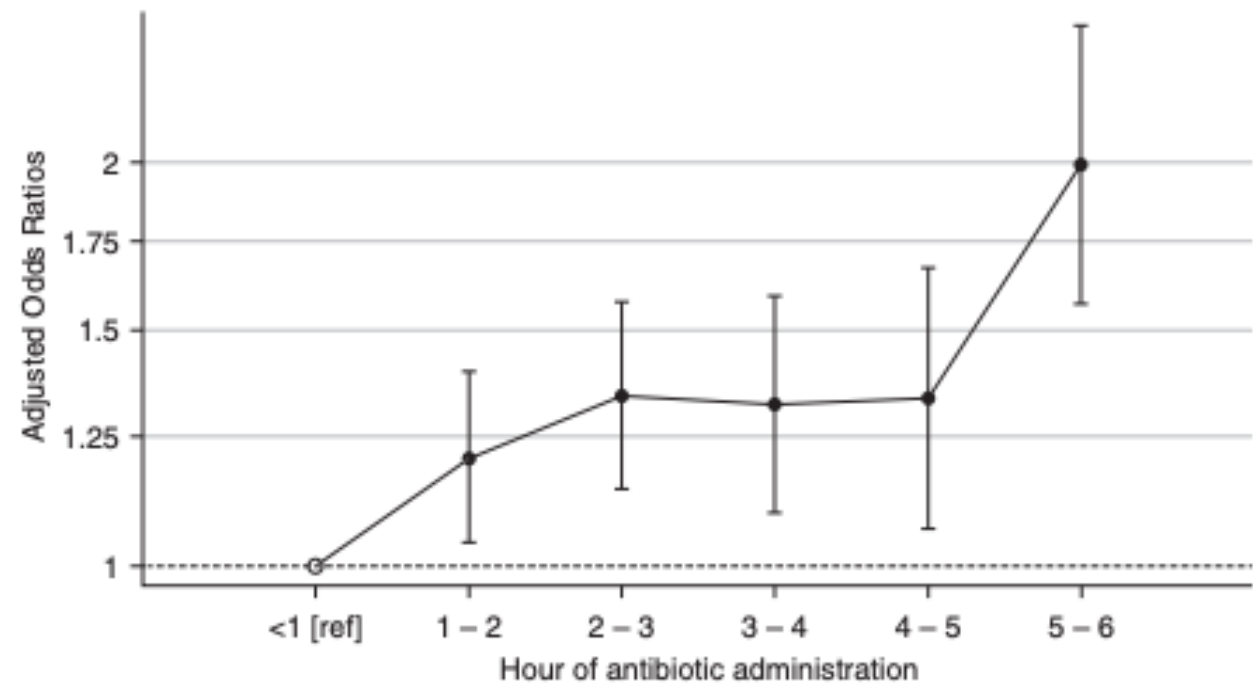
Sepsis Basics

- Best practices include:
 - Blood cultures (ideally before antibiotics are given)
 - Early broad-spectrum antibiotics
 - Measurement of lactate level (and repeat if $>2\text{mmol/L}$)
 - 30mL/kg of crystalloid (for hypotension or lactate $\geq 4\text{mmol/L}$)
 - Vasopressors if hypotensive during or after fluid resuscitation for goal MAP $\geq 65\text{mmHg}$

Surviving Sepsis
Campaign®

Antibiotics in Sepsis

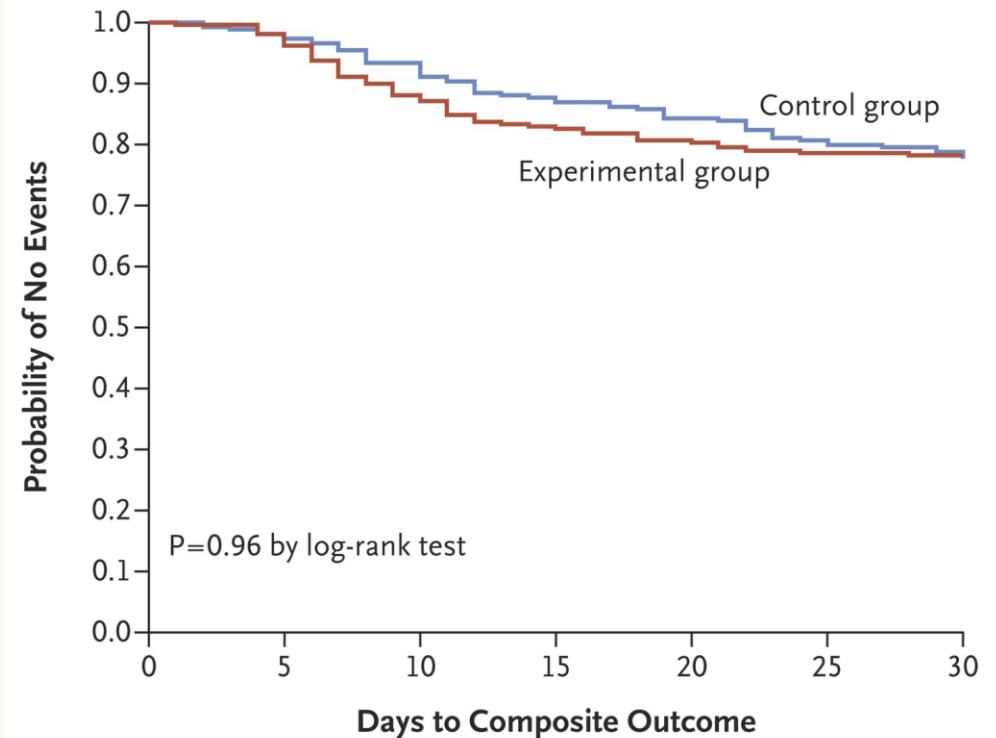
- Timing of antibiotics impacts hospital mortality even before 6 hours
- Retrospective study of 35,000 patients given antibiotics within 6 hours of arrival to the ED
 - Adjusted in-hospital mortality differed based on every 1-hour difference in timing of antibiotics



Liu, V. et al. "The Timing of Early Antibiotics and Hospital Mortality in Sepsis." *AJRCCM* 2017; 196:856-863.

Antibiotics for Intraabdominal Infections

- Study of patients with complicated intrabdominal infection (gross contamination of peritoneal space)
 - Compared short course of antibiotics (4 ± 1 day) versus variable longer course (mean 8 days) of antibiotics with stop date determined by resolution of physiologic abnormalities (WBC, fever, ileus)
 - No difference in composite outcome: surgical site infection, recurrent intrabdominal infection, and death



Sawyer, R. et al. "Trial of Short-Course Antimicrobial Therapy for Intraabdominal Infection." NEJM 2015; 372: 1996-2005.

Explaining other answers...

- (A) Antibiotics must be continued for a total of 14 days. → There is no benefit to continuing antibiotics for this length of time.
- (B) Her chance of dying in the hospital is the same as it would have been if she had received antibiotics in the ED, since both were in the first 6 hours after presentation. → If she had received antibiotics earlier than 2 hours after her arrival, her chance of dying in the hospital would be lower.
- (C) Antibiotics may be stopped after a total of 4 days. → Correct answer!
- (D) Her mortality will improve by continuing antibiotics until 2 days after resolution of fever, leukocytosis, and ileus. → This approach does not improve outcomes compared to a shorter defined course of abx.
- (E) The ceftriaxone should be discontinued, and metronidazole monotherapy should be continued for a total of 5 days. → Acceptable empiric antibiotic regimens for intrabdominal infections do not include metronidazole monotherapy.

Learning Objectives: Intrabdominal Sepsis

- In patients with **sepsis, in-hospital mortality increases with every 1-hour delay in antibiotic administration** (AJRCCM, 2017)
 - This is true even when antibiotics are administered within 6 hours
- After obtaining adequate surgical source control of a complicated intrabdominal infection, **treating with antibiotics for a fixed short course 4 ± 1 day is acceptable**
 - No difference in composite clinical outcome

Question 2: Part B

- The patient remains hemodynamically stable and afebrile. She is weaned off sedation and her mental status improves so that she now follows simple commands.
 - SBT this morning went well
 - Remains on pressure support ventilation with low level support
 - She has strong cough when suctioned
 - She has minimal secretions

Question 2: Part B

- It has been 48hrs since she was intubated in the OR for her surgery.
- Anesthesia documented that the intubation was challenging and there was minimal trauma to the airway during the intubation.
- She currently has a 7.5mm endotracheal tube in place.

