Infections in the ICU

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The George Washington University

Disclosures

Off-Label Usage
• None

Financial Relationships with Relevant Commercial Interests
• None

The ID Consultant and the ICU

• Hyperthermia Syndromes
• Sepsis
• Catheter Infections
• Ventilator Associated Pneumonia
• Miscellaneous

Question

• Which of the following patient populations with Foley catheters should be screened for bacteriuria and treated if positive
  a) All ICU patients
  b) Renal transplant patients in ICU
  c) All neutropenic patients in ICU
  d) Urologic surgical patients where the procedure is likely to cause mucosal bleeding
  e) All patients with Type I diabetes in ICU

Answer

For patients who will have a Foley catheter inserted, screening for bacteriuria and antibiotic prophylaxis are not generally recommended except
• Men undergoing urologic procedures where mucosal bleeding is anticipated

For women post Foley catheter
• screening for bacteriuria 48 hrs after Foley is removed with treat if positive is indicated

For patients without a Foley catheter, screening and treatment is indicated in pregnant women early in pregnancy and then periodically
• to reduce pyelonephritis, low birth weight infants, and prematurity
Additional Points for Foley Catheters

- **Recommended**
  - Closed drainage system
- **Not Routinely Recommended**
  - Enhanced meatal care
  - Antibiotic/Antiseptic coated catheters
  - Antibiotics in drainage bag
  - Bladder irrigation
  - Periodic cultures to screen for bacteruria
  - Routine catheter changes over time
  - Antibiotics at time of catheter removal

Additional Points

- **Bacteriuria**
  - Men
    - one voided urine >100,000 colonies of one isolate
  - Women
    - two voided urines >100,000 of one isolate
  - Catheterized patient
    - >100 colonies of one isolate
- **Pyuria plus asymptomatic bacteriuria**
  - NOT indication for Rx

Hyperthermia

- A patient presents with temperature = 41°C
  - WBC=25,000
- Differential Diagnosis
  - Multiple
- What non infectious causes should you look for on the boards if T>40-41°C

Hyperthermia >40.5°C

- **Heat Stroke** (No diaphoresis!)
  - Classic-non exertional
  - Exertional
- **Neuroleptic Malignant**
- **Malignant Hyperthermia**
- **Serotonin Syndrome**
  - (Cocaine, Ecstasy....)

Note: Many of these can be associated with leukocytosis of 20k-40k

Management of Hyperthermia

- **ABC’s**
  - Airway, Breathing, Circulation
- **Promote Cooling**
  - Evaporation with H2O mist and fans
  - Suppress shivering (benzodiazepine)
- **Treat complications**
  - Respiratory alkalosis, pulmonary edema, ARDS
  - Coma
  - Coagulopathy
  - Rhabdomyolysis, renal failure
  - Liver failure

Question

You are called at 9 a.m. to the surgical floor to see a 29-year-old previously health male status/post anterior cruciate ligament repair with a fever of 40°C who returned 14 hours previously from the operating room.

He did well post operatively except for some nausea, rx metoclopramide (Reglan). He received linezolid pre-operatively.

The patient is agitated and rigid. His blood pressure is rose from 130/70 to 180/100 twenty minutes ago. Now the BP is 110/60. He is given one ampule of Narcan, but does not respond.

Which of the following would you give:

A. Antihistamines
B. High-dose corticosteroids
C. Dantrolene
D. IVIG
E. Dilantin
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Three Syndromes You Should Know

Malignant Hyperthermia
- Syndrome- 5% Mortality
  - Muscle contraction (masseter spasm)
  - “Lead pipe rigidity”
  - Cardiovascular instability
- Genetic defect
  - Ca++ transport in skeletal muscle
  - Autosomal dominant
  - (excessive calcium accumulation)
- Triggers
  - Usually < 1 hour after trigger (up to 10 hours)
  - Classic: Halothane, succinylcholine

Neuroleptic Malignant Syndrome (NMS)
- Frequent trigger = haloperidol
  - Any “neuroleptic” (antipsychotic)
  - Antiemetics such as metoclopramide
  - Withdrawal of antiparkinson drugs (L dopa)
- Onset 1-3 days
  - Time of drug initiation
  - When dose changed
- Management
  - Dantrolene (direct muscle relaxant for up to 10 days)
  - Dopamine agonists (bromocriptine and others)

