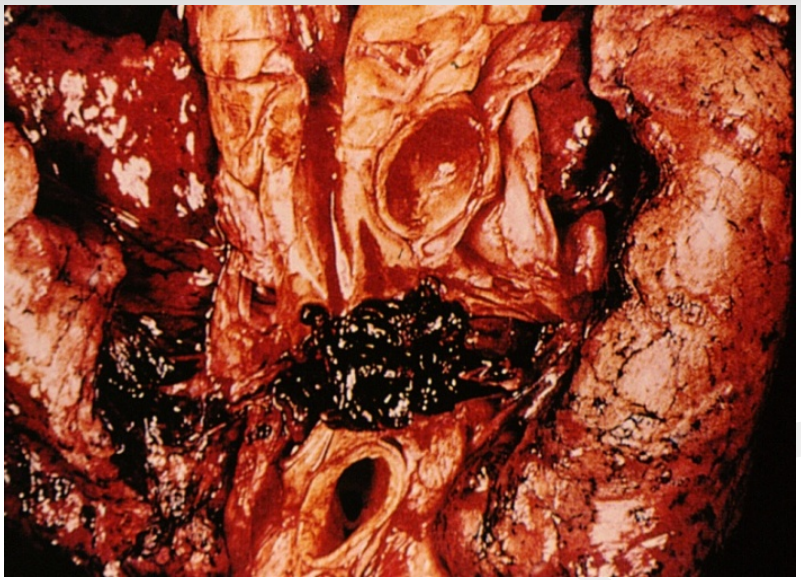
Pulmonary: Physiology, VAP, DVT/PE

ACS Surgical Critical Care Update 2013



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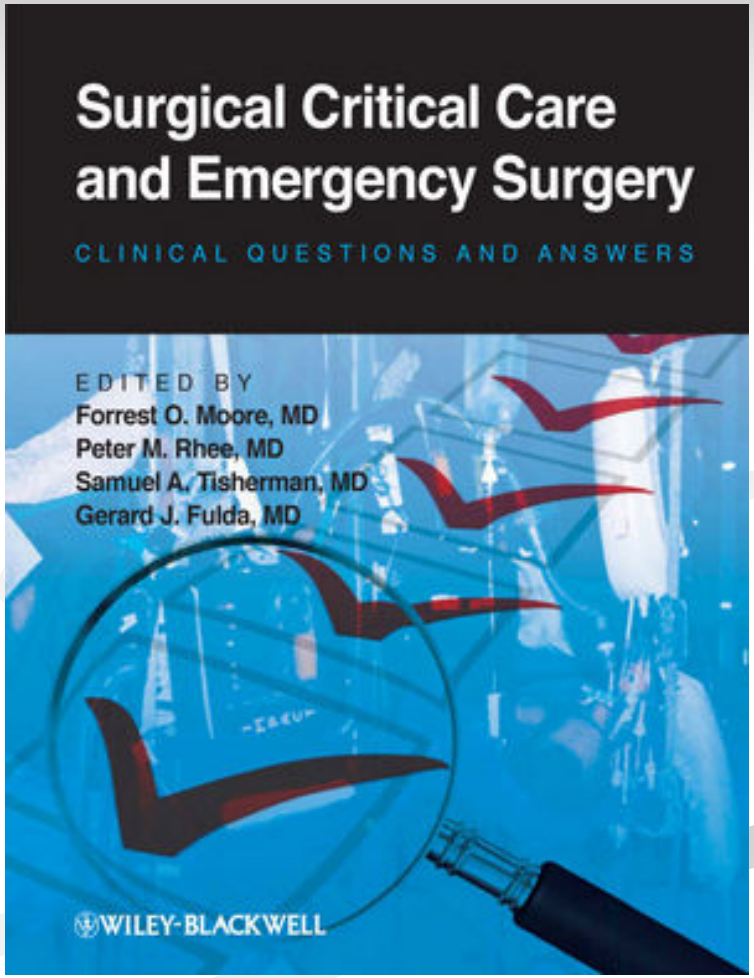
Disclosure

Royalties from Wiley-Blackwell



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VAP Diagnostic Strategies

CLINICAL

- Lung infiltrate that is new or progressing

+

- ≥ 2 clinical signs of infection
  - Fever/hypothermia
  - Leukocytosis/leukopenia
  - Purulent sputum
  - Decline in oxygenation

- Clinical signs/+culture *without* an infiltrate:
  - ventilator-associated tracheobronchitis (VAT)

BACTERIOLOGIC

- Use of quantitative cultures of the lower respiratory tract
  - ESA
  - BAL
  - PSB
- Growth above a set threshold = VAP