Question 2: Part A

Which of the following statements regarding liberation from mechanical ventilation is correct?

- (A) Only patients at high risk for extubation failure should have a spontaneous breathing trial (SBT) before extubation
- (B) Using non-invasive ventilation (NIV) immediately after extubation for patients at high risk for extubation failure does not impact mortality
- (C) Patients who fail a cuff leak test but are otherwise ready for extubation should have extubation delayed by at least 48 hours
- (D) Patients who fail a cuff leak test but are otherwise ready for extubation should receive systemic steroids prior to extubation
- (E) Men are at higher risk than women for developing postextubation stridor

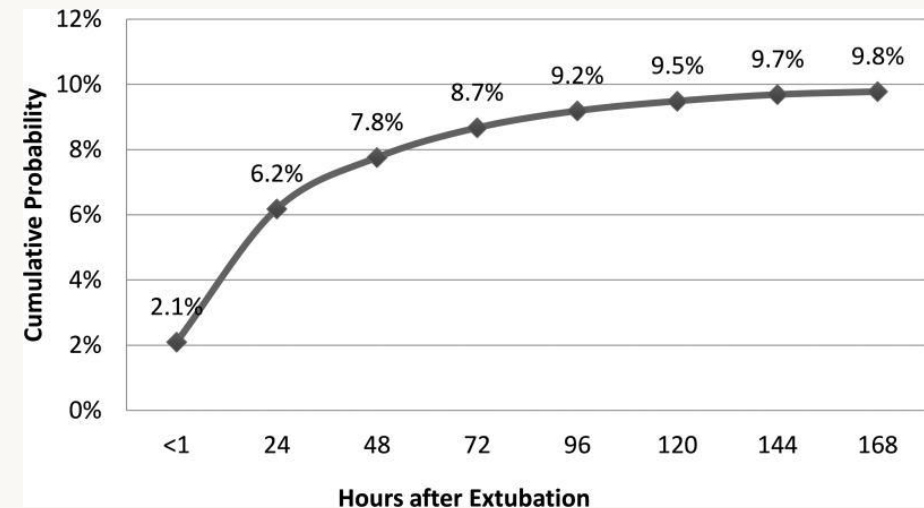
Liberation from Ventilation

- Daily SAT + SBT (if no contraindications) for all patients who have been on mechanical ventilation >24 hours is standard of care
 - RCT from Lancet 2008 → improved ICU outcomes (MV days, ICU LOS, and mortality- NNT 7.4)
 - Initial SBT should be performed with 5-8 cm H₂O inspiratory pressure augmentation (ATS/CHEST consensus recommendation, 2017)

Girard, T. et al. "Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care: a randomized controlled trial" Lancet 2008; 371: 126-134.

Liberation from Ventilation: Risk of Failure

- Failure of liberation = requirement for reintubation
 - Approximately 10% patients require reintubation
 - Median time to reintubation 15 hours
 - In the ICU, 90% of reintubation occurs within 96hrs of initial extubation

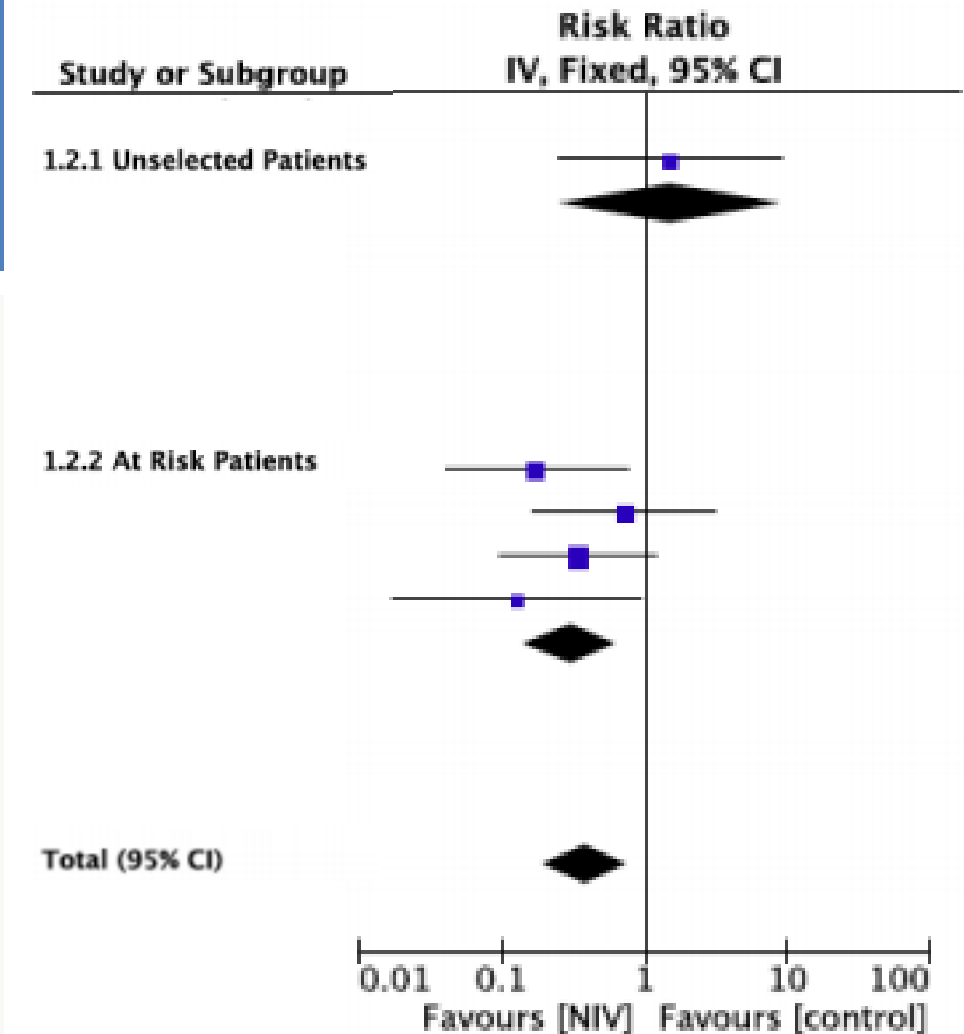


Miltiades, A. et al. "Cumulative Probability and Time to Reintubation in US ICUs" *Critical Care Medicine*. 2017; 45: 835.

Postextubation NIV

- Patients at risk for failure of liberation
 - >65 years and/or significant underlying cardiac and respiratory disease
- ATS/ERS clinical practice guidelines from 2017 support **use of NIV immediately postextubation for high risk patients** based on pooled analysis from RCTs demonstrating mortality benefit

Mortality



Postextubation Stridor (PES)


- Laryngeal edema is an established complication of intubation that can cause a decrease diameter of laryngeal lumen
- Clinically, LE presents as postextubation stridor (PES) and/or postextubation respiratory distress
- Stridor in PES occurs are a result of increase in airflow velocity through narrow laryngeal lumen

Pluijms et al. *Critical Care* (2015) 19:295
DOI 10.1186/s13054-015-1018-2



REVIEW

Open Access

Postextubation laryngeal edema and stridor resulting in respiratory failure in critically ill adult patients: updated review 

Wouter A. Pluijms^{1*}, Walther NKA van Mook², Bastiaan HJ Wittekamp³ and Dennis CJJ Bergmans²

Postextubation Stridor (PES)