Serotonin Syndrome
- Syndrome = Excess Serotoninergic Activity
  - Therapeutic drugs, drug interactions, self poisoning
- Clinical Manifestations
  - Acute onset in 24 hrs of new drug/drug change
  - Hyperreflexive>bradyreflexia
  - Nausea and vomiting followed by shivering
- Treatment
  - Rapid resolution after withdrawal offending drug
- Triggers
  - Linezolid = MAO Inhibitor: beware with drugs below
    - SSRIs (Bupropion)
    - Selective serotonin reuptake inhibitors

Teaching Points for Hyperthermia
Rigid/Somnolent vs Rigid Agitated
- Muscular rigidity (lead pipe) in Operating Room and Somnolent
  - Malignant hyperthermia
- Muscular rigidity and agitated with drug list
  - Neuroleptic Malignant Syndrome
  - Muscular hyperreactivity and agitated with clonus/nausea and vomiting
  - Serotonin syndrome
Guide for the Pharmacologically Impaired

**Drug Categories and Examples**

**Hyperthermia Concerns**

- Monoamine Oxidase Inhibitors
  - Depression: Malignant Neuroleptic
    - Phenelzine (Nardil)
  - Serotonin Release: Tranylcypromine (Parnate)
    - Isocarboxazid (Marplan)

- Butyrophenones
  - Psychosis: Malignant Neuroleptic
    - Haldol

- Tricyclic Antidepressants
  - Serotonin Release: Imipramine (Tofranil)
    - Stellazine (Elavil)

- Dopamine Agonists
  - Malignant Neuroleptic: Bromocriptine (Parlodel)

- Selective Serotonin Release Inhibitors
  - Psychosis: Malignant Neuroleptic
    - Citalopram (Celexa)
  - Depression: Serotonin Release
    - Fluoxetine (Prozac)
    - Paroxetine (Paxil)
    - Sertraline (Zoloft)
    - Escitalopram (Lexapro)

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**Shock**

- Distinguishing different causes of shock
- Treatment of shock
- Technology
  - Out of favor: Swan Ganz catheter
  - In favor: Ultrasound/Echo/Cardiac output catheters

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**Question**

You are asked to consult on a 30 year old patient with fever and hypotension in the ICU. The patient had been previously healthy, had multiple traumatic injuries 3 weeks ago, and has been in the ICU being weaned from the ventilator.

Which of the following hemodynamic profiles would be most consistent with septic shock?

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<th>RV</th>
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<th>PCWP</th>
<th>SV02</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Values</td>
<td>2.6-4.2</td>
<td>700-1600</td>
<td>150</td>
<td>153</td>
<td>&lt;10</td>
</tr>
<tr>
<td>a.</td>
<td>5.0</td>
<td>500</td>
<td>20/10</td>
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**Differential Diagnosis of Shock**

- Distributive
- Hypovolemic
- Cardiogenic
- Extracardiac Obstructive

For the boards: hemodynamics are getting to be outdated (Swan Ganz rarely used) but...could they ask you to recognize some typical patterns?
Sepsis is the Most Common Cause of Distributive Shock But....Not the Only One!

- Sepsis
- Toxic Shock Syndrome
- Anaphylaxis
- Adrenal/Thyroid
- Neurogenic (spinal)
- Toxic (Organophosphates, Abacavir)
- Hepatic
- Pancreatic
- Severe anemia

Management of Sepsis

- Diagnosis
  - Only 50% of clinically defined cases will have a positive blood culture
  - “Time to positivity” of blood culture is useful for determining source

Differential Time to Positivity

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<td>1</td>
</tr>
<tr>
<td>60-99</td>
<td>2</td>
</tr>
<tr>
<td>30-59</td>
<td>3</td>
</tr>
<tr>
<td>15-29</td>
<td>0</td>
</tr>
<tr>
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<td>6</td>
</tr>
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<td>Total</td>
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</table>

Antimicrobial Therapy for Sepsis

- “Right drug, right dose, right time”
- Empiric regimens should be broad
  - Consider anti-candida
  - Narrow spectrum as data return
- Specific Therapy for single pathogen
  - Combination therapy almost never indicated
    - Possible indications
      - Pseudomonas
      - Endocarditis due to Enterococcus etc
      - Highly resistant organisms

