FEVER IN THE ICU

Infectious Diseases in Clinical Practice
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Learning Objectives

• To know the differential diagnosis for fever in a patient in the ICU

• To know the common clinical presentation, diagnosis, and management of common infections in the ICU

• To recognize the common non-infectious etiologies for fever in the ICU

Fever: Definition and Measurement

• Definition of fever is arbitrary
  • ≥38.3°C (101°F) commonly used, IDSA/ACCCM guidelines
  • Use a lower threshold in immunocompromised patients
  • T < 36.0°C should also prompt an investigation for infection
  • Note that patients on CRRT or ECMO may not mount a fever

Fever in the ICU: Epidemiology

<table>
<thead>
<tr>
<th>Reference</th>
<th>Setting</th>
<th>Number of Patients</th>
<th>Fever Definition (°C)</th>
<th>Fever Incidence (%)</th>
<th>Infectious Fever Etiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ciri et al.</td>
<td>General ICU</td>
<td>93</td>
<td>≥38.4</td>
<td>70</td>
<td>53%</td>
</tr>
<tr>
<td>Pena et al.</td>
<td>General ICU</td>
<td>493</td>
<td>≥38.3</td>
<td>38.2</td>
<td>55%</td>
</tr>
<tr>
<td>Barie et al.</td>
<td>Surgical ICU</td>
<td>2,419</td>
<td>≥38.2</td>
<td>26</td>
<td>46%</td>
</tr>
<tr>
<td>Lupardi et al.</td>
<td>General ICUs 1 CVICU</td>
<td>20,466</td>
<td>≥38.3</td>
<td>44%</td>
<td>MSS Culture positive</td>
</tr>
</tbody>
</table>

• At least 50% of febrile episodes are non-infectious!
• Most common infectious etiologies: PNA, bloodstream, abdominal infections
• Most common non-infectious etiologies: post-op fever, central fever

Differential: Head-to-Toe Approach

- Cerebrospinal meningitis (post-NSG)
- Nosocomial Sinusitis (hospital-acquired)
- Hospital-acquired pneumonia (HAP)
- Empyema
- ARDS
- Endocarditis
- Pericarditis
- Abdominal abscess
- SBP
- Surgical site infection (SSI)
- Osteomyelitis/septic arthritis
- Gout
- Cellulitis at PIV/CVC
- Infected decubitus ulcer
- Adrenal insufficiency
- Drug Fever/Withdrawal
- DVT/PE
- Malignancy
- Transfusion reaction
- Transplant rejection
- Central fever

Disclosures

• NONE
Differential: Head-to-Toe Approach

- **CNS**
  - Nosocomial meningitis (post-NSG)
  - Sinusitis

- **HEENT**
  - Hospital acquired PNA
  - Empyema
  - ARDS

- **Pulmonary**
  - Endocarditis
  - Pericarditis

- **Cardiac**
  - Abdominal abscess
  - SBP
  - Acute pancreatitis
  - C. difficile

- **GI/GU**
  - Osteomyelitis/septic arthritis
  - Gout

- **MSK**
  - Cellulitis at PIV/CVC
  - Infected decubitus ulcer
  - Surgical site infection

- **Skin**
  - CLABSI
  - Candidemia

- **Systemic**
  - Drug Fever/Withdrawal
  - DVT/PE

- **Other non-infectious etiologies**

Parts of the Exam to Remember

- **CNS**
  - Careful neuro exam

- **HEENT**
  - Look for nasal discharge

- **Pulmonary**
  - Back and joint exam

- **Cardiac**
  - Cellulitis at PIV/CVC

- **GI/GU**
  - Examine line sites
  - Take off bandages

- **Skin**
  - CLABSI
  - Examination of skin

Diagnostics

- Avoid “automatic” order sets for fever (i.e., the “pan-culture”)
- Expensive
- Time-consuming
- Patient discomfort
- Unnecessary radiation
- Transfer out of the controlled unit for imaging/procedures
- With more testing, you will find more colonizers/contaminants

- Use a rational approach
- Start with a history and physical
- Order labs/diagnostics based on clinical suspicion

Case #1

35 y/o man with alcoholic cirrhosis is admitted to the ICU with severe influenza A and is intubated and eventually requires ECMO. He was slowly improving but then over the last 2 days has started having fevers to 38.3 with increasing O2 requirement. He has trouble following commands when sedation is lifted.

Blood and urine cultures are negative. CXR is unchanged. Head CT shows pansinusitis but is otherwise negative.

