



Brigham and Women's Hospital

Founding Member, Mass General Brigham

Evidence-Based Preventative Therapy in the ICU

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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, Vitaflo, Sanofi-Aventis/Regeneron, and Organon.



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- Clinical focus: Critical Care Medicine
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Common ICU Complications

DVT

GI bleeding

Ventilator-associated events/Lung injury

Delirium

Pressure injuries



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



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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}

DVT and PE have significant attributable morbidity and mortality

- Asymptomatic proximal DVT carries 11 - 13% risk of death at 90 days compared to 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 ¹⁻³, ASH 2018 Guidelines⁴)

Pharmacologic (medical and non-orthopedic surgical patients)

- Low molecular weight heparin (LMWH)
- Unfractionated heparin (UFH)

Additional pharmacologic approaches for orthopedic surgical patients

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

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

- Types: Stockings, compression boots, venous foot pumps (≥ 18 hr/day)
- 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. MK Gould et al., Chest 2012; vol 141 (2Suppl) pp e227s – e277S
3. Y Falck-Ytter et al., Chest 2012; vol 141 (2Suppl) pp e278S – e325S
4. HJ Schunemann et al., Blood Advances 2018; vol 2 pp 3198 - 3225



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 1-2%

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



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)

- 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 ThromboEmobolism Prevention in a Medical Indications Study: ARTEMIS trial)¹
- Renal excretion – need to dose adjust for renal insufficiency²
- Only 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



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
 - In addition to allergic symptoms, Abs delays clearance
- Renal excretion

Argatroban

- Only IV administration – monitor with aPTT
- Hepatic clearance
- Interferes with INR assay

Oral agents (dabigatran) not FDA approved for this

- 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 POD 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.



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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 anesthesia ⁴

- 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: hypercoaguable state persists beyond hospital DC

Available evidence from multicenter RCTs:

Betrixaban lowered PE incidence but increased clinically relevant bleeding (APEX, 7513 patients)¹

Rivaroxaban decreased PE incidence but increased bleeding (MAGELLAN, 8101 patients)²

Rivaroxaban at discharge did not decrease symptomatic or fatal PE (MARINER, 12024 patients)³

Persistent unknowns

Are there subgroups who would benefit from extended prophylaxis?

Should both arterial and venous thromboses be considered?

References

1. AT Cohen et al., NEJM 2016; vol. 375 pp 534 – 544
2. AT Cohen et al., NEJM 2013; vol. 368 pp 513 – 523
3. AC Spyropoulos et al., NEJM 2018; vol. 379 pp 1118 - 1126



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



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.



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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:

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
 - Avoid chlorhexidine
 - IV Antibiotics for GI tract decontamination may have role

Rocking beds helpful but expensive

Early tracheostomy not effective³

- Multicenter study, 600 patients, showed 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



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

The patient tolerates extubation on ICU day 7. That evening he is irritable and mistakes his TV remote for a phone. Shortly after midnight he tried to climb out of bed and pulled at his central line. He was verbally abusive to his nurse and insisted that he has to leave for an appointment. Which of the following are the best “next steps”?

- A. Re-orient the patient and provide a medication such as lorazepam to promote sleep.
- B. Check a head CT to evaluate patient’s acute mental status change.
- C. Order restraints to prevent the patient from getting out of bed.
- D. Re-orient the patient and use PRN doses of a medication such as haloperidol to control refractory agitation.
- E. Re-orient the patient and arrange for a sitter to stay with the patient.



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Case, continued

What measures, if instituted earlier, might have been effective at decreasing patient's symptoms?

- A. Give diphenhydramine shortly before bedtime to promote sleep.
- B. Taper his opioid analgesic and use only non-opioid analgesics.
- C. Make sure patient has a nap during the afternoon; minimize visitors to decrease overstimulation, start q2h glucose checks to monitor for possible hypoglycemia
- D. Adjust analgesics to keep patient drowsy but still responsive to voice, give melatonin shortly before bedtime to promote sleep, increase lab check frequency to monitor for hypoglycemia.
- E. Adjust analgesics to keep pain score <4, give melatonin shortly after dinner to promote sleep, remove any non-essential devices, ask his family to provide family photographs.