Which Antibacterials Can Be Given By Rapid Infusion

<table>
<thead>
<tr>
<th>Drug</th>
<th>Minimum Infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pen G</td>
<td>60-120 min</td>
</tr>
<tr>
<td>Pip-tazo</td>
<td>20-30 min</td>
</tr>
<tr>
<td>Ticar-clav</td>
<td>30 min</td>
</tr>
<tr>
<td>Cefepime</td>
<td>30 min</td>
</tr>
<tr>
<td>Daptomycin</td>
<td>10 min</td>
</tr>
<tr>
<td>Meropenem</td>
<td>3-5 min</td>
</tr>
<tr>
<td>Imipenem</td>
<td>20-30 min</td>
</tr>
<tr>
<td>Ertapenem</td>
<td>30 min</td>
</tr>
<tr>
<td>Doripenem</td>
<td>60 min</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>BSIs per 10,000 admissions</th>
<th>Percentage of BSIs Total (n = 20,978)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coagulase-negative staphylococci</td>
<td>15.8</td>
<td>31.3</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>10.3</td>
<td>20.2</td>
</tr>
<tr>
<td>Enterococcus species</td>
<td>4.8</td>
<td>9.4</td>
</tr>
<tr>
<td>Candida species</td>
<td>4.6</td>
<td>9.0</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>2.8</td>
<td>5.6</td>
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Wisplinghoff et al. CID 2004;39:348

Management of Sepsis for the Boards

- Initial Fluid Resuscitation
  - Crystalloid with albumen
  - Crystalloid 1L over 30 min and total 2 liters over 4-6 hours
  - Hetastarch: Do Not Use (renal dysfunction)
  - Hg 7-8 g/dl adequate unless fluid resuscitation fails to improve O2 tissue delivery: then Hg 10g/dl

- Pressors
  - Norepinephrine is preferred
  - Vasopressin useful if shock is refractory
  - Low dose dopamine: Do NOT use for renal perfusion
  - Dobutamine indicated for myocardial dysfunction or refractory hypotension

- Physiologic Targets
  - Mean arterial pressure >65 mmHg
  - Central venous pressure 8-12 mmHg (12mm for mechanically ventilated patients)
  - Urine output 0.5 cc/kg/hr
  - Central venous oxygen saturation (SvO2) >65-75
  - If blood lactate >4 mM, target at 10-20% / initial 2 hour reduction

Management of Sepsis

- Glucocorticosteroids (Hydrocortisone 100mg q8h)
  - Enhance shock reversal
  - No survival benefit
  - Except perhaps for highest risk patients
  - No role for ACTH stimulation test

- Tight glucose control
  - Harmful, no benefit

- Adjunctive Antiendotoxin / Anticytokine /Antithrombosis
  - None marketed or effective
  - APC(Activated Protein C) removed from market

Catheter Related Infections

- Prevention

- Management

The 100,000 Lives Campaign

Prevent Central-Line Infections

- Hand Hygiene
- Maximal Barrier Precautions Upon Insertion
- Chlorhexidine Skin Antisepsis
  - (Skin site preparation; also consider chlorhexidine body washes and patches)
- Optimal Catheter Site Selection, with Avoidance of the Femoral Vein for Central Venous Access in Adult Patients
- Daily Review of Line Necessity

- http://www.ihi.org/IHI/Programs/Campaign/CentralLineInfection.htm

Bob Weinstein Rule Regarding Source

- Short Term Vascular Catheter-Skin
- Long Term Catheter-Lumen
Antibiotic Impregnated Catheters and Hubs Plus Antibiotic Lock Solutions

- Not likely testable on the boards
- They have a role but..... not well defined

Catheter Related Infections

- Prevention
- Management

Categorization of Intravascular Line Infections

- Local Catheter Infection
  - Exit Site
    - Might be salvaged medically
  - Tunnel
    - Almost never salvaged medically
- Catheter Colonization
  - Do not routinely culture tips-maybe if infection suspected!
  - If Staph aureus grows from tip, you should treat
  - Catheter is source
    - >15cfu from 5 cm segment of tip
    - >100 cfu from broth culture

Question

The laboratory reports that both blood cultures are growing gram positive cocci in clusters.