Limitations of Both Strategies

- Sensitivity
- Specificity
  - Low specificity (SCX, clinical) leads to over-treatment
- Lack of a "gold standard" for comparison
- "Ventilator-associated" arbitrary
- No consideration of pre-intubation aspiration

Am J Respir Crit Care Med 2005 Feb

Controversies of VAP Diagnosis

- **Is the clinical strategy sufficiently accurate?**
- **Is one diagnostic strategy superior?**
- **Are outcomes improved with either method?**
- **Which quantitative threshold should be used?**

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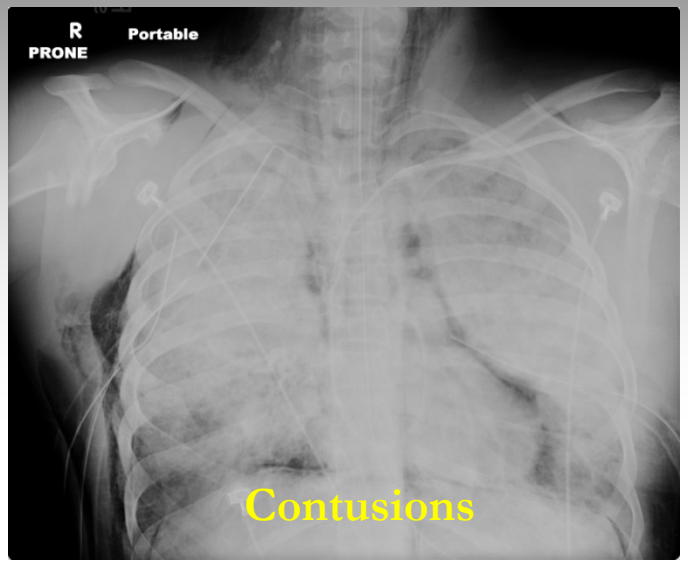
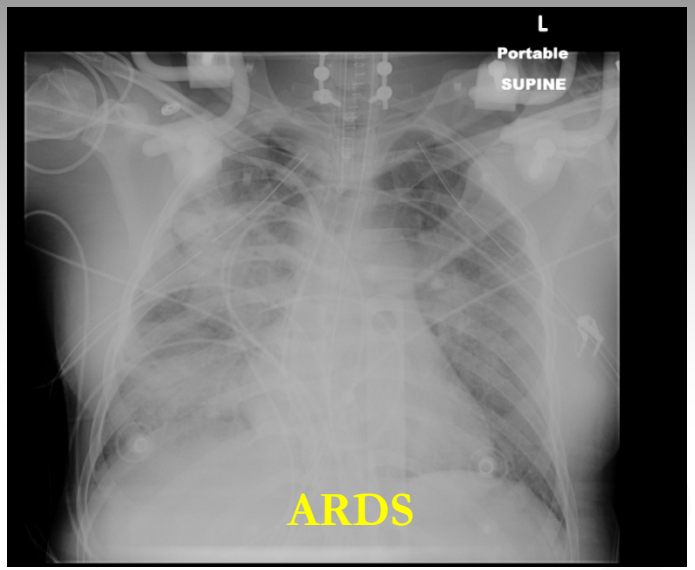
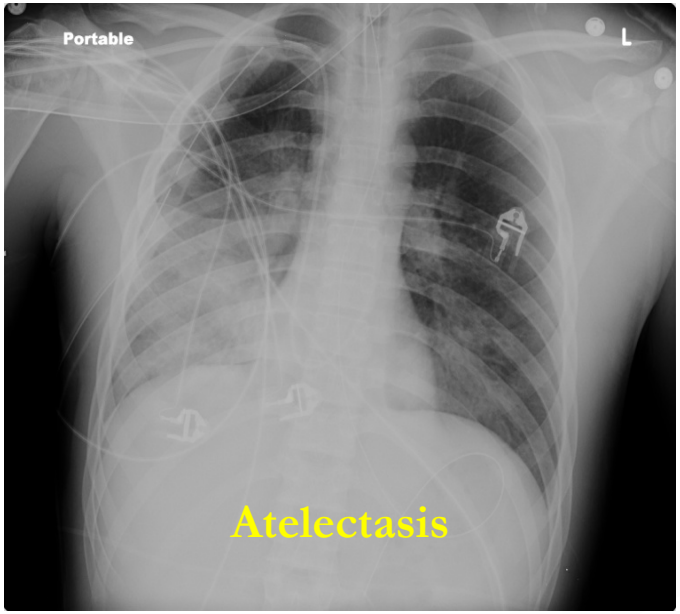
Radiologic findings nonspecific



