



Brigham and Women's Hospital

Founding Member, Mass General Brigham

Evidence-Based Preventative Therapy in the ICU

Kathleen J. Haley, MD

Associate Physician

Department of Medicine, Division of Pulmonary and

Critical Care Medicine

Brigham and Women's Hospital

Assistant Professor of Medicine

Harvard Medical School



Kathleen Haley, MD



Pennsylvania State University Medical College
Medicine Residency and Pulmonary Medicine
Fellowship @ NEDH

Critical Care and Research Fellowship @ BWH
Assistant Professor of Medicine @ HMS

- Clinical focus: Critical Care Medicine
- Research focus: Chronic Critical Illness and Asthma
- Member of the BWH Ethics Committee
- Director, Spaulding Cambridge Hospital Ventilator Service

Conflict of Interest/Financial Disclosure

I am a co-investigator on the NIH-funded PrecISE Trial Network and the IDEA Trial. Within the last three years, the following companies have provided study drugs for the PrecISE Trial Network: GlaxoSmithKline, Laurel, Sun Pharma, Vifor, Vitaeris/CSL Behring, Vataflo, Sanofi-Aventis/Regeneron, and Organon.

I am a co-investigator on industry-sponsored trials, which use study drugs supplied by Sanofi, TEVA, Astra Zeneca, and AMGEN.



Common ICU Complications

DVT/PE

GI bleeding

Ventilator-associated events

Central line infections

Pressure injuries

(Delirium)



Case

72yo man, h/o CAD (on ASA), HTN, severe COPD, s/p RUL resection 1 month prior to admission admitted to the ICU with respiratory failure and sepsis due to pneumonia. He was intubated in the ED and is currently on 3 micrograms/kg/hr norepinephrine. His labs show a creatinine 0.7, INR of 2.1, PTT 33, and platelets of 95. What is the best approach for DVT prophylaxis for this patient?

- A. No prophylaxis needed since the patient has an elevated INR and he is already on daily ASA
- B. Enoxaparin, 40mg QD SQ
- C. Unfractionated heparin 5000U SQ BID or TID
- D. Intermittent compression boots (“pneumoboots”)
- E. Enoxaparin 40mg QD SQ and stop ASA



Case

72yo man, h/o CAD (on ASA), HTN, severe COPD, s/p RUL resection 1 month prior to admission admitted to the ICU with respiratory failure and sepsis due to pneumonia. He was intubated in the ED and is currently on 3 micrograms/kg/hr norepinephrine. His labs show a creatinine 0.7, INR of 2.1, PTT 33, and platelets of 95. What is the best approach for DVT prophylaxis for this patient?

A. No prophylaxis needed since the patient has an elevated INR and he is already on daily ASA

B. Enoxaparin, 40mg QD SQ

C. Unfractionated heparin 5000U SQ BID or TID

D. Intermittent compression boots (“pneumoboots”)

E. Enoxaparin 40mg QD SQ and stop ASA



The problem: Deep Venous Thrombosis (DVT)

DVT and PE are common in ICU patients

- 10 - 33% ICU patients in MICU >48hr had DVT on ultrasound study^{1,2,3}
- Risk in ICU patients > floor medical patients

DVT and PE have significant attributable morbidity and mortality

- Asymptomatic proximal DVT has 11 - 13% risk of death at 90; 2 – 4.8% without DVT^{4,7}
- DVT and PE occur together – 10% ICU patients with DVT also had PE^{2,5}
- PE is not commonly suspected on clinical grounds – > 50% of the PEs detected on autopsy were unexpected⁶

References:

1. DR Hirsch et al. JAMA 1995; vol 274 pp 335-337
2. DJ Cook et al. Crit Care Med 2005; vol 31 pp 48-55
3. PE Marik et al. Chest 1997; vol 111 pp 661-664
4. PT Vaitkus et al., Thromb Haemost 2005; vol 93 pp76-79
5. EH Ibrahim et al., Crit Care Med 2002; vol 30 pp 771-774
6. LA Pineda et al., Chest 2001; vol 120 pp791-795
7. GE Raskob et al., J Am Heart Assoc 2021; vol 10; e019459



ICU patients are at-risk for DVT

Patient Characteristics

- Immobilization
- Cancer (due to disease itself and cancer therapies)
- Hypercoagulable state
- Age
- Cardiac failure
- Burns/trauma and recent surgery
- CVA
- Obesity

Risks associated with ICU care

- Medications (sedation, paralytics)
- Mechanical ventilation
- Central venous lines