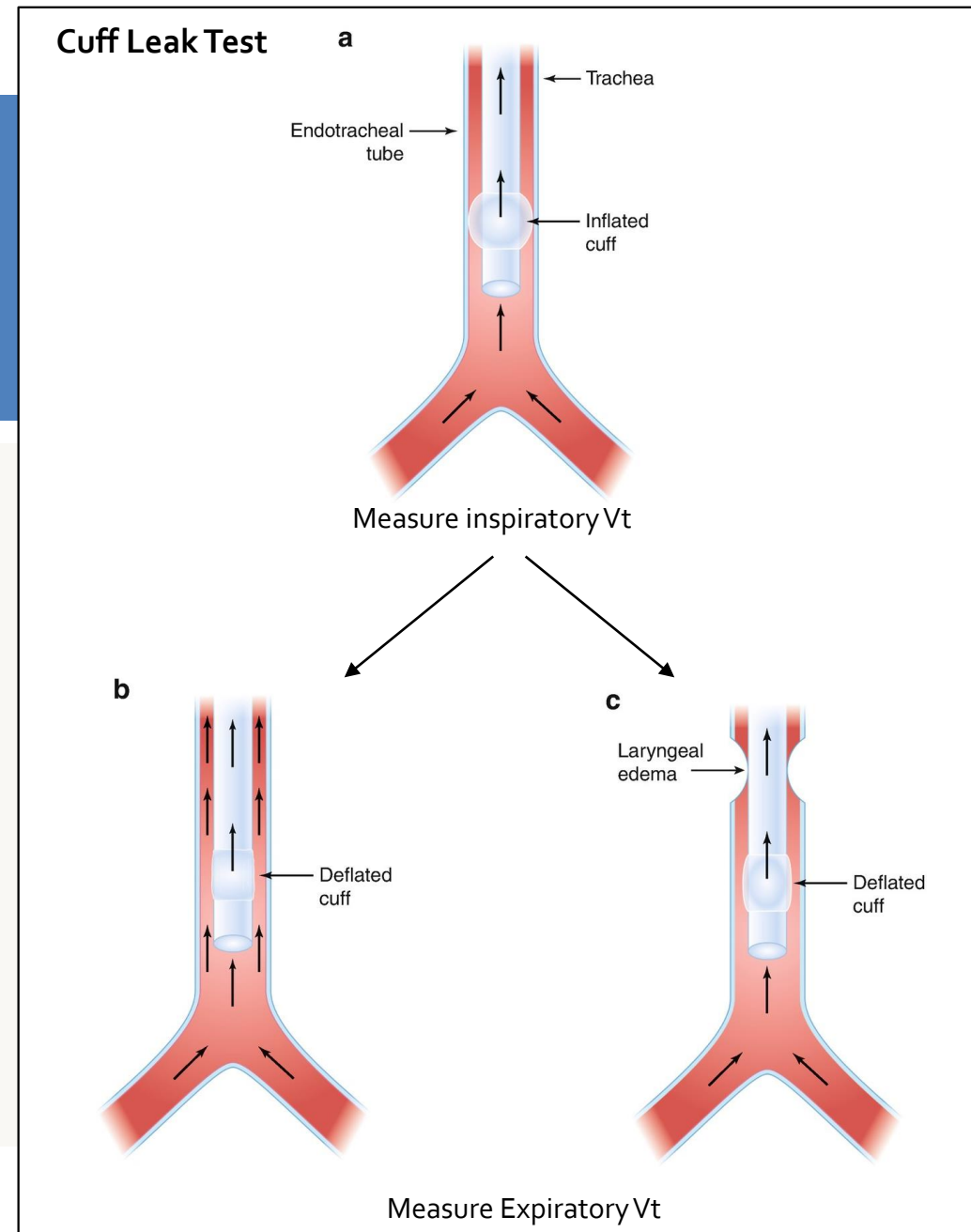
- PES incidence varies
 - reported from 5% - 54%
- Reintubation rate in patients with PES varies (10%-100%)
 - Not all patients with PES require reintubation

Risk Factors for PES

Female gender
Longer duration of intubation
Difficult/traumatic intubation
Higher endotracheal tube size
Higher cuff pressure

Cuff Leak Test

- One approach to predicting PES is to perform a **cuff leak test** prior to extubation



Cuff Leak Test

Positive

Potential identification of LE and PES prior to extubation

Potential to minimize postextubation risk

Negative

Potential delay in extubation may lead to increased risks associated with prolonged duration MV

Indirect assessment of LE (just surrogate)

Variable sensitivity/specificity

PES Prevention

- 3 RCTs of steroid vs placebo for patients who failed cuff leak test pooled data demonstrate:
 - Decreased PES (10.8 vs 31.9%, RR 0.35, 95%CI 0.20 – 0.63)
 - Decreased reintubation (5.8 vs 17.0%, RR 0.32, 95%CI 0.14 – 0.76)
- RCT of methylprednisolone (20mg x4 over 12hr) vs placebo before extubation for all patients (no cuff leak performed)
 - Steroids reduced PES, reintubation, and reintubation due to PES

ATS/CHEST recommendations.

- For adults who have failed a cuff leak test but are otherwise ready for extubation, we suggest administering systemic steroids at least 4 hours before extubation, (conditional recommendation, moderate certainty in the evidence).

Explaining other answers...

- | | | |
|--|---|---|
| (A) Only patients at high risk for extubation failure should have a spontaneous breathing trial (SBT) before extubation | → | All patients receiving mechanical ventilation should have a daily SBT paired with SAT. |
| (B) Using non-invasive ventilation (NIV) immediately after extubation for patients at high risk for extubation failure does not impact mortality | → | NIV used immediately after extubation for high risk patients is associated with a mortality benefit. |
| (C) Patients who fail a cuff leak test but are otherwise ready for extubation should have extubation delayed by at least 48 hours | → | There is no evidence to support this. In fact, delay of extubation is a concern related to routine cuff leak testing. |
| (D) Patients who fail a cuff leak test but are otherwise ready for extubation should receive systemic steroids prior to extubation | → | Correct answer! |
| (E) Men are at higher risk than women for developing post-extubation stridor | → | Women are at increased risk for developing post-extubation stridor. |

Learning Objectives: Ventilator Liberation

- Performing a **daily SAT and SBT for all mechanically ventilated patients in the ICU** decreases the duration of MV and improves mortality
- Using **NIV immediately following extubation for patients at high risk for extubation failure** improves mortality
- Giving **systemic steroids prior to extubation to patients who fail a cuff leak test** can improve ventilator liberation outcomes.
 - Less likely to develop postextubation stridor
 - Less likely to require re-intubation

Question 3

A 72-year-old man with PMH of HTN, renal insufficiency, hypothyroidism, moderate COPD, and PVD, is now POD1 from a fem-pop bypass. He was transferred to the ICU intubated because he was slow to wake from anesthesia; he was extubated yesterday afternoon.

Medications include:

- Opioid PCA for pain
- Metoprolol for BP
- Levothyroxine for hypothyroidism
- Furosemide x 1 dose

Question 3

Social history:

- He is a high-level executive in the financial industry.
- History of 45 pack-year cigarette smoking, quit 1 month ago.
- 1-2 drinks with dinner, sometimes more. No history of withdrawal.
- He reports remote history of cocaine use, last used 40 years ago. Currently no illicit substance use.

Question 3

- You are asked to come and evaluate the patient because he has become restless. The ICU nurse tells you that the patient did not sleep last night and was drowsy this morning, but now the patient is agitated and combative.

Vitals:

Afebrile

BP- 165/84
(baseline 130/75)

HR- 110 bpm (NSR)

RR 20

SpO2 98% on RA

Pre-op labs:

Urine tox negative

Yesterday's labs:

TSH normal

Na 134

Cr 1.5 (baseline 1.4)

WBC 6

Exam:

Awake and alert

No diaphoresis.

Speaking in full sentences

Poor attention

No facial droop

Moving all 4 extremities

No tremor or tongue
fasciculations

Surgical site clean; no
evidence of infection.

Question 3

What intervention would have been most likely to prevent delirium in this patient?

- (A) Use benzodiazepines for sedation in the ICU.
- (B) Standing high dose opiates for pain control.
- (C) Prophylaxis with haloperidol while in the ICU.
- (D) Night-time dexmedetomidine while in the ICU.
- (E) Use of the ABCDE bundle in the ICU.