Your Next Diagnostic Step is:

1. Sinus puncture
2. Lumbar puncture
3. Mini-BAL or endotracheal aspirate

Defining CAP, HAP, VAP, HCAP

- Community-acquired pneumonia (CAP)
- Pneumonia acquired in association with a healthcare setting, not meeting criteria for HAP or HCAP
- Hospital-acquired pneumonia (HAP)
- Ventilator-associated pneumonia (VAP)
- Healthcare-associated pneumonia (HCAP)

Defining CAP, HAP, VAP, HCAP

**Community-acquired pneumonia (CAP)**
- PNA not acquired in association with a healthcare setting (i.e. not meeting criteria for HAP or HCAP)
- Risk for MDR pathogens when hospitalized for ≥5 days.

**Hospital-acquired pneumonia (HAP)**
- PNA acquired after 48 hours in the hospital and not incubating at the time of admission.
- Risk for MDR pathogens when hospitalized for ≥5 days.
- Risk by days intubated:
  - Days 1-5 (3%/d)
  - Days 5-10 (2%/d)
  - Days > 10 (1%/d)

**Ventilator-associated pneumonia (VAP)**
- PNA acquired after 48 hours of intubation. This is a subset of HAP.
- Risk by days intubated:
  - Days 1-5 (3%/d)
  - Days 5-10 (2%/d)
  - Days > 10 (1%/d)

**Healthcare-associated pneumonia (HCAP)**
- PNA in a non-hospitalized patient with any one of the following:
  - Hospitalization for ≥2 days in the last 90 days
  - Residence in a nursing home or long-term care facility
  - Intravenous antibiotics, wound care, dialysis, or chemotherapy within the last 30d
  - Family member with an MDR pathogen

Why do we care about these distinctions?

- To characterize the risk of MDR bacteria, and therefore inform your empiric antibiotic approach
- Risk of MDR organisms in PNA:
  - HCAP
  - HAP/VAP with ≥5 days in the hospital
  - Immunosuppression
  - Abx in last 90 days
  - High frequency of ABx resistance in a specific unit

VAP: Diagnosis

**STEP 1**
Clinical suspicion for PNA?

1. New or progressive CXR infiltrate
2. 2 out of 3 clinical criteria:
   - F > 38°C
   - Adult or B WBC
   - Purulent secretions
   - 65% sensitive, 75% specific
   - With ARDS: consider PNA when have 2 clinical criteria b/c may not see CXR changes

**STEP 2**
Lower respiratory tract culture before Abx

- Quantitative cultures preferred
- BAL (cutoff 10⁷ or 10⁶) and mini-BAL (cutoff 10⁵ or 10⁴) both are ~80% sensitive and specific
- Even 24 hrs of prior Abx can make a sample negative

**STEP 3**
Start empiric therapy

- Re-evaluate each day based on culture results, clinical course
- Consider stopping Abx if cultures are negative

- Other diagnostics:
  - Sensitivity of blood cultures <25%
  - Thoracentesis if an effusion is large or the patient is toxic
VAP/HAP: Empiric ABx (IDSA Guidelines)

- Risk Factors for MDR Pathogens Present?
  - HCAP
  - HAP/HAP with ≥ 5 days in the hospital
  - Immunosuppression
  - ABx in last 90 days
  - High frequency of ABx resistance in a specific unit

- Use local resistance patterns for guidance
- Use linezolid or vancomycin
- Use anti-pseudomonal beta lactam
- Use anti-pseudomonal FG or AG

Duration of ABx

- Chastre et al: RTC of 400 pts dx’d with VAP by quantitative BAL, randomized to 8 vs. 15 days of ABx therapy
- No difference in: mortality, recurrent infections, length of ICU stay
- 8-day group had:
  - More ABx-free days (9 vs 13%)
  - Less MDR organisms if had recurrent infections (42 vs 65%)
  - But, higher pulmonary reinfection rate (41 vs 25%) if had a glucose nonfermenter (Pseudomonas, Acinetobacter, or Stenotrophomonas)

- Take-home:
  - Pseudomonas, Acinetobacter, Stenotrophomonas: 14 (or 15) days
  - MRSA: 7-21 days depending on extent of infection (IDSA MRSA guidelines)
  - 7 (or 8) days for everyone else

Linezolid vs. Vancomycin for MRSA?