Evidence for Prevention

Prophylaxis works

- VTE decreased up to 57%
- Pharmacologic > Mechanical

Prophylaxis is not used consistently

- Underuse
 - Average of 70% ICU patients on prophylaxis in 16 studies (range 33 – 100%)
- Interruptions
 - Bleeding
 - Procedures
 - Coagulopathy



Regimens (ACCP Guidelines, Ninth edition ¹⁻², ASH 2018 Guidelines³, Seminars in Resp and Crit Care Med⁴)

Pharmacologic (medical and non-orthopedic surgical patients)

- Heparin: Low molecular weight heparin (LMWH) or unfractionated (UFH)
- Rivaroxaban

Additional approaches for orthopedic surgical patients

- Direct thrombin inhibitor (dabigatran – off label use)
- Additional selective Xa inhibitors: apixaban, rivaroxaban
- Fondaparinux
- Anti-vitamin K agent: warfarin (goal INR 2 – 3)

Mechanical (all patients, can be added to pharmacologic methods)

- Problems: Not as effective as pharmacologic prophylaxis, can cause skin ulcerations
- Benefits: No bleeding

References:

1. SR Kahn et al., Chest 2012; vol 141 (2 Suppl) pp e195S-226S
2. Y Falck-Ytter et al., Chest 2012; vol 141 (2Suppl) pp e278S – e325S
3. HJ Schunemann et al., Blood Advances 2018; vol 2 pp 3198 – 3225
4. K MacDougall and AC Spyropoulos, Semin Resp Crit Care Med 2021; vol 42: 308 - 315



Low molecular weight heparins (LMWH)

Advantages over unfractionated heparin¹

- Once daily dosing
- Fewer side effects

Effective

- Enoxaparin 40 mg SQ daily decreased DVT with side effects similar to placebo (MEDENOX trial)²

Problems

- More dependent on renal clearance, varies among LMWH
- Not usually weight based – “capped” doses hard to adjust for obese patients

References:

1. JI Weitz, NEJM 1997; vol 337 pp 688-698
2. MM Samama et al. NEJM; vol 341 pp 793-800



Unfractionated heparin

Long track record of effectiveness

- Decreases DVT approximately 60%¹

BID or TID

- TID more effective, but more bleeding²

Doesn't depend on renal clearance

Complications

- Heparin-induced thrombocytopenia (HIT) up to 0.5 - 3%

References:

1. JF Cade, Crit Care Med 1982; vol 10 pp 448-450
2. CS King et al., Chest 2007; vol 131 pp 507-516



Heparin-Induced Thrombocytopenia (HIT)

>50% decrease in platelet count in patients who have received heparin

Differentiated from the early (<2d exposure), transient, <50% platelet decrease

HIT is antibody-mediated (anti-PF4); occurrence UFH >> LMWH

Associated mortality up to 30%

Incidence 0.5 – 5%

Risk factors:

Female patients 2X increased risk

Prolonged exposure (>5d)

Bovine heparin > porcine

Surgical patients (cardiac, trauma, orthopedic) 1 – 5% incidence >> medical (<1%)

Cancer

Extracorporeal membrane oxygenation

Major complication is thrombosis – 50 – 89% patients with HIT

Treatment is anticoagulation: argatroban, bivalirudin

Defer warfarin until platelets have returned to baseline



What about Alternative Agents?

ASA

- Decreased thrombosis risk compared to placebo
- BUT: Less effective and increased risk of bleeding

Direct Xa inhibitors (fondaparinux, rivaroxaban, apixaban)

- 2020 Rivaroxaban approved by FDA for DVT prophylaxis in medical patients
- Can be used for patients with HIT (off label)
- Effective - decreased DVT 46% compared to placebo, same major bleeding as placebo (0.2%) (Arixtra for ThromboEmbolism Prevention in a Medical Indications Study: ARTEMIS trial)¹
- Renal excretion – need to dose adjust for renal insufficiency²
- All anti-Xa agents are FDA approved only for post-operative DVT prophylaxis and treatment of PE and DVT

References:

1. AT Cohen et al., BMJ 26 January 2006
2. R Selby and W Geerts, Hematology 2009; pp 286-292
3. K MacDougall and AC Spyropoulos Semin Resp Crit Care Med 2021; pp 308 - 315



Direct thrombin inhibitors

Approved for patients with heparin-induced thrombocytopenia (HIT)

Lepirudin (Hirudin derivative)

- Available for SC injection – monitor with aPTT
- Allergic reactions and anaphylaxis
 - Antihirudin in up to 40% treated patients; Ab presence delays clearance
- Renal excretion