DSM 5: Defining Delirium

- Delirium is a syndrome characterized by:
 1. **Disturbance in attention** (ability to direct, focus, sustain, shift attention)
 2. Additional **disturbance in cognition** (memory, disorientation, language, perception...)
 3. Development over **hours-days** that is change from baseline and that **fluctuates** over the course of day
 4. **Not explained by pre-existing condition**
 5. Evidence that the disturbance is due to a **medical condition, substance intoxication or withdrawal, or medication side effect**

Predisposing Factors for Delirium

- Advanced age
- Underlying dementia
- Functional impairment in ADLs
- High medical comorbidity
- History of alcohol abuse
- Male gender
- Sensory impairment

ICU Delirium

- Impact
 - Independent risk factor for mortality among intubated patients in the ICU
 - 3x higher at 6 months
 - Fewer ventilator-free days
 - 5 days fewer on average
 - \$15,000-25,000 higher hospital costs
 - 9 times higher incidence of cognitive impairment at hospital discharge

JAMA[®]
The Journal of the American Medical Association

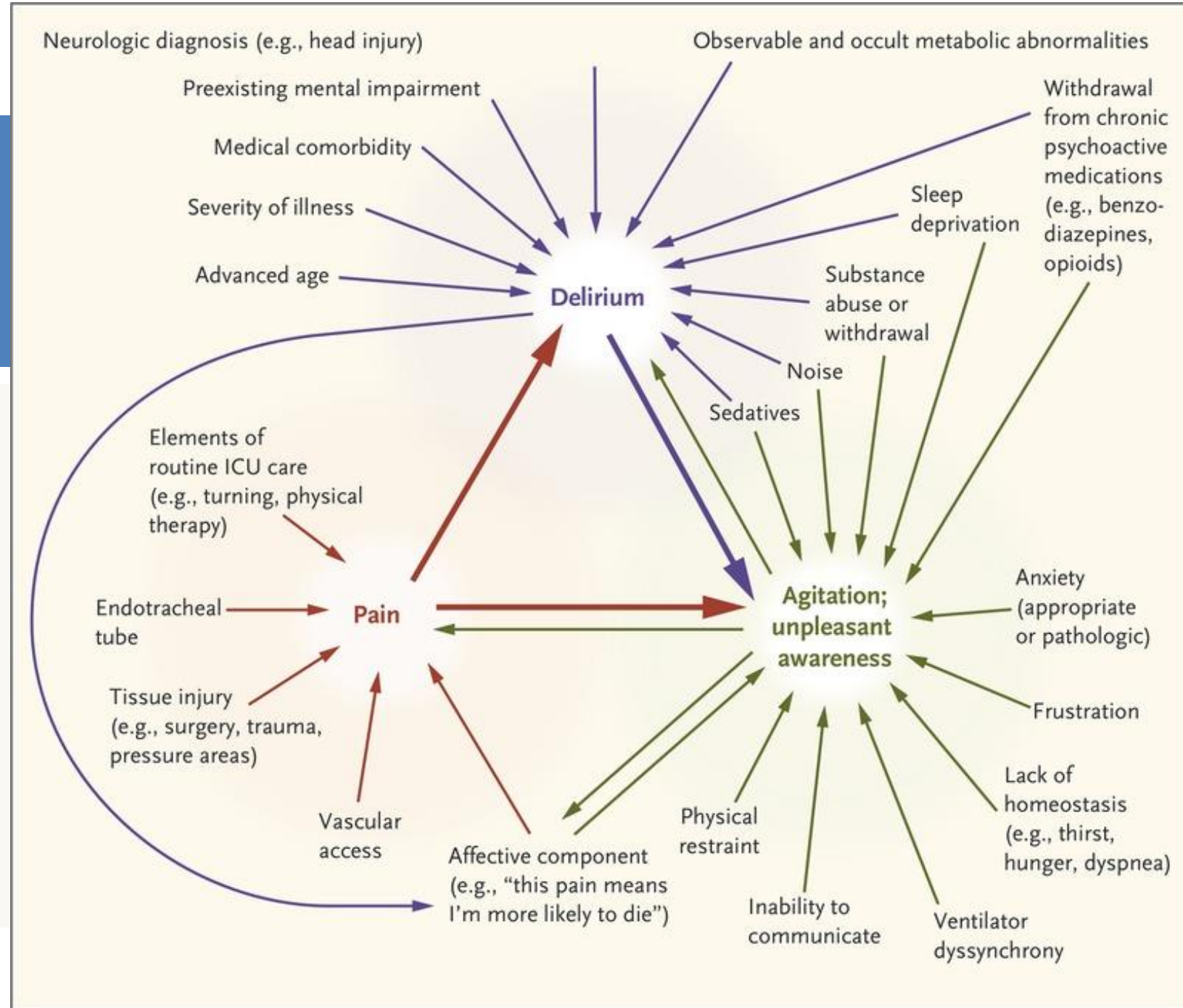
April 14, 2004



Wesley, E. "Delirium as a Predictor of Mortality in Mechanically Ventilated Patients in the Intensive Care Unit." *JAMA*. 2004; 291 (14): 1753-1762.

ICU Delirium

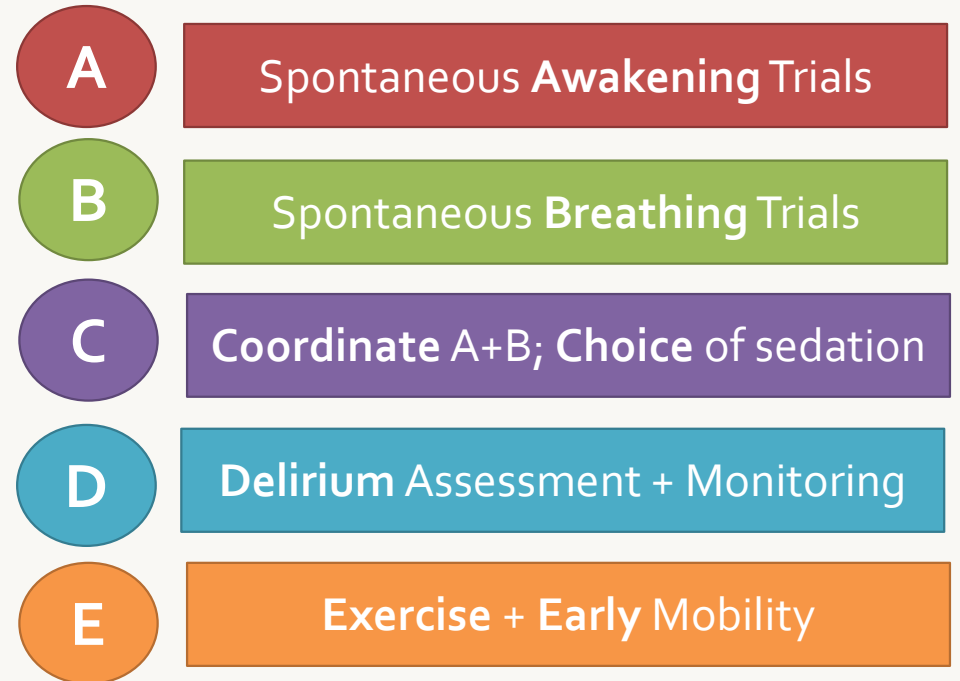
- Causes and interactions: pain, agitation, and delirium in the ICU



Reade, M. et al. "Sedation and Delirium in the Intensive Care Unit." NEJM 2014; 370: 444-454.

ICU Delirium

- Treatment
 - The best treatment is prevention
 - Treat underlying etiology
- Prevention
 - No evidence for pharmacologic agent
 - Trials of dexmedetomidine and antipsychotics as ppx: no effect (AJRCCM 2018, NEJM 2018)
 - ICU bundle protocol has shown to decrease prevalence (38% to 23%) and duration (3.8 to 1.72 days) of delirium in ICU



Learning Objectives: ICU Delirium

- In mechanically ventilated patients in the ICU, **delirium is an independent risk factor for mortality**
 - It is also associated with increased hospital and ICU length of stay, and cognitive impairment at time of discharge
- While there is no clear evidence for pharmacologic prevention of delirium, **use of the ABCDE bundle can decrease prevalence and duration of delirium in the ICU**

Question 4

- A 73-year-old man with a history of prostate cancer collapses while boarding a bus in a crowded urban bus terminal.
- Bystander CPR is begun, a transit policeman arrives, attaches an AED which recommends “shock” and discharges with return of spontaneous circulation.