- Phase 4, double-blind, randomized, controlled multicenter trial, pts with MRSA HAP/VAP/HCAP
  - IV linezolid 600 mg Q12h vs. IV vancomycin (15 mg/kg Q12h)
  - Vanco dose-optimized by unblinded pharmacist
  - Treated for 7-14 days (up to 21 d if bacteremia)

- Primary outcome: Clinical response
  - Cure defined as: resolution of clinical signs and sx, improvement or lack of progression of CXR, no additional abx required

Study Conclusions

- Linezolid has a modest benefit in clinical response over vancomycin in MRSA HAP/VAP
- Limitations:
  - Vanco pts sicker: Compared to linezolid group, more ventilated, concurrent MRSA bacteremia, kidney disease and diabetes
  - No difference in hard outcomes:
    - No mortality benefit
    - Did not evaluate length of ICU stay, length of hospitalization, mechanical ventilation

Linezolid vs. Vancomycin: Outcomes

- No difference in:
  - Clinical Cure
  - Micro-eradication

Nosocomial Transmission of Resp Viruses

- Has been described with:
  - RSV
  - Influenza
  - Parainfluenza
  - Adenovirus

- Transmission can be between patients or from visitors/staff
HAP/VAP: Take Home Points

- Think about risk factors for MDR pathogens and use that to guide empiric therapy
- Diagnosis is based on a combination of clinical and microbiologic parameters
- Duration of therapy 7 days with the exception of the glucose nonfermenters +/- MRSA
- Consider linezolid for MRSA if not responding to vancomycin

Nosocomial Sinusitis

- Epidemiology:
  - Radiographic sinusitis in 25-75% of ICU pts
  - But etiology of nosocomial fever in ~5%
  - Radiographic sinusitis ≠ infectious sinusitis
- Micro: Pseudomonas, S. aureus, can be polymicrobial
- Clinical: classic signs/sx of sinusitis often absent
- Dx: CT, aspirate by ENT to confirm dx and guide ABx therapy
- Treatment duration: 7 days

Case #2

A 65 y/o M is admitted with an STEMI. 4 days into his hospitalization he spikes a fever to 39, drops his SaO2 to the low 90s on RA, and becomes altered. He has a foley. He is started on vancomycin and pip/tazo and improves.

Work-up reveals:
- CXR with a new LLL infiltrate
- Blood cultures and sputum culture negative at 48h
- UA (from his catheter) shows 30 WBC, Urine cx >100K VRE

What would you do with his ABx?

1. Continue pip-tazo and d/c vanco
2. Continue pip-tazo and change vancomycin to linezolid to cover VRE

CA-UTI is a Diagnosis of Exclusion!

- Catheter-associated bacteriuria is common (up to 25% of patients with short term catheters)
- CA-bacteriuria usually represents colonization (asymptomatic bacteriuria = ASB) and NOT infection
- What about pyuria?
  - Pyuria is common in catheterized patients (up to 75% with short term catheters)
  - The presence or degree of pyuria cannot differentiate ASB from UTI
  - But, the absence of pyuria suggests an alternative diagnosis

Catheter-associated UTI: Definition

1. Patient with a catheter currently or within the last 48 h
2. Symptoms or signs c/w UTI
3. No other source of infection (i.e., diagnosis of exclusion)
4. ≥10³ cfu of ≥1 bacterial species in a urine culture
The million dollar question...

- What are “signs and symptoms compatible w/UTI” in a patient with a catheter?
  - New onset or worsening of fever, rigors, altered mental status, malaise or lethargy with no other identified cause
  - Flank pain or CVAT
  - Acute hematuria
  - Pelvic discomfort
  - Spinal cord injury patients: increased spasticity, autonomic dysreflexia, or sense of unease

Signs and Symptoms of Systemic Infection without classic UTI signs/ sx

<table>
<thead>
<tr>
<th>Alternate Diagnosis Likely? (Signs/ sx of other illness present)</th>
<th>U/A, urine cx (-)</th>
<th>U/A (+), urine cx (-)</th>
<th>U/A (+), urine cx (+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>Do not order U/A, urine cx</td>
<td>U/A (+), urine cx (+)</td>
<td>Treatment for UTI if no alternate dx identified</td>
</tr>
<tr>
<td>No</td>
<td>Send U/A, urine cx</td>
<td>Do not treat for UTI</td>
<td>On abx No abx</td>
</tr>
</tbody>
</table>

*Exceptions: pregnancy, pre-urological procedure, neutropenic host

Empiric Therapy for Complicated UTI

- Community acquired:
  - Ertapenem
  - Ceftriaxone
- Healthcare associated:
  - Pip/tazo
  - Ertapenem
  - Ceftriaxone

Treatment

- Duration:
  - 7 days if there is prompt resolution of symptoms
  - 10-14 days if response is delayed
- Catheter change?
  - Yes, if the catheter has been in for >2 weeks, change it
  - This has been associated with:
    - CA-bacteriuria and CA-UTI at 28d
    - Time to resolution of sx

Candidurias: Who to Treat?