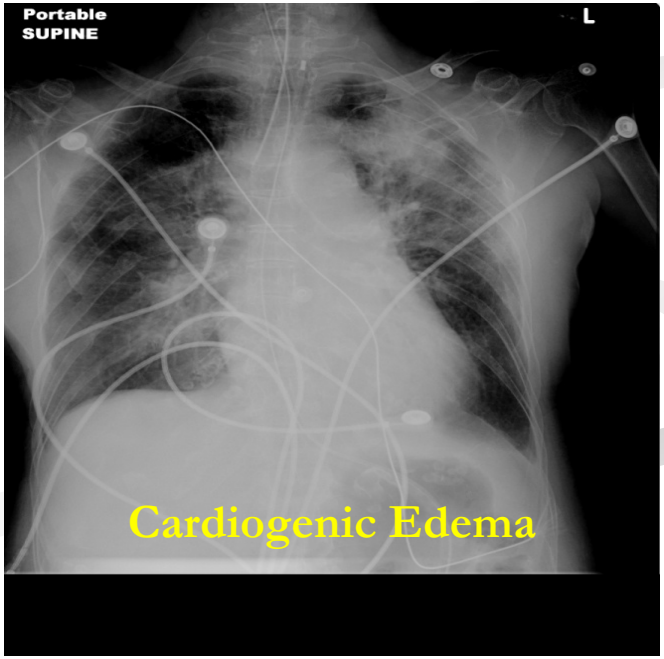
Contusions



ARDS



Atelectasis



Cardiogenic Edema

VAP

- No reliable, valid definition of VAP (NHSN)
  - CDC's healthcare-associated infections (HAIs like CRBSI, CAUTI) surveillance system
    - Standard methodology and definitions to collect data from nearly 5000 healthcare facilities
  - NHSN PNA definitions last updated in 2002
    - Designed for surveillance of all healthcare-associated PNA events and not limited to VAP
    - Need more accurate diagnosis
    - PNA that occurs at the time a ventilator is in place, or within 48 hours after a ventilator has been in place
    - ***No required duration for the ventilator to qualify as a VAP***
  - Surveillance and prevention practices difficult to track

VAP

- **Elements**
  - **No required amount of time that ETT must be in place for PNA to count as a VAP**
  - **CXR – lacks specificity *(not required in new definitions)***
  - **Clinical signs/symptoms – lacks sensitivity and specificity; highly subjective**
  - **Microbiology – lacks sensitivity and specificity; varies among practitioners; what is best practice?**

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Commentary

Eight initiatives that misleadingly lower ventilator-associated pneumonia rates

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Decline in VAP Rates

- Evidence-based preventive measures
- Ways to lower VAP rates ***without improving patient care***
  - Strict interpretation of clinical signs included in surveillance definitions
  - Strict interpretation of CXR findings included in surveillance definitions
  - Requirement for consensus approach to determine if VAP, or physician approval
  - Transferring patients needing prolonged mechanical ventilation
  - Admitting uncomplicated vented postop patients

CDC

- **VAP Surveillance Definition Working Group**
  - **Division of Healthcare Quality Promotion**
  - **CDC Prevention Epicenters**
  - **Critical Care Societies Collaborative**

No gold standard, valid, reliable definition of VAP

VAP Definition Modification

- Achieve validity/clinical credibility/reliability
  - Improve accuracy of reporting HAIs
    - Using criteria that are less likely to be influenced by variability in resources, subjectivity, and clinical practices
    - Amenable to electronic data capture
  - Comparisons among facilities
  - Pay-for-performance

Klompas M. Curr Opin Crit Care 2013 June
http://www.hhs.gov/ash/initiatives/hai/Events/2012-hai-progress-meeting-vae.pdf
http://www.cdc.gov/nhsn/acute-care-hospital/vae/

Ventilator-Associated Events

- Tiered approach
  - Not intended for use in management of patients
  - Not a clinical definition algorithm
- Tiers 1 and 2
  - Ventilator-associated conditions (VAC)
  - Infection-related complications (IVAC)
  - Potential use for public reporting
- Tier 3
  - Internal use for quality improvement
  - Possible VAP and Probable VAP

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Algorithm

(Respiratory Component)

- **Patient on mechanical ventilation > 2 days**
- **Baseline period of stability or improvement, followed by sustained period (> 2 days) of worsening oxygenation**
  - **Increasing FI02 (>0.20) or PEEP (>3 cmH20)**

Ventilator-Associated Condition (VAC)

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Algorithm

(Infection/Inflammation Component)

- **VAC *and***
- **Evidence of infection/inflammation**
  - **On or after day 3 of mechanical ventilation**
  - **Elevated temperature or leukocytosis (SIRS) *and***
  - **New antimicrobial agent continued for ≥ 4 days**

Infection-Related Ventilator-Associated Complication (IVAC)

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Algorithm

(Additional Evidence)