Question 4

- The patient is brought to the closest hospital; he remains unconscious but with a stable blood pressure.
- Upon arrival, he is emergently taken to the cath lab; a suspicious, non-obstructing plaque is found in the circumflex artery.
- He is transferred to the ICU. His BMP, CBC, and coagulation panel are normal.

Question 4

What is the best next step to improve the outcome for this patient?

- (A) STAT head CT to rule out CNS catastrophe.
- (B) Refer for hyperbaric oxygen for possible hypoxic brain injury.
- (C) Begin external cooling of patient to 32° C for 12 hours
- (D) Activate protocol for targeted temperature management of patient.
- (E) Hold a family meeting to relay his poor neurologic prognosis and discuss withdrawal of care.

Targeted Temperature Management (TTM)

- **Indication:**

- AHA 2020 guidelines class 1 (strong) recommendation
- TTM with goal temp 32-36°C for at least 24 hours once target temp reached for adults who do not follow commands with ROSC after:
 - out of hospital cardiac arrest with any initial rhythm
 - in hospital cardiac arrest with initial non-shockable rhythm
 - In-hospital cardiac arrest with initial shockable rhythm*

*based on non-randomized trials

Targeted Temperature Management (TTM)

- **Contraindications:**

- Active non-compressive bleeding (relative, increased bleeding risk with lower temps)
- Pregnancy (relative, increased bleeding risk)
- Hemodynamically unstable (relative, increased bleeding risk)

- Key component for TTM device is a continuous feedback mechanism
 - Requires ability to measure and monitor core temperature (e.g. via bladder probe)

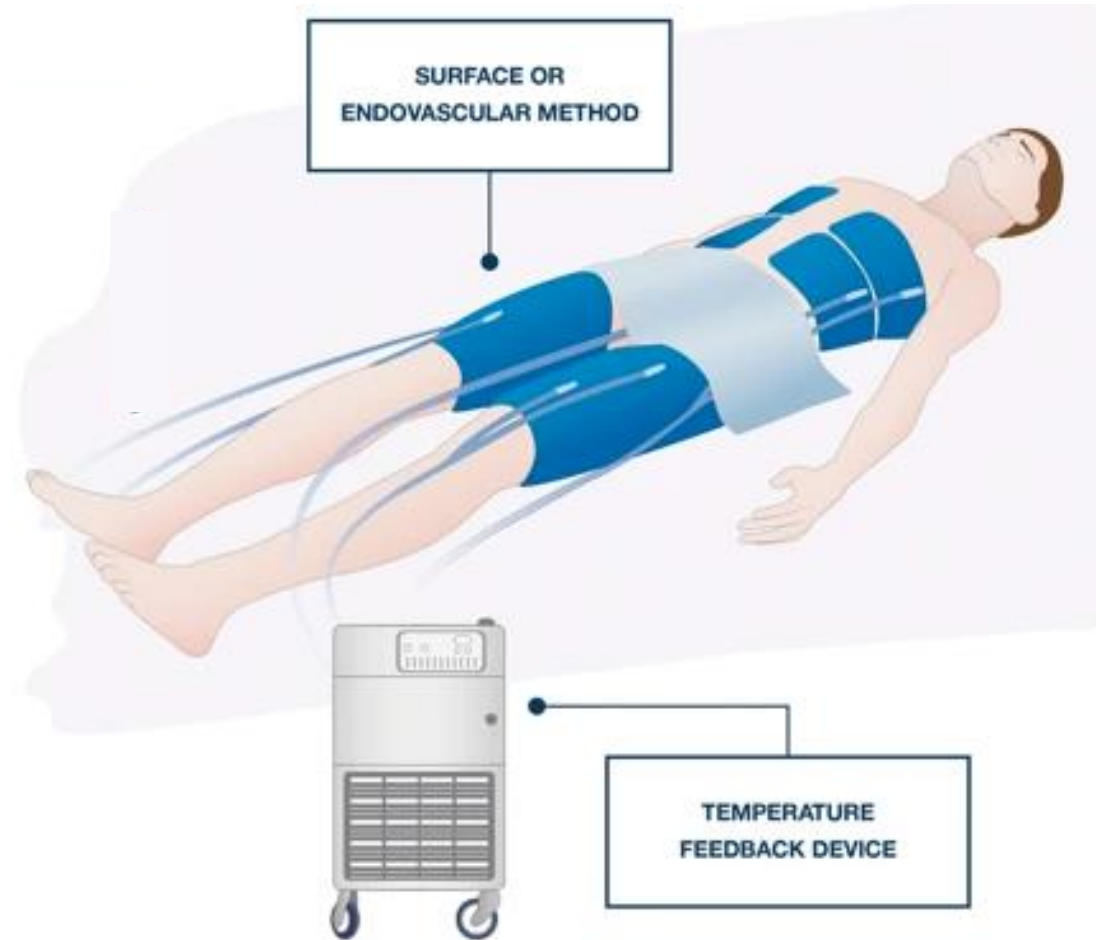


Image source: <<https://ccforum.biomedcentral.com/articles/10.1186/s13054-019-2721-1>>

TTM: External Cooling Device

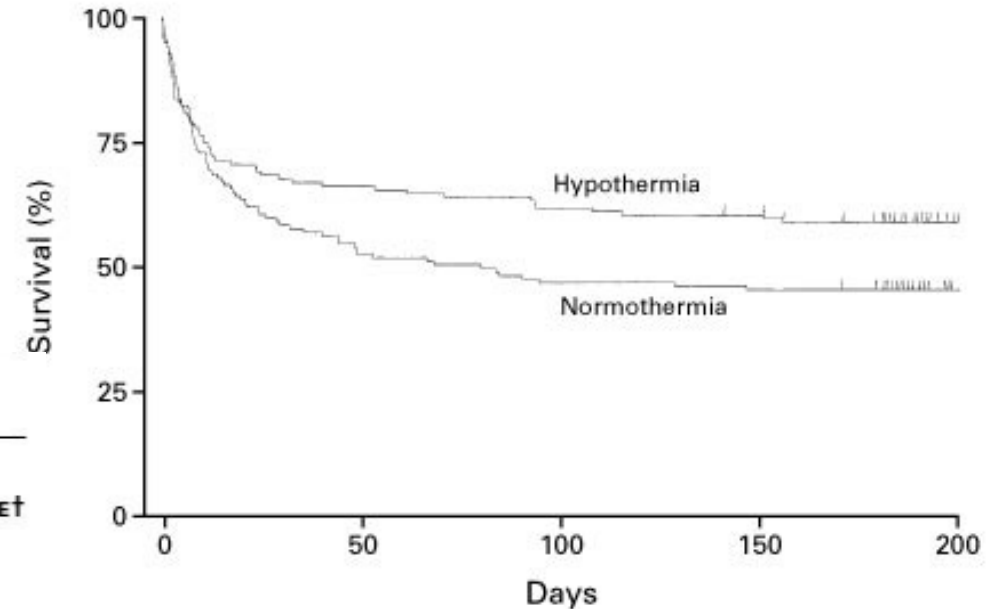
Why do TTM?

- Two landmark trials in 2002 published in NEJM showed that cooling:
 - Improves survival
 - NNT = 7 (to prevent 1 death)
 - Improves neurologic outcome

TABLE 2. NEUROLOGIC OUTCOME AND MORTALITY AT SIX MONTHS.