Argatroban and Bivalirudin

- Only IV administration – monitor with aPTT
- Half-life dramatically impacted by clearance
 - Argatroban affected by hepatic function; FDA approved for HIT
 - Bivalirudin affected by renal function; off label use in HIT
- Interfere with INR assay (Argatroban > Bivalirudin)

Oral agents (e.g. dabigatran) off label use in HIT

- Very limited clinical experience so far
- Available studies show similar VTE and PE rates
 - Higher major bleeding rates with DOAC
 - Use only if required for another reason



Case, continued

On HD 2 the patient has a witnessed aspiration with desaturation. That evening he developed hypotension and a new infiltrate on his CXR. He was started on vancomycin and cefepime for possible pneumonia. Overnight he became oliguric and his OGT output was noted to have “coffee grounds”. This morning’s labs show that his creatinine has increased from a baseline of 0.7 to 1.5. Also, his platelets have decreased from an initial value of 95 to 85.



Case, continued

Are there any changes that need to be made to his DVT prophylaxis?

- A. Since the patient is tolerating his current regimen no change is needed.
- B. Since his platelets have decreased, HIT must be excluded. Stop enoxaparin and start fondaparinux.
- C. Since his creatinine has increased and his platelets have decreased pharmacologic prophylaxis should be stopped and mechanical prophylaxis started.
- D. Since his creatinine has increased his enoxaparin should be changed to unfractionated heparin.
- E. Since his platelets have decreased and he has signs of GI bleeding the enoxaparin should be stopped, and mechanical prophylaxis started.



Case, continued

Are there any changes that need to be made to his DVT prophylaxis?

- A. Since the patient is tolerating his current regimen no change is needed.
- B. Since his platelets have decreased, HIT must be excluded. Stop enoxaparin and start fondaparinux.
- C. Since his creatinine has increased and his platelets have decreased pharmacologic prophylaxis should be stopped and mechanical prophylaxis started.
- **D. Since his creatinine has increased his enoxaparin should be changed to unfractionated heparin.**
- E. Since his platelets have decreased and he has signs of GI bleeding the enoxaparin should be stopped, and mechanical prophylaxis started.



Special considerations

Renal Insufficiency or failure

- LMWH is renally cleared, so unfractionated heparin generally preferred for severe renal dysfunction
- Dalteparin has been shown to be safe with GFRs to 30 ml

Morbid obesity³

- Need weight-based dose adjustments (actual, not ideal)
- Different proportion lean body to fat
- If enoxaparin used, a BID schedule is more effective than QD

References:

1. D Cook et al., Crit Care 2008; vol 12 R32
2. J Douketis et al., Arch Internal Med 2008 vol 168 pp 1805 – 1812
3. NP Clark Thrombosis Research 2008; vol 123 pp S58 – S61



But what about....

Coagulopathic patients

- Abnormalities in coagulation due to uremia or hepatic dysfunction are not protective^{1,2}
- Medical patients with thrombocytopenia are still at risk of VTE
- Mechanical means may be preferred here

GI bleeding

- Major GI bleeding in only 0.2% on DVT prophylaxis³

Spinal anesthesia⁴

- Increased risk of spinal hematoma – may need mechanical prophylaxis

References:

1. O Dabbagh et al., Chest 2010; vol. 137 pp 1145-1149
2. J Douketis et al., Arch Internal Med 2008; vol 168 pp 1805-1812
3. MJ Leonardi et al., Arch Surg 2006; vol 141 pp 790-797
4. R Selby and W Geerts, Hematology 2009; pp 286-292



What About Extended Prophylaxis?

Rationale: hypercoagulable state persists beyond hospital DC

VTE rates in patients at in-patient rehab 49/1000 admissions before prophylaxis QI¹

Available evidence from multicenter RCTs:

Enoxaparin lowered VTE in older women with poor morbidity (EXCLAIM, 7415 patients)²

Betrixaban lowered PE incidence but increased clinically relevant bleeding (APEX, 7513 patients)³

Rivaroxaban decreased PE incidence but increased bleeding (MAGELLAN, 8101 patients)⁴

Rivaroxaban at discharge did not decrease symptomatic or fatal PE (MARINER, 12024 patients)⁵

Apixaban (30 days) similar VTE/PE but higher bleeding c/w enoxaparin (ADOPT, 6528 patients)⁶

Persistent unknowns

Are there subgroups who would benefit from extended prophylaxis?

Should both arterial and venous thromboses be considered?