- VAC and IVAC *and*
- Positive results of microbiological testing
  - Purulent secretions
    - ≥ 25 neutrophils and ≤ 10 squamous cells/LPF
  - Other positive lab evidence
    - Positive SCX, BAL, PSB

Possible or Probable VAP

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Possible VAP

Patient meets criteria for VAC and IVAC

AND

On or after calendar day 3 of mechanical ventilation and within 2 calendar days before or after the onset of worsening oxygenation, ONE of the following criteria is met:

1) Purulent respiratory secretions (from one or more specimen collections)
   - Defined as secretions from the lungs, bronchi, or trachea that contain ≥25 neutrophils and ≤10 squamous epithelial cells per low power field [lpf, x100].
   - If the laboratory reports semi-quantitative results, those results must be equivalent to the above quantitative thresholds.

2) Positive culture (qualitative, semi-quantitative or quantitative) of sputum*, endotracheal aspirate*, bronchoalveolar lavage*, lung tissue, or protected specimen brushing*

**Excludes the following:*

- Normal respiratory/oral flora, mixed respiratory/oral flora or equivalent
- *Candida* species or yeast not otherwise specified
- Coagulase-negative *Staphylococcus* species
- *Enterococcus* species

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Probable VAP

(VAC + IVAC)

On or after calendar day 3 of mechanical ventilation and within 2 calendar days before or after the onset of worsening oxygenation, ONE of the following criteria is met:

1) Purulent respiratory secretions (from one or more specimen collections—and defined as for possible VAP)

AND one of the following (see Table 2):

- Positive culture of endotracheal aspirate*, ≥ 10^5 CFU/ml or equivalent semi-quantitative result
- Positive culture of bronchoalveolar lavage*, ≥ 10^4 CFU/ml or equivalent semi-quantitative result
- Positive culture of lung tissue, ≥ 10^4 CFU/g or equivalent semi-quantitative result
- Positive culture of protected specimen brush*, ≥ 10^3 CFU/ml or equivalent semi-quantitative result

**Same organism exclusions as noted for Possible VAP.*

2) One of the following (without requirement for purulent respiratory secretions):

- Positive pleural fluid culture (where specimen was obtained during thoracentesis or initial placement of chest tube and NOT from an indwelling chest tube)
- Positive lung histopathology
- Positive diagnostic test for *Legionella* spp.
- Positive diagnostic test on respiratory secretions for influenza virus, respiratory syncytial virus, adenovirus, parainfluenza virus, rhinovirus, human metapneumovirus, coronavirus

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VAEs

- **Identifies a broad range of events in patients on mechanical ventilation, not limited to VAP alone**

Requires thinking more broadly about prevention

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Which of the following is NOT considered a best practice for the prevention of ventilator-associated pneumonia?

- a. Daily drug sedation holiday
- b. Early tracheostomy
- c. Gastrointestinal and DVT prophylaxis
- d. Elevation of head-of-bed

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Which of the following is NOT considered a best practice for the prevention of ventilator-associated pneumonia?

- a. Daily drug sedation holiday
- b. *Early tracheostomy*
- c. Gastrointestinal and DVT prophylaxis
- d. Elevation of head-of-bed

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Early (< 7 days) tracheostomy has been shown conclusively to:

- a. Decrease incidence of VAP
- b. Decrease mortality
- c. Decrease hospital and ICU length of stay
- d. None of the above

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Early (< 7 days) tracheostomy has been shown conclusively to:

- a. Decrease incidence of VAP
- b. Decrease mortality
- c. Decrease hospital and ICU length of stay
- d. ***None of the above***

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VAP Bundle

- Reducing complications by improving quality
  - Benchmarking
  - Reducing incidence of VAP

VAP Bundle

- Daily spontaneous breathing trial
- Daily sedation holiday
- Stress gastritis prophylaxis
- Elevation of head of bed
- DVT prophylaxis
- Daily oral care
  - Chlorhexidine

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Craven DE et al. CHEST 2006 July

Am J Respir Crit Care Med 2005 Feb

Not Part of VAP Bundle

(But Is Evidence-Based and Should Be Considered)

- Restrictive blood transfusion policy
- Use of noninvasive positive pressure ventilation
- Continuous aspiration of subglottic secretions
- Strict glycemic control
- ***Early tracheostomy***[1-5] in select populations
  - Severe TBI
  - ***May*** decrease incidence of VAP, mortality, and hospital and ICU length of stay

[1]Barquist ES et al. J Trauma 2006 Jan

[2]Griffiths J et al. BMJ 2005 May

[3]Rizk EB et al. Neurocrit Care 2011 Dec

[4]Young D et al. JAMA 2013 May

[5]Gomes SBN et al. Cochrane 2012 Mar

Which of the following organisms is LEAST likely to require a prolonged course of antibiotics for the treatment of ventilator-associated pneumonia (VAP)?