OUTCOME	NORMOTHERMIA	HYPOTHERMIA	RISK RATIO (95% CI)*	P VALUE†
	no./total no. (%)			
Favorable neurologic outcome‡	54/137 (39)	75/136 (55)	1.40 (1.08–1.81)	0.009
Death	76/138 (55)	56/137 (41)	0.74 (0.58–0.95)	0.02

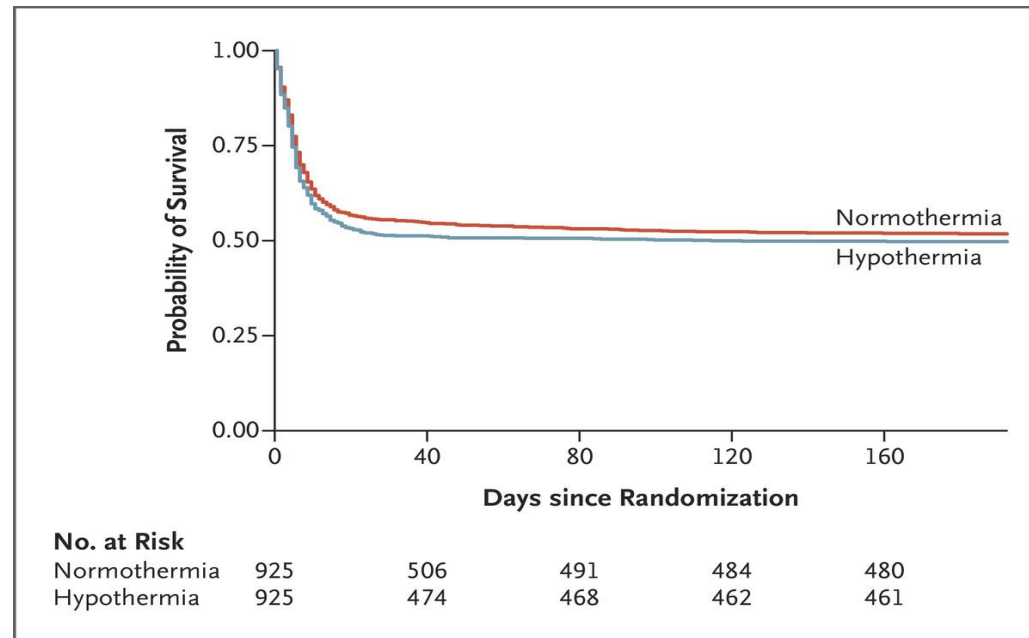
“Mild Therapeutic Hypothermia to Improve the Neurologic Outcome after Cardiac Arrest.” NEJM 2002; 346: 549-556.



Bernard, S. et al. “Treatment of Comatose Survivors of Out-of-Hospital Cardiac Arrest with Induced Hypothermia.” NEJM 2002; 346: 557-563.

2021 Update

- TTM-2 Trial (June 2021)
 - 1900 patients with OHCA enrolled, 1861 randomized
 - Targeted hypothermia (33°C) vs Targeted normothermia (<37.8 °C)
 - Primary outcome = death @6 months → no difference
 - Secondary outcome = functional status @ 6 months → no difference



Dankiewicz, J et al. "Hypothermia versus Normothermia After Out-of-Hospital Cardiac Arrest." NEJM 2021; 346: 2283-2294.

TTM-2 Controversies

- The trial did not include a group without TTM – does the trial simply demonstrate the benefit of using a protocolized approach to temperature management and/or avoidance of large temperature swings?
- The patient population in this trial (OHCA, s/p bystander CPR, no shock) is different than that of prior TTM trials that have shown benefit – does the trial indicate that we have yet to identify the subgroup of patients who benefit most from TTM?
- Still unclear how the findings from TTM-2 will be incorporated into practice guidelines – will recommendations change?

Explaining other answers...

- (A) STAT head CT to rule out CNS catastrophe. → With no focal neuro deficits, likely low yield.
- (B) Refer for hyperbaric oxygen for possible hypoxic brain injury. → Hypoxic brain injury is not an indication for hyperbaric oxygen.
- (C) Begin external cooling of patient to 32° C for 12 hours → TTM is recommended for at least 24 hours.
- (D) Activate protocol for targeted temperature management of patient. → Correct answer!
- (E) Hold a family meeting to relay his poor prognosis and discuss withdrawal of care. → In patients who are candidates for TTM, neuro-prognostication should occur 72 hrs after the patient returns to normothermia.

Prognosis after arrest

- Poor neurologic outcome associated with:

Clinical Finding	Time after cardiac arrest
Absence of pupillary light reflex	72 hours
Presence of status myoclonus	During first 72 hours
Absence of N20 somatosensory evoked potential cortical wave	24-72 hours
Marked reduction in gray-white ratio on Brain CT	Within 2 hours
Extensive restriction of diffusion on brain MRI	2-6 days
Persistent absence of EEG reactivity to external stimuli	72 hours
Persistent burst suppression or intractable status epilepticus	After rewarming

Prognosis after arrest

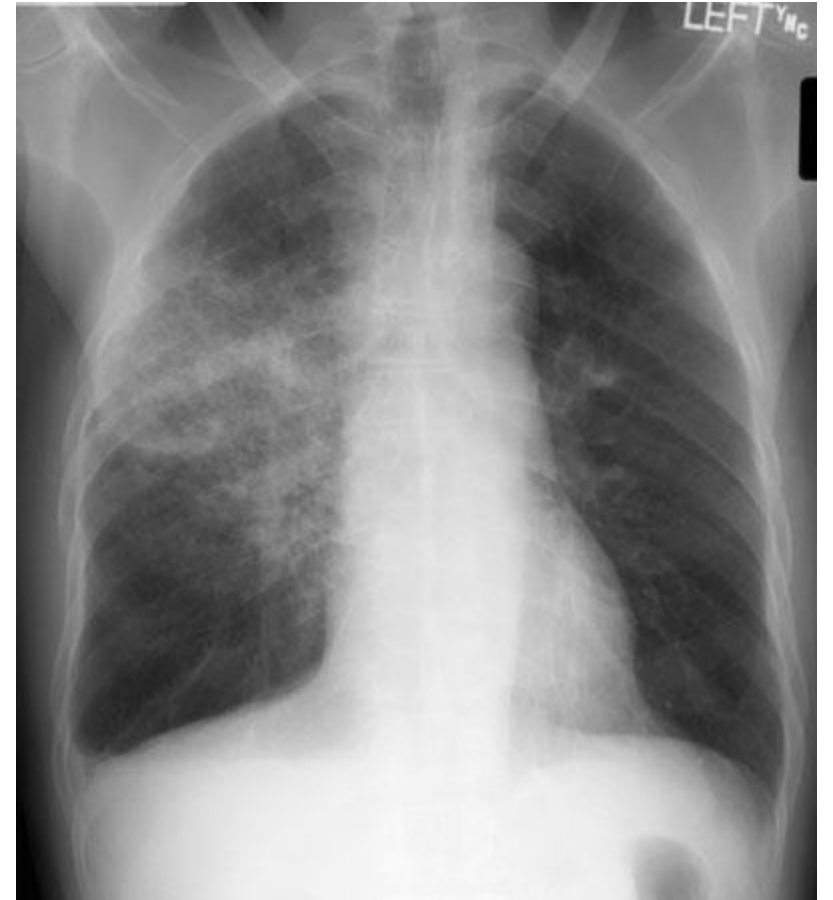
- Neurologic prognostication **can not** occur when a patient is cooled
 - Wait 72 hrs after normothermia is achieved to examine and assess
 - Multiple modalities of testing and examination should be used together to predict neurologic outcome

Learning Objectives: Targeted Temperature Management (TTM)

- TTM **improved outcomes** in patients who remain unconscious with ROSC after out of hospital cardiac arrest
 - Improvement in survival and neurologic function
- TTM with a goal temperature of 33°C does not confer benefit compared to 36°C (NEJM 2013)
- Neuro-prognostication can not be performed when a patient is hypothermic
 - Though there are clinical markers of poor prognosis earlier, wait 72 hours after the patient is normothermic to formally assess and prognosticate

Question 5: Part A

- An 81-year-old man with a past medical history of HTN, DM2, and mild emphysema is admitted with pneumonia.
- Vital signs:
 - BP 100/60 (baseline 140/80)
 - HR 110 bpm
 - SpO2 92% on 10L
 - Temp 101.8 F
- Labs:
 - WBC 15K
 - Cr 1.2 (baseline 1)
 - Electrolytes normal
 - Glucose 220



Question 5: Part A

Which of the following is true?