References

1. RS Mayer et al., PMR 2011; vol. 3 pp 1111 – 1115
2. RD Hull et al. Ann Int Med 2010; vol. 153 pp 8 – 18
3. AT Cohen et al., NEJM 2016; vol. 375 pp 534 – 544
4.  AT Cohen et al., NEJM 2013; vol. 368 pp 513 – 523
5. AC Spyropoulos et al., NEJM 2018; vol. 379 pp 1118 – 1126
6. SZ Goldhaber et al NEJM 2011; vol. 365 pp 2167 - 2177

Special Considerations: Primary Neurologic Diagnoses¹

All patients: pneumatic compression boots (IPC) on admission

CLOTS 3 study showed ARR 3.66% with IPC after ischemic stroke

Primary neuromuscular disease: pharmacologic prophylaxis (PP) on admission

Neurologic diagnoses with risk of hemorrhage: delay PP until hemorrhage risk decreased

- Ischemic CVA: pharmacologic prophylaxis once risk of hemorrhagic conversion decreases
- Aneurysmal subarachnoid hemorrhage: start UFH 24h after surgery or coiling
- Patients treated with thrombolysis or hemicraniectomy: delay PP for 24 hours
- Intracranial hemorrhage: PP if hematoma has been stable for 48h and no additional coagulopathy
- CNS malignancy: PP if no signs of hemorrhagic conversion
- Traumatic brain injury: PP timing depends on associated intracranial hemorrhage (stable x 24h) or craniectomy (24h postoperatively)
- Spinal cord injury: minimize time using IPC alone; start PP < 72h of admission

References:

1. Nyquist P. et al., Neurocritical Care 2016; vol. 24 pp 47 – 60
2. Dennis M. et al., Lancet 2013; vol. 382 pp 516 - 524



The Bottom Line

DVT/PE remains an important clinical problem but prophylactic therapy is effective

LMWH (enoxaparin) is the default prophylactic agent

- Even with minor bleeding and/or coagulopathies

- Antiplatelet agents less effective

- If oral agent desirable rivaroxaban now approved in medical patients

Patients with estimated GFR <30cc/hr should receive unfractionated heparin

Surgery patients have special considerations

- Orthopedic procedures – full anticoagulation or anti-Xa

- Neurosurgery procedures/CNS injury or CVA – wait until bleed risk subsides



Case, continued

Despite antibiotics and pulmonary toilet, the patient is unable to be extubated. What is true about GI prophylaxis for this patient?

- A. GI prophylaxis should be avoided since he already has signs of a pneumonia and GI prophylaxis increases the risk of ventilator associated pneumonia.
- B. GI prophylaxis is not needed since the patient has been on mechanical ventilation for less than one week.
- C. GI prophylaxis should be started using a high-dose proton pump inhibitor given the signs of recent GI bleeding.
- D. GI prophylaxis should be started with either a proton pump inhibitor or H2 blocker.
- E. Medications for GI prophylaxis are not needed since the patient has been started on tube feeds.



Case, continued

Despite antibiotics and pulmonary toilet, the patient is unable to be extubated. What is true about GI prophylaxis for this patient?

- A. GI prophylaxis should be avoided since he already has signs of a pneumonia and GI prophylaxis increases the risk of ventilator associated pneumonia.
- B. GI prophylaxis is not needed since the patient has been on mechanical ventilation for less than one week.
- C. GI prophylaxis should be started using a high-dose proton pump inhibitor given the signs of recent GI bleeding.
- D. GI prophylaxis should be started with either a proton pump inhibitor or H2 blocker.**
- E. Medications for GI prophylaxis are not needed since the patient has been started on tube feeds.



The Problem: Stress ulcers

Abnormal GI mucosa

- Common (approximately 75% patients) by EGD evaluation¹
- Clinically important bleeding in 0.2 – 6 % ICU patients^{2,3}

Risk factors

- Mechanical ventilation >48 hours²
- Coagulopathy²
- Older age³
- Sepsis and septic shock³
- Steroid therapy³
- MSOF³
- Liver disease⁴
- Renal replacement therapy⁴
- GI ulcer or bleeding within past year⁴
- Burns >35% BSA⁴
- Traumatic brain injury or spinal cord injury⁴

References:

1. DA Peura et al., Annals of Int Med 1985; vol 103 pp 173-177
2. DJ Cook et al., NEJM 1994; vol 330 pp 377-381
3. M Pimentel et al., Am J Gastroenterology 2000; vol 95 pp 2801-2806
4. D Cook and G Guyatt, NEJM 2018; vol. 378: pp 2506 - 2516