- a. Acinetobacter
- b. Pseudomonas
- c. Stenotrophomonas
- d. Escherichia

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Which of the following organisms is LEAST likely to require a prolonged course of antibiotics for the treatment of ventilator-associated pneumonia (VAP)?

- a. Acinetobacter
- b. Pseudomonas
- c. Stenotrophomonas
- d. *Escherichia*

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Length of Treatment

- Chastre J et al.[1]
  - RCT 401 patients
  - 8 vs. 15 days
  - NFGN rods – similar outcomes; higher recurrence with 8 days of treatment
- Fekih Hassen et al.[2]
  - RCT 30 patients
  - 7 vs. 10 days
  - Outcomes similar

[1] JAMA 2003 Nov

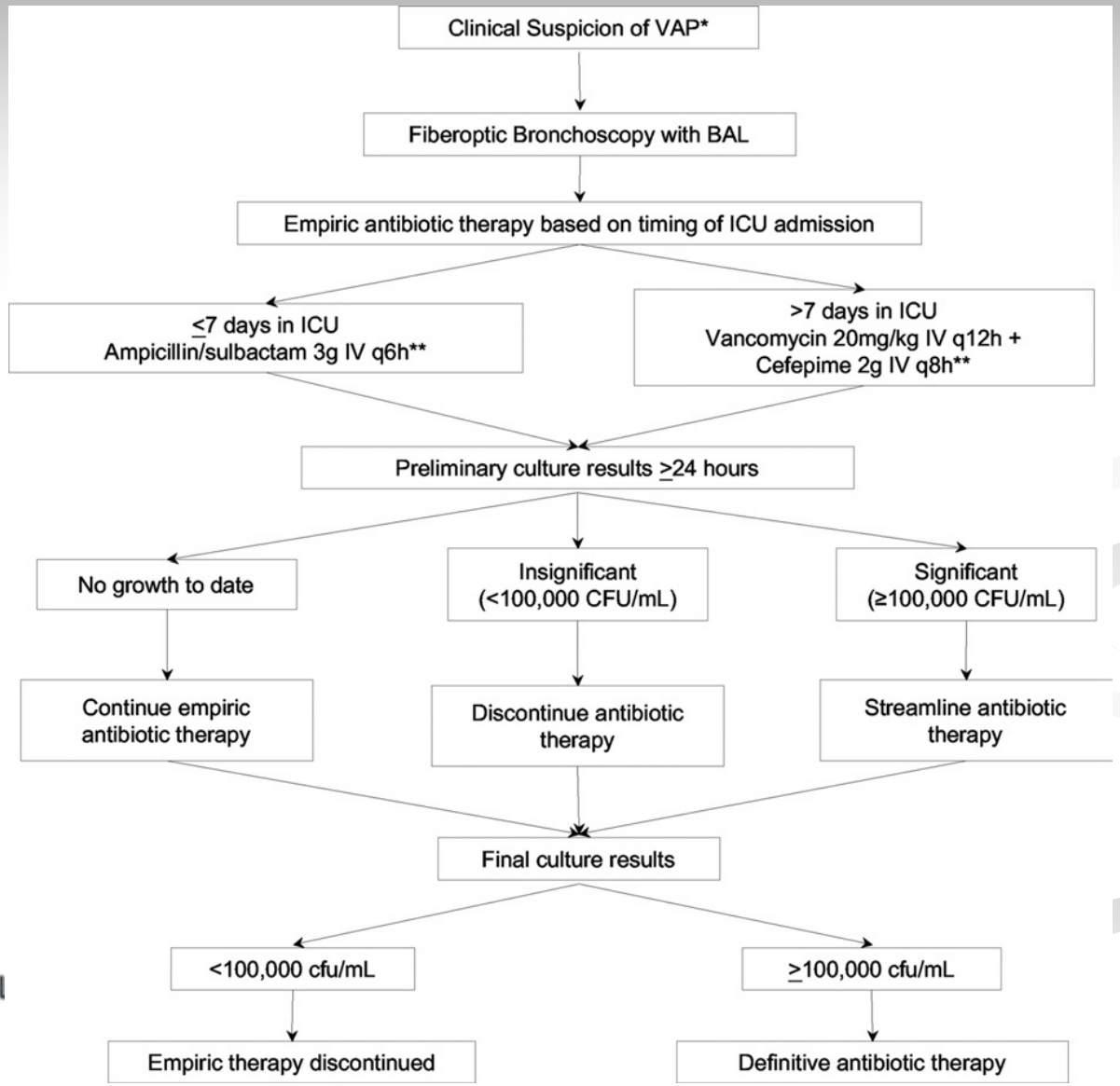
[2] Ann Fr Anesth Rean

Length of Treatment

- Short course (*7-8 days*):
  - Fewer antibiotic days
  - Lower recurrence with MDRO
  - No difference in overall recurrence, mortality, ICU days, ventilator free days
- Consider longer course (*10-14 days*)
  - Acinetobacter, Pseudomonas, Stenotrophomonas, MRSA
  - Higher recurrence of NFGNB with short course
  - Less relapses with long course treatment

Dimopoulos G et al. Chest 2013 June: Short vs. long-duration antibiotic regimens for VAP: a systematic review and meta-analysis

JACS 2011 Magnotti et al.