Which of the following would be the most convincing evidence that the line was the source of the infection?

The blood culture drawn through the IV line turns positive:

A) 1 hour prior to blood culture drawn peripherally
B) 3 hours prior to blood culture drawn peripherally
C) 1 hour after blood culture drawn peripherally
D) 4 hours after blood culture drawn peripherally
E) Time to positivity is not a reliable indicator of source of bacteremia

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Rand, Ann Intern Med 1/2004
Suspected Catheter Related Bacteremia
What if the Blood Culture is Negative
But the Cath Tip Grows Staph Aureus?

- Catheter tips are not routinely cultured!!
- Risk of subsequent bacteremia is high
  - 24% if no antibiotics within 24 hrs
  - 4% if antibiotics
  - (Non randomized, retrospective, Bonten CID 2008)
- Treat for at least 5-7 days

Always Remove Catheter

- Syndromes
  - Severe Sepsis
  - Septic thrombophlebitis/Venous obstruction
  - Endocarditis
  - Positive blood cultures>72 hrs after appropr Rx
- Organisms
  - Staph aureus
  - Pseudomonas aerug
  - Atypical mycobacteria
  - Bacillus species
  - Candida species
  - Malassezia
  - Propionibacteria
  - Micrococcus

Duration of Therapy for Catheter Related Infections

- Testable only for Staph aureus
- Otherwise: look up

Question

A 42 year old male in the ICU for cardiogenic shock has Staph aureus line related bacteremia
Which of the following would mandate a course of therapy >14 days, ie 4-6 weeks?

a) Positive blood culture positive at 24 hrs of appropriate therapy but negative at 72 hrs
b) Temp 38.5 after 48 hrs of appropriate therapy but afebrile by 72 hrs
c) Staph is MRSA
d) Prolonged neutropenia pre and post bacteremia
e) Negative TEE on day 2 of appropriate therapy

Who Is Low Risk and Eligible for 14 Day Therapy for Staph aureus Bacteremia?

- TEE negative (performed at least 5-7 days post pos BC)
  - Cardiac abnormalities do not mandate long therapy by themselves
- Patient has None of the Following
  - Neutropenia, steroids, immunosuppression, diabetes
  - Prosthesis
    - joint
    - recent endovascular graft
  - Valve
  - Prolonged endocarditis or suppurative phlebitis
  - Metastatic foci
  - No Fever after 72 hrs and no positive blood culture > 72-96 hrs after therapy initiated
**Question**

To prevent ventilator associated pneumonia, which of the following interventions is most effective?

a) Twice weekly surveillance cultures of tracheal secretions  
b) Silver impregnated endotracheal tube  
c) Oral care daily with chlorhexidine  
d) H2 blockers to suppress gastric acidity  
e) Rifaxamin by nasogastric tube

**Prevention of Ventilator Associated Pneumonia**

- **General strategies**
  - Hand hygiene, prompt weaning
- **Prevent aspiration**
  - Use cuffed tube with inline suctioning
- **Prevent aerodigestive colonization**
  - Avoid H2 blockers and PPIs  
  - Oral hygiene (evidence marginal)  
  - (Oral/Gut decontamination controversial)
- **Minimize contamination of equipment**
  - Routine tubing change unnecessary

**Appendix**
**Ventilator Bundle Elements**

1. Elevation of the head of the bed to between 30 and 45 degrees
2. Daily awakening: “sedation vacation”
4. DVT prophylaxis (unless contraindicated)
5. Stress bleeding prophylaxis

---

**Diagnosis of Line Infection Involving Short-term Central Venous or Arterial Catheter**

<table>
<thead>
<tr>
<th>Mild or moderate H (no hypotension or organ failure)</th>
<th>Severe H (hypotension, hypoperfusion, signs &amp; symptoms of organ failure)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood cultures, 2 sets (1 peripheral)</td>
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<tr>
<td>Consider antibiotics</td>
<td>Initiate appropriate antibiotic therapy</td>
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- If no source of fever identified, remove CVC and AC, culture tip and insert at new site or exchange over a guidewire or culture insertion site plus hubs where available.
- Blood cultures (+) & AC cultures (+) for Staphylococcus aureus, Bacillus, etc.
- Blood cultures (+) & AC cultures (+) for Coagulase negative staphylococci, etc.
- Blood cultures (+) & AC cultures (+) for Steplococcus aureus, Enterococcus, Gram-negative bacilli
- Blood cultures (+) & AC cultures (+) for Yeast, Candida
- Blood cultures (+) & AC cultures (+) for Endocarditis
- Blood cultures (+) & AC cultures (+) for Thrombophlebitis
- Blood cultures (+) & AC cultures (+) for Osteomyelitis

If continued fever & no other source found, remove & culture CVC and AC.