Current Evidence

Stress Ulcer Prophylaxis in the Intensive Care Unit (SUP-ICU)¹

- Multicenter, blinded trial in 33 European ICUs
 - 3298 patients: 1645 pantoprazole, 1653 placebo
- Compared pantoprazole prophylaxis to placebo
- Outcomes
 - Primary: 90-day mortality – no differences
 - Composite outcomes (clinically important GI bleed, C difficile infection, pneumonia, myocardial ischemia) – no difference
 - Clinically significant bleeding – PPI less (2.5 versus 4.2%) but not statistically significant

Reference:

1. M. Krag et al., NEJM 2018; vol. 379 pp 2199 – 2208.



Regimens

Histamine receptor blockers (IV or enteral)

- Significant drug interactions

Proton pump inhibitors (PPI, IV or enteral)

- Slightly more consistent acid suppression than histamine receptor blockers¹
- May interfere with clopidogrel – due to inhibition of cytochrome P450 2C19²
 - Clopidogrel must be activated by cytochrome P450 2C19 to work
- Concern regarding side effects, especially association with C. difficile

Enteral feeding

- Early data suggest this may be very effective

Sucralfate (enteral)

- Significant downsides and less effective (not recommended)

References:

1. W Alhazzani et al., Critical Care Med 2013; vol 41 epub Jan 9
2. GM Mutlu et al., Am J Respir Med 2003; vol 2 pp 395 – 411
3. L Laine and C Hennekens, Am J Gastroenterology 2010; vol 105 pp 34 – 41
4. D Cook et al., NEJM 1998; vol 338 pp 791-797



Prophylaxis recommendations

Use prophylaxis only in patients with clear indications

- Mechanical ventilation >48h
- Coagulopathy and/or thrombocytopenia
- GI ulcer or bleeding within 1 year
- Multisystem disease
- Severe comorbid process with significant physiologic stress

Stop prophylaxis once increased risk resolved



The Problem: Ventilator-associated Events

Covers all complications of mechanical ventilation

Includes ventilator-associated pneumonia (VAP)¹

- Two days of stable or decreasing ventilator settings followed by at least two days of worsening ventilator settings
- Subclassifications of infectious ventilator complications: Infection-related ventilator-associated complication (IVAC) and

Possible ventilator-associated pneumonia

IVAC and VAP have significant morbidity and mortality

- Frequent complication of mechanical ventilation – 8 – 28% patients²
- Increases length of stay both surgical and medical patients
- Significant absolute mortality: up to 76%, depending on causative organism²
- In medical patients, attributable mortality approximately 30%³

References:

1. M Klompas Am J Resp Crit Care Med 2015; vol 192 pp 1420 - 1430
2. J Chastre and J-Y Fagon, Am J Resp Crit Care Med 2002; vol 165 pp 867-903
3. CA Fleming et al. Med Clin N Am 2001; vol 85 pp 1545 - 1563



Preventing IVAC and VAP: ventilator considerations

Type of suction – closed, in-line best

Humidifier considerations

- Heat and moisture exchangers are better than heated humidifiers
- Heat and moisture exchangers should be changed weekly
 - More frequent changes have higher VAP rates

Circuit changes

- Frequency increases costs and doesn't decrease VAP

References:

1. P Dodek et al., Annals of Int Med 2004 vol 141 pp305-313
2. M Klompas et al., Am J Resp Crit Care Med vol 191 pp 292 - 301



Preventing IVAC and VAP: prevent aspiration

Effective VAP prophylaxis reduces aspiration of infected secretions

- Head of bed up
- Subglottic suctioning can be considered
- Maintain adequate (20 cm water) cuff pressure
- Avoid nasotracheal intubation
- Maintain oral hygiene
 - Chlorhexidine is controversial for medical patients
 - IV Antibiotics for GI tract decontamination may have role

Rocking beds helpful but expensive

Early tracheostomy not effective³

- Multicenter study, 600 patients, showed only trends for decreased VAP

References:

1. P Dodek et al., Annals of Int Med 2004 vol 141 pp305-313
2. L. Bouadma et al., Crit Care Med 2010 vol 38 PP 789 – 796
3. PP Terragni et al. JAMA 2010 vol 303 pp 1483 - 1489



Selective Decontamination

Use of antibiotics to decrease bacterial burden in the GI tract

- Non-absorbable enteral regimens – colistin, polymyxin, tobramycin

- Sometimes with short course (<5d) IV antibiotics

Concern is that antibiotic use may affect local bacterial resistance patterns

Data on efficacy is mixed

- May depend on population:

 - Surgical populations, especially trauma

 - BMT patients

- Recent meta-analysis (Hammond et al., JAMA 2022 pp 1922 – 1934)