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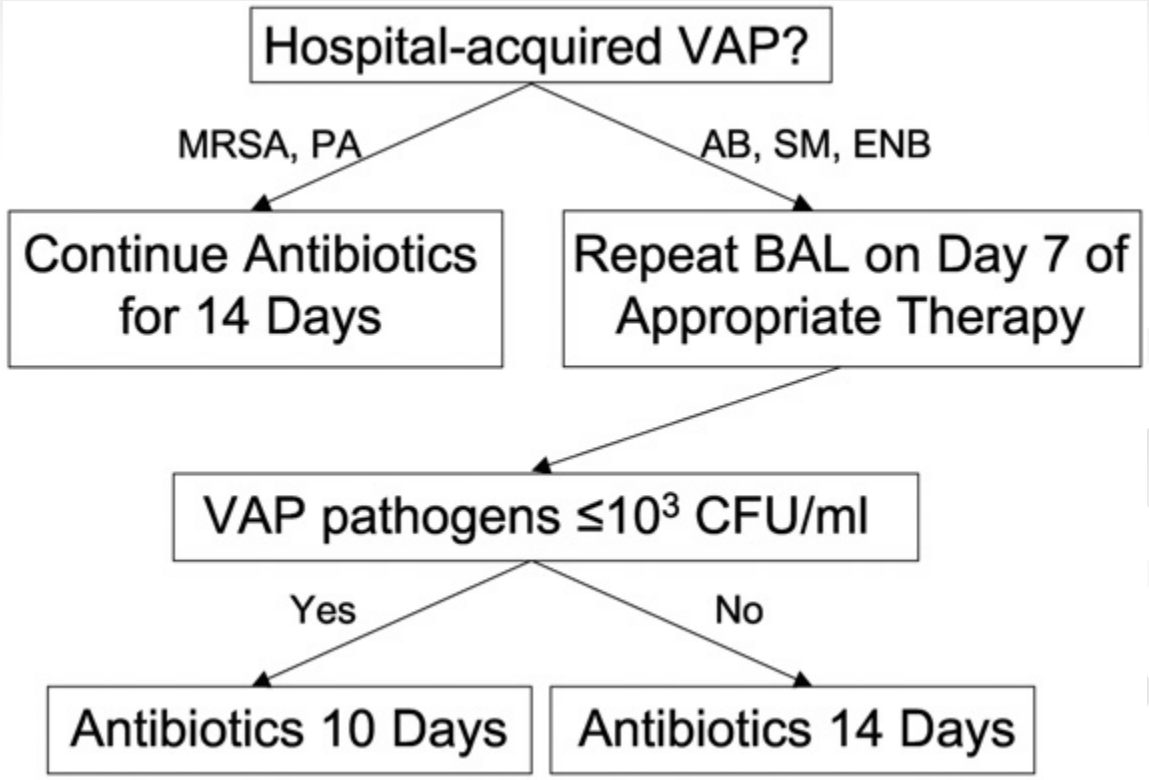
JACS 2011 Magnotti et al.



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VTE Epidemiology

- **Pulmonary embolism (PE) and deep venous thrombosis (DVT)**
- **Affects between 600,000 and 2 million patients annually; death in 100,000 to 300,000 per year**
- ***PE remains the most common preventable cause of in-hospital mortality***
- ***Fatal PE is the 3rd most common cause of death in trauma patients who survive the first 24 hours***

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VTE Incidence

	General Surgery	Trauma	Hip Fx	SCI
Overall DVT	20-30%	58%	50%	70-90%
Proximal DVT	7%	18%	20%	15%
PE	0.5%-2%	2-22%	5-25%	5%
Fatal PE	0.1-0.8%	1%	4-7%	3-5%

AHRQ - #1 strategy to improve patient safety in hospitals is prevention of VTE

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According to the ACCP, which of the following is not appropriate VTE prophylaxis in the injured patient?

a. **LDUH**
b. **LMWH**
c. **IVCF**
d. **Fondaparinux**

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According to the ACCP, which of the following is not appropriate VTE prophylaxis in the injured patient?