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The Problem: Delirium

Acute brain dysfunction with varying degrees of decreased attention, altered cognition and perception¹

- Frequently underdiagnosed¹
 - Confusion Assessment Method – ICU
 - Intensive Care Delirium Screening Checklist
- Three subtypes – Agitated (1.6%), Hypoactive (43.5%), Mixed (54.9%)²

Common problem

- Prevalence 32% among arousable patients in multicenter study³
- Prevalence in mechanically ventilated patients higher – up to 80%⁴

Associated with poor outcomes^{1,4}

- Independent risk factor for death – hypoactive has highest risk¹
- Increased number of complications and length of stay
- Increased costs

References:

1. C Hayhurst et al. Anesthesiology 2016 vol 125 pp 1229 – 1241
2. JF Peterson et al. J Am Geriatr Soc 2006 vol 54 pp 479 - 484
3. J Salluh et al. Critical Care 2010 vol 14 R210
4. E Wesley et al. JAMA 2004 vol 291 pp 1753 - 1762



Evidence for Prevention: Pharmacologic approaches

Mixed results for prophylaxis¹⁻⁴

- Studies of post-operative patients generally favor pharmacologic approach for prophylaxis
- Medical ICU patients no consistent effects

Difficulties in assessing success of pharmacologic approach

- Agitated symptoms controlled via sedation
- Delirium per se not treated
- Some successful trials may be early treatment instead of true prophylaxis

References:

1. K Neufeld et al., J Am Geriatric Soc 2016 vol 64 pp705 – 714
2. Y Wu et al., JAMA Psychiatry 2019 vol 76 pp 526 – 535
3. C Hayhurst et al., Anesthesiology 2016 vol 125 pp 1229 – 1241
4. W Hawkins et al., J Crit Care 2018 vol 44 pp 289 - 293



Evidence for prevention: nonpharmacologic approaches

More effective than pharmacologic^{1,2}

- Avoid exacerbating medications
 - Classes to avoid: Benzodiazepines, Anticholinergics, Steroids
 - Daily sedation interruption
- Maintain good symptom control
- Promote normal day/night and sleep cycles
- Remove invasive devices

Success increased when delirium prevention done as part of comprehensive approach³

- Society for Critical Care guidelines: Management of Pain Agitation and Delirium⁴

References:

1. I Abraha et al., PLOS One 2015 vol 10: e0123090
2. C Hayhurst et al., Anesthesiology 2016 vol 125 pp 1229 – 1241
3. A Trogrlic et al., Critical Care Med 2019 vol 47 pp 419 – 426
4. J Devlin et al., Critical Care Med 2018 vol 46 pp e825 – e873



Evidence-based recommendations

Proactive daily assessment for early signs of disordered cognition

Institute nonpharmacologic approaches as soon as feasible

Add pharmacologic symptom management if

- Agitation poses a safety risk
- Symptoms not controlled by nonpharmacologic interventions



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
5. Environmental controls can decrease the incidence of delirium and are more effective than pharmacologic management



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



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- 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 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



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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 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.

Antibiotic treatment with the goal of GI track decontamination is controversial but may be useful in specific patient groups such as bone marrow transplant patients or trauma patients.



Chlorhexidine – the controversy

Evidence in favor from several trials and meta-analyses

- Many of the positive trials are from cardiac surgical units, not medical units
- Definitions showing decreased infection may instead reflect decreased colonization

Evidence against benefit

- Studies showing decreased infection don't show mortality benefit
- Analyses limited to double-blind studies in medical unit don't show benefit

Evidence of possible harm

- Chlorhexidine aspiration can lead to lung injury/ARDS in animal models
- Chlorhexidine can cause oral ulceration (improves with decreased concentration)



References for Question 2

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Conflict of Interest/Financial Disclosure

I am a co-investigator on the NIH-funded PrecISE Trial Network and 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, Vitaflo, Sanofi-Aventis/Regeneron, and Organon .