 - 32 randomized studies, total of 24,389 patients (18,335 from three trials)

 - SDD decreased mortality only when regimens included both IV and enteral antibiotics

 - Decreased VAP and bacteremia

- No significant effects on antibiotic resistance but data was judged to be low quality



VAEs require a mechanical ventilator

Although “airway protection” frequently invoked for reason to intubate, functional laryngeal reflexes are better at protecting the airway

- Noninvasive ventilation
- Early extubation
 - Daily sedation holidays
 - Daily evaluation for readiness to extubate



Case, continued

On review of your patient's labs, you note that there is a new blood culture report. A blood culture drawn 3 nights ago during a febrile episode is now showing *S. epidermidis*. The patient has a central venous line that was placed when he was hypotensive in the emergency room. His current VS are Temperature 100.7, HR 85, BP 135/72, RR 16 and his exam does not show redness at the insertion site. Which of the following is the best course of action?

- A. Start vancomycin to treat bloodstream infection
- B. Add "ethanol lock" to the central line
- C. Start nafcillin to treat bloodstream infection
- D. Review the protocol for central line hub cleaning with the bedside nurse
- E. Review the need for central access, remove line if feasible



Case, continued

On review of your patient's labs, you note that there is a new blood culture report. A blood culture drawn 3 nights ago during a febrile episode is now showing *S. epidermidis*. The patient has a central venous line that was placed when he was hypotensive in the emergency room. His current VS are Temperature 100.7, HR 85, BP 135/72, RR 16 and his exam does not show redness at the insertion site. Which of the following is the best course of action?

- A. Start vancomycin to treat bloodstream infection
- B. Add "ethanol lock" to the central line
- C. Start nafcillin to treat bloodstream infection
- D. Review the protocol for central line hub cleaning with the bedside nurse
- E. **Review the need for central access, remove line if feasible**



The Problem: Central Line-Associated Infections

Definition: Bloodstream infection ≥ 48 h after placement without alternative source¹

Central line associated bloodstream infections (CLABSI/CRBSI) are important preventable complications¹

Majority of hospital acquired bacteremias (approximately 60%) are CLABSI/CRBSI²

Increased ICU and hospital length of stay -> Increased costs

Significant associated with possible significant attributable mortality

Reportable quality measure

Risk Factors^{1,2,3,4}

Line location/use (dialysis lines most common associated)

Emergent placement

Severe comorbid disease

Malnutrition/BMI>40

Duration of use – patients with CLABSI had average of >20 days, without 5 - 8 days^{2, 3}

References:

1. N.P. O'Grady NEJM 2023; vol 389: 1121 – 1131
2. V. H. Mortensen et al., Infect Dis; vol 54: 178 - 185
3. H. Toor et al., Cureus 2022; vol 14:e22809
4. K Moriyama et al., Medicine 2022; 101: e31160



Prevention Strategies

Mechanisms of CLABSI/CRBSI

- Insertion site contamination

 - During insertion

 - During management

- Luminal spread

 - Hub contamination

 - Contaminated infusion

Preventative Strategies

- Minimize site contamination

- Ensure infusate sterility



Prevention Approaches¹

Management Target: Site contamination during insertion

- Strict hand hygiene/checklists

- Full barrier precautions and operator protective equipment (sterile gown/gloves/mask/hat)

- Site choice

- Antiseptic/antibiotic catheter coatings

- Line carts/kits

Management Target: Site contamination during management

- Strict hand hygiene/checklists

- Chlorhexidine/antibiotic site dressings

- Transparent dressings over insertion site

- Minimize number of lumens/minimize entry

- Remove line as soon as feasible

Management Target: Maintain infusate sterility

- Dedicated sterile hoods for medication preparation

- Use “closed system” (perforated septa) instead of “open” (stopcocks) for infusions



Results

Hospitals highly motivated to decrease CLABSI/CRBSI

2009 CMS targeted 50% decrease in CLABSI over 5yr

CLABSI rate negatively impacted CMS reimbursement

Prior to 2009 hospitals had already brought down average number of CLABSI by 58%¹

Preventative efforts work²

4-year program to decrease CLABSI rate showed 68% decrease²

Decrease was sustained over 10 years³

References

1. Srinivasan A. et al. MMWR 2011; 60: 243 - 248
2. Muto C. et al., MMWR 2005; 54: pp 1013 – 1016
3. Pronovost, P. J. et al. Am J Med Qual 2016; vol 3: pp 197 - 202



But...