a. LDUH
b. LMWH
c. ***IVCF***
d. Fondaparinux

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IVCFs

- ***Not recommended as prophylaxis (ACCP '08 and '12)***[1]
  - **Highest quality is indirect coming from study in patients confirmed with symptomatic, proximal DVT**
- **2002 EAST guidelines[2] → level III evidence in favor of**
  - **Prophylactic placement in very high risk trauma patients who are unable to receive chemoprophylaxis**
- ***More commonly placed for prophylaxis than for treatment***

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[1]Gould MK et al. CHEST 2012 Feb
[2]Rogers FB et al. J Trauma 2002 July

IVCF

- **Decousas, *NEJM*, 1998 and PREPIC, *Circulation*, 2005**
  - ***Only* RCT of IVCFs in proximal DVT shown to prevent PE**
  - **400 patients with proximal DVT, randomized to permanent filter or no filter *AND* to LMWH or LDUH**
  - **Initial non-significant reduction in PE and at 8 years (63% risk reduction), but no difference in mortality**
  - **At 2 years and 8 years → increased DVT, no change in mortality, PTS similar**
  - ***LMWH = LDUH***

IVCFs

Conclusive data lacking that PE and death are reduced when used as prophylaxis, and may increase risk of DVT

Retrievable

- **Poor retrieval rates although improved to 60% with a dedicated filter registry in trauma patients**
- **Most extensively utilized and studied in trauma patients, however there is a lack of high quality literature**
  - **Decrease in PE and fatal PE**
  - **Contraindication to chemoprophylaxis**

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O'Keeffe T et al. Am Surg 2011 Jan
Rogers FB et al. J Trauma Acute Care Surg 2012 Feb

Prophylaxis (Chemical)

- **LDUH (5000 U's q12 or q8)**
  - **Major abdominal or thoracic surgery**
    - **Meta-analyses reduced all DVT (20-40%), proximal DVT, PE and fatal PE**
  - **2002 EAST guidelines → no support (level II)**
  - **LDUH 5000 U's q8 may be as effective as enoxaparin in trauma patients[1]**
    - **Retrospective, decreased cost, protocol change mid-year**
  - **RCT of LDUH vs. placebo in med-surg ICU patients reduced DVT from 29% to 13%**

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[1]Arnold JD et al. Am Surg 2010 June

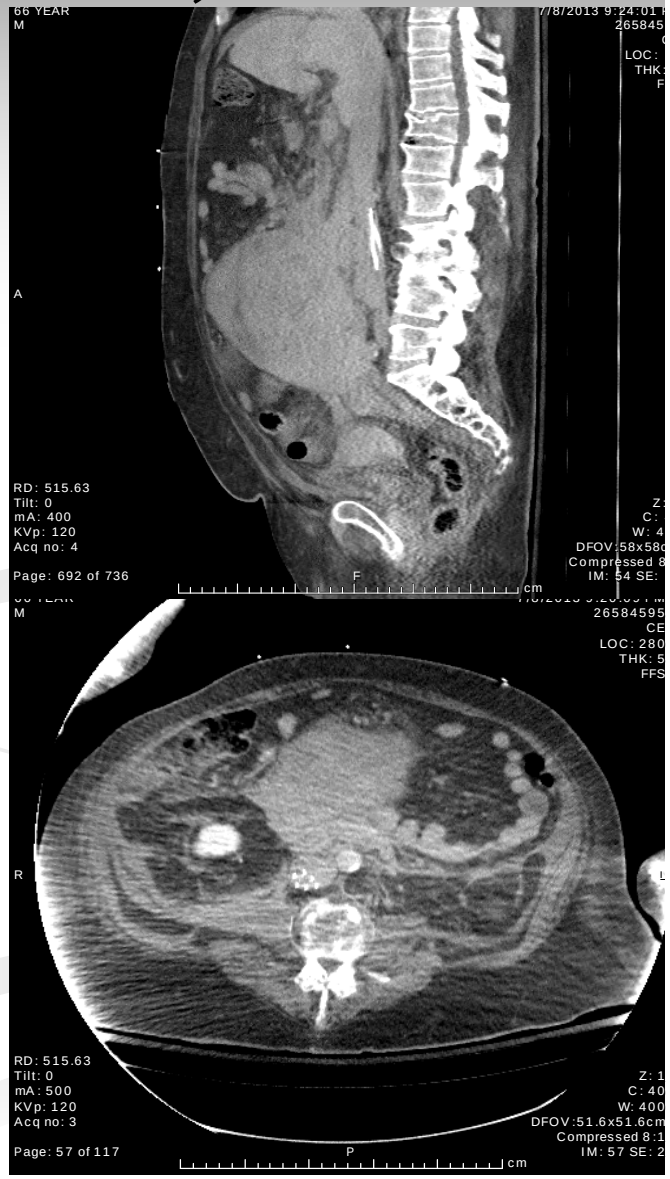
Prophylaxis (Chemical)