- (A) Hyperglycemia in the critically ill is associated with increased mortality.
- (B) Targeting “tight” glucose control (80-110 mg/dl) is associated with a mortality benefit compared to a goal of <180 mg/dl.
- (C) Targeting “tight” glucose control (80-110 mg/dl) is associated with shorter ICU length of stay.
- (D) Hyperglycemia is only problematic for critically ill patients with diabetes.
- (E) Episodes of hypoglycemia when targeting “tight” glucose control (80-110 mg/dl) are insignificant if protocols are adhered to.

Hyperglycemia in the ICU

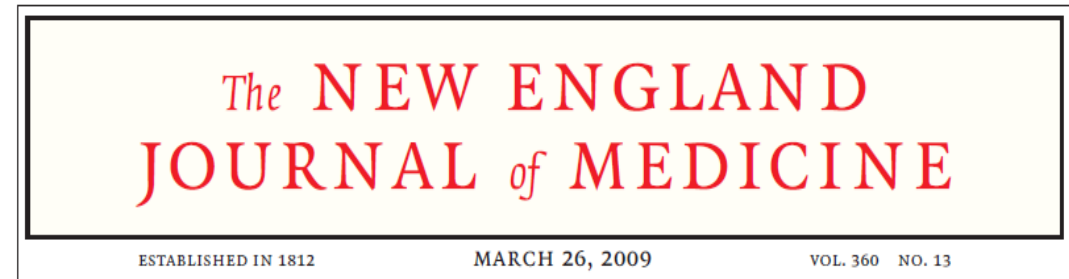
- Studies have shown that hyperglycemia is associated with worse outcomes in various populations of patients
 - Patients after MI (Lancet 2000)
 - Stroke patients (Stroke, 2001)
 - ICU patients (Mayo Clinic Proc, 2003)
 - Trauma patients (Am Surg, 2007)
- Does tight glucose control in the ICU mitigate this risk and improve mortality?

Hyperglycemia in the ICU

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 - Patients after MI (Lancet 2000)
 - Stroke patients (Stroke, 2001)
 - ICU patients (Mayo Clinic Proc, 2003)
 - Trauma patients (Am Surg, 2007)
- Does tight glucose control in the ICU mitigate this risk and improve mortality?
 - No! (NEJM, 2009)

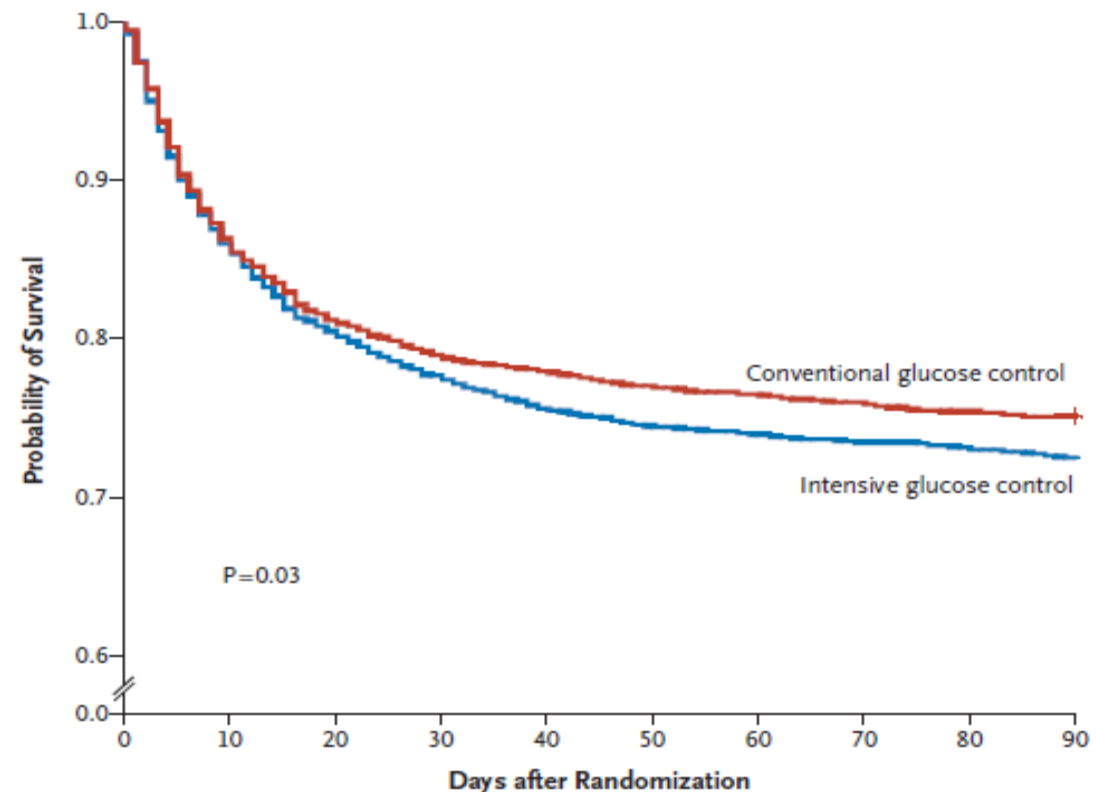
Glycemic Control in the ICU

- RCT with 6100 patients
 - Tight control (glucose goal 80-110 mg/dl)
 - Conventional control (glucose goal <180 mg/dl)
- Tight control associated with **higher** mortality
 - Absolute risk of death at 90 days up 2.6 %
 - Number needed to harm = 38
- Severe hypoglycemia (glucose \leq 40 mg/dl) more common in tight control group (6.8% vs 0.5%)



Intensive versus Conventional Glucose Control in Critically Ill Patients

The NICE-SUGAR Study Investigators*



Explaining other answers...

(A) Hyperglycemia in the critically ill is associated with increased mortality.

→ Correct answer!

(B) Targeting “tight” glucose control (80-110 mg/dl) is associated with a mortality benefit compared to a goal of <180 mg/dl.

→ Tight glucose control is associated with increased mortality compared to conventional glucose control.

(C) Targeting “tight” glucose control (80-110 mg/dl) is associated with shorter ICU length of stay.

→ There was no difference in ICU LOS for patients with tight versus conventional glucose control.

(D) Hyperglycemia is only problematic for critically ill patients with diabetes.

→ Hyperglycemia is associated with mortality in ICU patients regardless of presence/absence of DM.

(E) Episodes of hypoglycemia when targeting “tight” glucose control (80-110 mg/dl) are insignificant if protocols are adhered to.

→ Episodes of severe hypoglycemia occur **more frequently** with tight glucose control.

Learning Objectives: Glycemic Control in the ICU

- **Tight glucose control is not recommended for ICU patients** as it has been shown to be associated with increased mortality
 - Instead, target a glucose <180 mg/dl in critically ill patients