Preventative efforts deteriorated during pandemic

Prevalence increased by 28% nationally, 39% in ICUs¹

Why?

Resources diverted away from prevention³

Practice changes to limit preventative measures³

Decreased tracking³

References

1. Patel, P. R. et al. Infect Control and Hosp Epidem 2022; vol. 43: pp 790 – 793
2. O’Grady, N. P. New Engl J Med 2023; vol 389: pp 1121 - 1131



The Problem: Hospital-Acquired Pressure Injuries

Common problem in the ICU¹

- Incidence 10 – 26%, Prevalence 17 – 24%
- About 9% are deep tissue injuries
- Pressure injuries associated with medical devices²
 - Wide variability among studies: 0.9 – 41.2% and prevalence 1.4% - 121% with averages 10 and 12%, respectively

Significant morbidity

Important reportable quality measure

References:

1. WP Chaboyer et al., Crit Care Med 2018 vol 46 e1074 – e1081
2. M Barakat-Johnson et al., J Wound Care 2019 vol 28 pp 512 - 521



Risk Factors

Age

Immobility

Vasopressor-dependent

Sedation

BMI (U-shaped)

Renal failure

Increased APACHE and ASA scores

Standardized scales in use

- e.g. Braden scale
- Most ICU patients score in the “high risk” category



Evidence-based Prevention

Maintaining good tissue perfusion

Frequent skin inspection

Early treatment if pressure injury identified

Maintaining good turning schedules

- Patients sometimes too unstable for turns
- Weight shifts not as effective as full turns

Specialized linens to reduce friction



Take-Home Points

1. Critically ill patients are at increased risk for venous thromboembolic disease (DVT and PE)
2. DVT Prophylaxis is effective, but only if it is used
3. Histamine receptor blockers or PPIs are effective prophylaxis strategies for preventing stress ulcers
4. The common denominator in IVAC and VAP prophylaxis is to avoid aspiration



Question 1

- You have admitted a 68 yr old man with sepsis due to pneumonia. As part of his routine admission orders, subcutaneous heparin is started for DVT prophylaxis. The patient has required mechanical ventilation and pressor support. Pertinent laboratories include a creatinine of 2.6, INR 2.2, and platelets of 95K (150K on admission labs). What should be done regarding his DVT prophylaxis?
- a. The subcutaneous heparin should be discontinued and mechanical DVT prophylaxis started since patient has signs of a coagulopathy
 - b. The subcutaneous heparin should be continued
 - c. The subcutaneous heparin should be changed to enoxaparin since the patient has evidence of renal insufficiency
 - d. The subcutaneous heparin should be discontinued. No DVT prophylaxis is needed since the patient is auto-anticoagulated with an INR of 2.6
 - e. The subcutaneous heparin should be discontinued and fondaparinux used for DVT prophylaxis



Question 1

You have admitted a 68 yr old man with sepsis due to pneumonia. As part of his routine admission orders, subcutaneous heparin is started for DVT prophylaxis. The patient has required mechanical ventilation and pressor support. Pertinent laboratories include a creatinine of 2.6, INR 2.2, and platelets of 95K (150K on admission labs). What should be done regarding his DVT prophylaxis?

- a. The subcutaneous heparin should be discontinued and mechanical DVT prophylaxis started since patient has signs of a coagulopathy
- b. The subcutaneous heparin should be continued**
- c. The subcutaneous heparin should be changed to enoxaparin since the patient has evidence of renal insufficiency
- d. The subcutaneous heparin should be discontinued. No DVT prophylaxis is needed since the patient is auto-anticoagulated with an INR of 2.6
- e. The subcutaneous heparin should be discontinued and fondaparinux used for DVT prophylaxis



Question 1, Explanation

Both enoxaparin and unfractionated heparin are standard medications for pharmacologic DVT prophylaxis. Pharmacologic prophylaxis is superior to mechanical prophylaxis, and so mechanical prophylaxis would only be used if there was a significant contraindication to pharmacologic prophylaxis. Unfractionated heparin does not have renal clearance and so is preferred over enoxaparin in patients with renal insufficiency.

Critically ill patients with thrombocytopenia and coagulopathy are at risk for bleeding, but they are also hypercoagulable and require DVT prophylaxis.

Heparin-induced thrombocytopenia (HIT) is uncommon and is usually associated with platelets decreasing by at least 50% from baseline and thrombotic events, particularly arterial thromboses. Patients with newly diagnosed HIT require therapeutic anticoagulation, not DVT prophylaxis, using bivalirudin or argatroban.