- **Fondaparinux**
  - **Factor Xa inhibitor; blocks thrombin generation by accelerating rate of factor IIa, VIIa, IXa, Xa, Xia, and XIIa inactivation by antithrombin**
  - **No HIT**
  - ***No antidote*, long half-life**

  - **Superior (or at least equivalent) to LMWH in *ortho* patients**
  - **Equivalent to dalteparin (LMWH) in *major abdominal surgery* (PEGASUS study)**
  - **Small pilot study in *trauma* patients found 1.2% incidence of DVT with no PE, HIT or major bleeding**

Prophylaxis (Chemical)

- VKA
- DTIs
  - Argatroban
  - Lepirudin
- Oral agents
  - ***Rivaroxaban*** (factor Xa inhibitor)
    - Prophylaxis following TKR/THR
    - No lab monitoring
    - Prothrombin complex concentrate for reversal
  - Dabigatran (direct thrombin inhibitor)
    - Prophylaxis following TKR/THR
    - No lab monitoring
    - No antidote; consider HD; no effect with PCC



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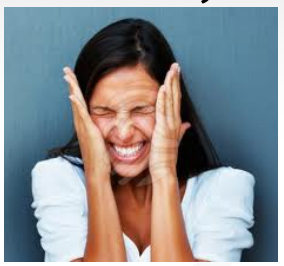
ASA

- 2012 ACCP[1] guidelines for major general and abdominopelvic surgery in ***high risk*** patients (VTE 6%, Caprini ≥ 5, not at risk for bleeding) ***AND contraindication to LMWH or UFH*** (?HIT)
  - Low dose ASA or fondaparinux or IPC (2C)



  - Re-evaluation of a subgroup analysis of the Antiplatelet Trialist Collaborative (1994) in general surgery patients by ACCP found reduced risk of asymptomatic proximal or distal DVT by 48%, symptomatic proximal DVT by 59%, and PE by 57%

  - ***Low quality evidence***: data with moderate heterogeneity, no blinding in two studies, inconsistent outcomes, imprecision in RR of bleeding, and six studies used fibrinogen scanning for surveillance

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[1]Gould MK et al. CHEST 2012 Feb

LDUH and Trauma

- ***LDUH*** **or LMWH or IPC (2012 ACCP - 2C)**
  - ***Low quality evidence*** **in support of asymptomatic proximal DVT which is reduced by 58% with LMWH and by 90% with LDUH plus continuous passive motion (ortho and skeletal trauma patients)**

- **Add mechanical prophylaxis in high risk**

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A 35-year-old woman sustains a 7mm epidural hematoma after being assaulted. According to the Delayed Versus Early Enoxaparin Prophylaxis I (DEEP I) study, enoxaparin may be started safely within ___ hours following injury and a stable head CT?

- a. 24
- b. 48
- c. 72
- d. 96

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- a. *24*
- b. 48
- c. 72
- d. 96

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Traumatic Brain Injury

(Timing of Prophylaxis Highly Controversial)

- **Incidence of VTE 3-5% when started within 24-48 hours**
  - **Up to 15% when delayed beyond 48 hours**
- **Risk of hemorrhage requiring craniotomy (0.5%) or change in management or outcome (1.1%)**
- **LMWH > LDUH**
  - **Norwood 2008; Dudley 2010; Koehler 2011; Minshall 2011**

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Traumatic Brain Injury

(Timing of Prophylaxis Highly Controversial)

- **Brain Trauma Foundation** ***(J Neurotrauma 2007)***
  - **Level III recommendation for LMWH or LDUH + mechanical**
  - **Insufficient evidence to support preferred *agent*, dose, or timing**

- **Phelan and *The Delayed Versus Early Enoxaparin Prophylaxis I study*[1]**
  - ***Low risk TBI patients with progression rates equal to placebo after starting enoxaparin at 24 hours after injury***

[1]Phelan HA et al. J Trauma Acute Care Surg 2012 Dec

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DEEP Study

- Randomized controlled study of patients with low risk TBI
  - SDH < 8mm
  - EDH < 8mm
  - IPH <2cm
  - Single contusion per lobe
  - SAH with normal angiogram
- Unchanged HCT at 24 hours post-injury
  - Randomized to enoxaparin 30mg SQ BID (n=34) or placebo (n=28)
  - Repeat HCT 48 hours post-injury
  - TBI progression rate of 5.9% with enoxaparin; 3.6% with placebo
    - Rates are similar
    - All were subclinical progression