- Look for another source of infection.
- See Figure 2

**Management of Long-Term Central Venous Catheter or Port - Related Bloodstream Infection**

**Uncomplicated (Fig. 1)**

- Remove CVC/P & treat with systemic antibiotics for 5-7 days.
- For CVC, continue antibiotic lock.

**Complicated**

- Remove CVC/P & treat with systemic antibiotics for 5-7 days.
- For CVC, continue antibiotic lock.

- If catheter is retained, treat with systemic antibiotics. + antibiotic lock for 10-14 days.
- If catheter is removed, start antibiotics 10-14 days.

**Resolution of bacteremia/fungemia**

- Persistent bacteremia/fungemia
- Organ failure

**Management of Catheter-Related Bloodstream Infection (Short-term Central Venous Catheter or Arterial Catheter)**

**Uncomplicated bloodstream infection and fever resolves within 72 hours in a patient who has no intravascular hardware and no evidence of endocarditis or infective endocarditis.**

- Blood cultures, 2 sets (1 peripheral)
- Remove catheter & treat with systemic antibiotics for 5-7 days.
- If catheter is retained, treat with systemic antibiotics. + antibiotic lock for 10-14 days.
- If catheter is removed, start antibiotics 10-14 days.

**Complicated**

- Blood cultures, 2 sets (1 peripheral)
- Remove catheter & treat with systemic antibiotics for 5-7 days.
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**Resolution of bacteremia/fungemia**

- Persistent bacteremia/fungemia
- Organ failure

**Management of Catheter-Related Bloodstream Infection and Tunneled Hemodialysis Catheters**

**Uncomplicated**

- Blood cultures, 2 sets (1 peripheral)
- Remove CVC/P & treat with systemic antibiotics for 5-7 days.
- For CVC, continue antibiotic lock.

**Complicated**

- Blood cultures, 2 sets (1 peripheral)
- Remove CVC/P & treat with systemic antibiotics for 7-14 days.
- For CVC, continue antibiotic lock.

- If catheter is removed, start antibiotics 10-14 days.

**Resolution of bacteremia/fungemia**

- Persistent bacteremia/fungemia
- Organ failure

**Surgical Site Infection Prevention**

1. Appropriate use of antibiotics within 60 min pre skin incision
2. Appropriate hair removal
3. Controlled 6 AM postoperative serum glucose in cardiac surgery patients
4. Immediate postoperative normothermia in colorectal surgery patients

http://www.ihi.org/IHI/Programs/Campaign/SurgicalComplications.htm
Findings in Patient with Moderately Severe Serotonin Syndrome

- Mydriasis
- Agitation
- Diaphoresis
- Clonus (greater in lower extremities)
- Tremor (greater in lower extremities)
- Hyperreflexia (greater in lower extremities)
- Tachycardia


Antiseptic or Antibiotic Impregnated Devices-Not Testable on Boards

- Catheters
  - Indicated if, after full implementation of bundle recommendations, institutional goals are not met
  - Should goal be zero infections?
- Hubs
  - Not standard of care and not testable

Antibiotic Lock Solutions and Antibiotic Impregnated Hubs

- Probably not testable
- Lock Therapy indications
  - Long term catheters as adjunct to systemic rx
  - No sign of exit site or tunnel infection
  - Salvage is goal
- Dwell time
  - 24-48 hrs
- Drug Concentrations: Look up
- Both are used, but evidence of efficacy is inconsistent

The End

Management of Sepsis for the Boards

- Activated protein C
  - NO LONGER MARKETED IN US
- Tight glucose control
  - No
- Stress dose steroids
  - OK but controversial, as is Cosyntropin stimulation test
- Pressors
  - Prefer levophed
- Swan Ganz catheter
  - Not routinely indicated