Question 5: Part B

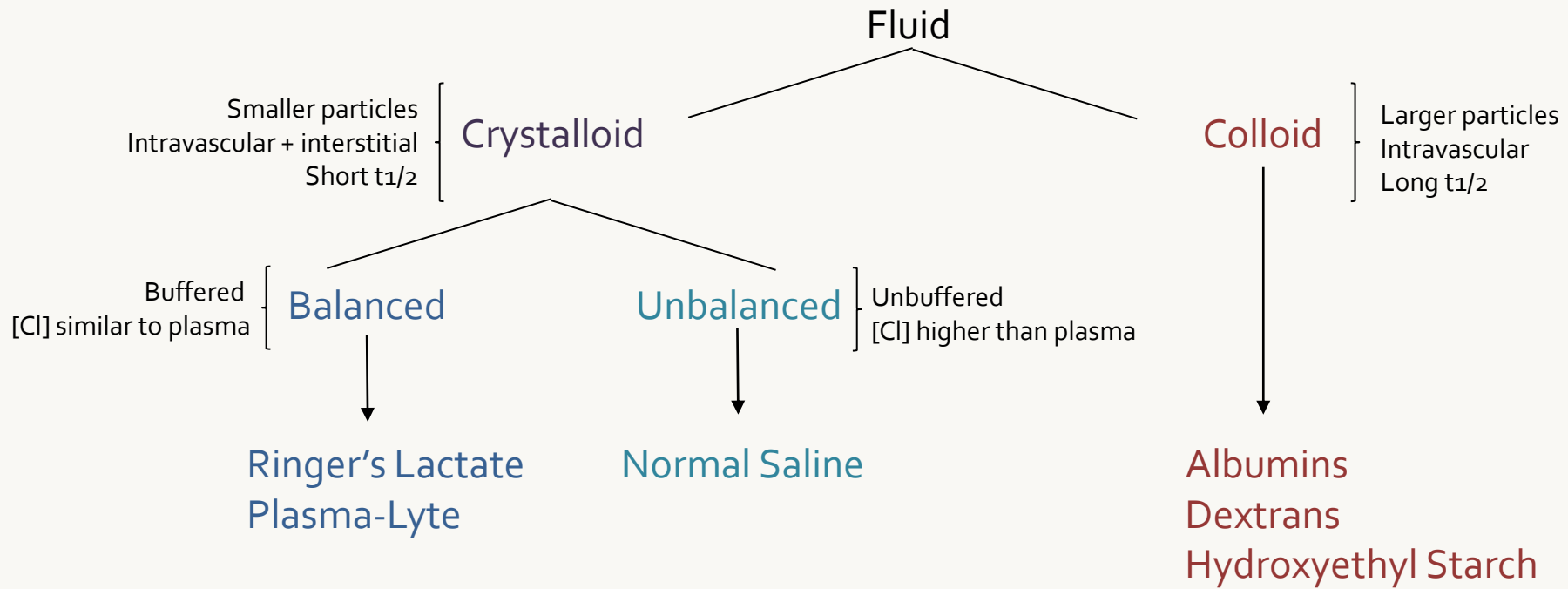
- Before transfer out of the ED, the patient was given 1L of normal saline, blood cultures were drawn, and empiric broad spectrum antibiotics started.
- He became progressively altered and was ultimately intubated for acute hypoxemic and hypercarbic respiratory failure prior to transfer to the ICU.
 - Blood pressure remains low
 - Urine output 10cc in the last hour
 - Lactate is elevated

Question 5: Part A

Which of the following is true regarding fluids for this patient with septic shock?

- (A) Compared to crystalloids, resuscitation with colloids cause less renal dysfunction but increased mortality.
- (B) Resuscitation with hydroxyethyl starch is associated with decreased mortality.
- (C) Resuscitation with balanced crystalloids may cause less renal dysfunction than unbalanced crystalloids.
- (D) Normal saline is the most commonly used balanced crystalloid resuscitation fluid.
- (E) Resuscitation with crystalloids combined with albumin is associated with a mortality benefit.

Fluid Resuscitation: Types of Fluid



Fluid for Resuscitation in Sepsis

- Colloid vs Crystalloid?
 - **Point:** Colloid may be protective of renal function given its tendency to remain intravascular as this could help the kidney maintain an adequate GFR.
 - **Counterpoint:** With the capillary dysfunction that occurs with sepsis, the potential benefit of colloid fluid remaining intravascular may be minimal or non-existent.

Fluid for Resuscitation in Sepsis

- Colloid vs Crystalloid?
 - SAFE 2004 (NEJM): albumin vs. saline
 - no difference in new organ failure, need for RRT, volume of fluid needed
 - CRISTAL 2013 (JAMA): colloid (albumin, dextran, HES, etc.) vs. crystalloid (NS, LR etc.)
 - no difference mortality or need for RRT
 - ALBIOS 2014 (NEJM): crystalloid + albumin vs. crystalloid alone
 - no diff mortality, renal injury, need for RRT
 - Meta-analysis of 9 studies with HES vs. crystalloids or albumin
 - Higher risk mortality and dose dependent effect causing AKI and need for RRT

Finfer, S. et al. "A comparison of albumin and saline for fluid resuscitation in the intensive care unit". NEJM. 2004. 350:2247-2256.

Annane D, et al. "Effects of fluid resuscitation with colloids vs. crystalloids on mortality in critically ill patients presenting with hypovolemic shock" JAMA. 2013. 310: 1809-1817.

Caironi P, et al. "Albumin replacement in patients with severe sepsis or septic shock". NEJM. 2014. 370(15):1412-1421.

Rhodes, A., et al. "Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2016." Intensive Care Medicine. 2017. 43: 304-377.

Fluid for Resuscitation in Sepsis

- Colloid vs Crystalloid?
 - No difference in outcomes aside from hydroxyethyl starches
 - Guidelines recommend against use of hydroxyethyl starches
 - **Guidelines recommend use of crystalloids for resuscitation** over colloids
 - Given similar outcomes and lower cost in most of the world

Fluid for Resuscitation in Sepsis

- Balanced vs unbalanced crystalloids?
 - **Point:** Fluids with $[Cl] >$ plasma chloride may cause GFR to fall by offsetting natural compensatory mechanism of kidney to maintain GFR via sensing at the macula densa
 - **Counterpoint:** Unclear if this natural compensatory mechanism, and the impact of high $[Cl]$ fluids, is altered in patients with septic physiology.

Fluid for Resuscitation in Sepsis

- **Balanced vs unbalanced crystalloids?**
 - Yunos et al., JAMA 2012: pre/post study, chloride-rich vs chloride-poor IVF
 - Balanced fluids associated with less AKI and less need for RRT
 - Limited by pre/post design + changing standard of care re. timing of initiating RRT
 - SPLIT, JAMA 2015: multicenter RCT of balanced vs unbalanced fluid, med/surg ICUs
 - No difference AKI or need for RRT
 - SALT-ED, NEJM 2018: open-label single center RCT (LR/PL vs. NS), ED patients
 - No difference in median hospital-free days (to day 28)
 - Balanced fluids better on composite outcome (death, new RRT, persistent renal dysfunction)
 - SMART, NEJM 2018: open-label single center RCT (LR/PL vs NS) med/surg ICUs
 - Balanced fluid better on composite outcome (death, new RRT, persistent renal dysfunction)

Yunos, N., et al. "Association Between a Chloride-Liberal vs Chloride-Restrictive Intravenous Fluid Administration Strategy and Kidney Injury in Critically Ill Adults." JAMA. 2012; 308: 1566-1572.

Young, P., et al. "Effect of a Buffered Crystalloid Solution vs Saline on Acute Kidney Injury Among Patients in the ICU." JAMA. 2015. 314: 1701-1710.

Self W, et al. "Balanced crystalloids versus saline in noncritically ill adults". NEJM. 2018. 378(10):819-828.

Semler MW, et al. "Balanced Crystalloids versus Saline in Critically Ill Adults". NEJM. 2018. 378(9):829-839.

Fluid for Resuscitation in Sepsis

- Balanced vs unbalanced crystalloids?
 - 2016 surviving sepsis campaign recommendation does not favor one over the other given variable evidence
 - With more recent trials, may shift recommendation in favor of balanced crystalloids
 - However there are still limitations to these studies, and more evidence is likely needed before guidelines are adjusted

Explaining other answers...

- (A) Compared to crystalloids, resuscitation with colloids cause less renal dysfunction but increased mortality. → There is no difference in renal dysfunction or mortality associated with use of crystalloids or colloids for resuscitation.
- (B) Resuscitation with hydroxyethyl starch is associated with decreased mortality. → Hydroxyethyl starch is associated with renal dysfunction, not decreased mortality.
- (C) Resuscitation with balanced crystalloids may cause less renal dysfunction than unbalanced crystalloids. → Correct answer!
- (D) Normal saline is the most commonly used balanced crystalloid resuscitation fluid. → Normal saline is an unbalanced crystalloid fluid.
- (E) Resuscitation with crystalloids combined with albumin is associated with a mortality benefit. → There is no mortality benefit to resuscitation with crystalloids with albumin compared to crystalloids alone.

Learning Objectives: Fluid Resuscitation

- Type of fluid for resuscitation in septic shock seems to impact outcomes
 - Crystalloids are recommended over colloid for initial resuscitation because there is no clear benefit (regarding renal dysfunction or mortality) to using colloids and colloids often cost more
 - Hydroxyethyl starches should be avoided for resuscitation, they cause renal dysfunction in a dose-responsive pattern
 - Data suggests balanced crystalloids may be associated with improved outcomes (renal dysfunction and mortality)

Thank you
very much for
your time!

- Please feel free to email any questions to the course directors!