Fondaparinux is not FDA-approved for anticoagulation in patients with HIT, although it does have supportive clinical investigations. Fondaparinux is approved for DVT/PE treatment and also approved for DVT prophylaxis in post-operative orthopedic patients.



References for Question 1

Antithrombotic Therapy and Prevention of Thrombosis, 9th ed. American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2012; 141 (2Suppl)

- SR Kahn et al., Chest 2012; vol 141 (2 Suppl) pp e195S-226S
- MK Gould et al., Chest 2012; vol 141 (2Suppl) pp e227s – e277S
- Y Falck-Ytter et al., Chest 2012; vol 141 (2Suppl) pp e278S – e325S

MM Samama and F Kleber, Thrombosis Journal 2006; vol4: 8; doi:10.1186/1477-9560-4-8



Question 2

A 45 yr old man with respiratory failure due to pulmonary edema in the setting of cardiomyopathy and renal failure has just been admitted to your ICU. On admission, he is on norepinephrine to maintain his BP. He was intubated in the ED. Which of the following could decrease his risk of ventilator-associated pneumonia?

- a. Keep the head of the bed elevated, use in-line suctioning apparatus changed every 2days, add IV antibiotics for GI tract decontamination
- b. Keep the head of the bed elevated, change the humidifier circuit every week, proceed to tracheostomy if the patient requires ventilator support for more than 7d
- c. Use subglottic suctioning, add IV antibiotics and antifungals for GI tract decontamination, use in-line suctioning changed daily
- d. Use subglottic suctioning, keep the head of the bed elevated, maintain oral hygiene
- e. Keep the head of the bed elevated, proceed to early tracheostomy if the patient requires ventilator support for more than 7d, use oral topical (polymixin B) and IV antibiotics for GI tract decontamination



Question 2

A 45 yr old man with respiratory failure due to pulmonary edema in the setting of cardiomyopathy and renal failure has just been admitted to your ICU. On admission, he is on norepinephrine to maintain his BP. He was intubated in the ED. Which of the following could decrease his risk of ventilator-associated pneumonia?

- a. Keep the head of the bed elevated, use in-line suctioning apparatus changed every 2days, add IV antibiotics for GI tract decontamination
- b. Keep the head of the bed elevated, change the humidifier circuit every week, proceed to tracheostomy if the patient requires ventilator support for more than 7d
- c. Use subglottic suctioning, add IV antibiotics and antifungals for GI tract decontamination, use in-line suctioning changed daily
- d. Use subglottic suctioning, keep the head of the bed elevated, maintain oral hygiene**
- e. Keep the head of the bed elevated, proceed to early tracheostomy if the patient requires ventilator support for more than 7d, use oral topical (polymixin B) and IV antibiotics for GI tract decontamination



Explanation, Question 2

Aspirating infected material is the mechanism of ventilator-associated infectious complications. Interventions that decrease aspiration can decrease the incidence of ventilator-associated infectious complications.

Good oral hygiene decreases the bacterial burden of oral secretions. The use of chlorhexidine in medical patients is controversial and is no longer recommended for medical patients. The data supporting chlorhexidine largely comes from a limited number studies examining post-operative patients.

Chlorhexidine can cause oral ulcers (clinical studies) and lung damage (animal studies).

Antibiotic treatment with the goal of GI track decontamination may have a role, particularly in specific patient groups such as bone marrow transplant patients or trauma patients.



References for Question 2

M Kompas. Potential Strategies to Prevent Ventilator-associated Events. Am J Respir Crit Care Med 2015; vol 192: 1420-1430

M. Klompas et al. JAMA Int Med 2014; vol 174 pp 751 – 761

R. Price et al. BMJ 2014; vol 348 pp 2197



Bibliography

- SR Kahn et al. Prevention of VTE in nonsurgical patients. Antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest 2012; vol 141 (2) (Suppl): e195S – e226S
- C Minet et al. Venous thromboembolism in the ICU: main characteristics, diagnosis and thromboprophylaxis. Crit Care 2015; vol 19: 287
- PP Terragni et al. Early vs late tracheotomy for prevention of pneumonia in mechanically ventilated adult ICU patients: a randomized controlled trial. JAMA 2010 vol 303: 1483-1489
- M Krag et al. Pantoprazole in patients at risk for gastrointestinal bleeding in the ICU. New Engl J Med 2018; vol 379: 2199 - 2208
- M Kompas. Potential strategies to prevent ventilator-associated Events. Am J Respir Crit Care Med 2015; vol 192: 1420-1430
- NP O’Grady. Prevention of central line-associated bloodstream infections. NEJM 2023; vol 389: 1121 – 1131