- Asymptomatic candiduria:
  - In general, don’t treat!
  - Change the Foley: can eliminate candiduria in 20-40%
  - Exceptions: Patients at high risk of dissemination
    - Neutropenia
    - Patients undergoing urologic procedures
- Symptomatic candiduria: treat
## Candida UTI: Treatment Options

1st line: Fluconazole
- Excellent urine levels, 10-fold higher than serum levels
- Can get concentrations in the urine that are higher than the MIC for organisms that are intermediate or resistant
- 200-400mg PO daily

## Fluconazole-Resistant Candida UTI

- Can try fluconazole and re-check Urinary Culture (UCx) if not systemically ill
- Other options:
  - Flucytosine
  - Amphotericin B
  - Amphotericin B bladder washes: Resolve candiduria in >90% but ○ relapses
- Other azoles?
  - Voriconazole, posaconazole, itraconazole have poor urinary penetration
- Caspofungin?
  - Poor urinary penetration, but use if suspect systemic disease

## CA-UTI: Take-home points

- ASB and pyuria are common in patients with a foley
- To diagnose a CA-UTI, the patient must have:
  - Signs and symptoms compatible with UTI
  - No other source for infection
- Treat for 7-14 days depending on clinical response
- Candiduria is almost always asymptomatic and does not require treatment

## Case #3

A 55 year old man is admitted to the ICU with severe gallstone pancreatitis. He has been afebrile and slowly improving on TPN and with conservative measures. He spikes a fever to 39°C associated with new hypotension and rigors. Blood cultures drawn from his triple lumen subclavian line turn positive 6 hours before his peripheral blood culture. Both are growing *E. coli*.

The most sensitive test to determine the source of the *E. coli* is:

1. Differential time to positivity
2. Inflammation around the central line exit site
3. Remove the catheter and culture the tip

The IDSA Guidelines recommend:

1. Pull the line
2. Ok to attempt line salvage with ABx lock therapy
3. Ok to attempt line salvage by giving systemic ABx through the line
**CLABSI: Diagnosis**

- Clinical findings unreliable:
  - Inflammation at the exit site is extremely insensitive (<3%)
- Positive peripheral bxt and > 15 CFU/plate of same organism from catheter tip
  - 79% sensitive, 92% specific
  - But >80% of catheters withdrawn b/c of clinical suspicion of CLABSI are removed unnecessarily
- Quantitative blood cultures (line vs peripheral) may be most sensitive/specific, but not routinely available


**CLABSI: Differential Time to Positivity**

- Allows for diagnosis without removing the line
- Draw culture from central line and peripheral blood at the same time
- CLABSI = blood culture drawn from central line turns positive at least 2 hrs before peripheral culture turns positive
- Test characteristics
  - 95% sensitive
  - 90% specific (but only ~40% specific for yeast)


**CLABSI: Management**

- Possible scenarios:
  - Line (+)/ peripheral (+)
    - DTTP ≥ 2 hrs → CLABSI → remove line and treat
    - DTTP < 2 hrs → look for another source and treat
  - Line (+)/ peripheral (-) → colonization/ contaminant

- Duration of treatment (with line removal):
  - 5-7 days: coagulase negative Staphylococci
  - 7-14 days: GNRs, Enterococcus
  - 14 days: S. aureus, Candida

Mermel et al CID 2009

**CLABSI: Line Management**

- Remove line whenever possible:
  - Guidewire exchange only if no alternative insertion site
  - If septic, hemodynamically unstable, persistent bacteremia → remove line
  - Long term catheters: remove if S aureus, Pseudomonas, Candida
  - Short term catheters: remove if S aureus, GNRs, Candida, Enterococcus

- Line salvage
  - Antibiotic lock therapy + systemic antibiotic therapy
  - Studied primarily in long-term catheters

Mermel et al CID 2009

**Case #4**

85 y/o man is admitted with fever and respiratory failure to the ICU and treated with vanc/pip-tazo. He initially responds but then 5 days into therapy he began spiking high fevers up to 39 ºC daily. His respiratory status is unchanged. He is escalated to vanc/meropenem with no change in his fever or respiratory status after another 5 days. Extensive work-up for other sources of infection is negative.

**What is Your Next Step?**

1. Change vanco to linezolid
2. Add tobramycin
3. Stop antibiotics
Drug Fever

- 3-4% of all drug reactions
- Multiple mechanisms:
  - Altered Thermoregulatory Mechanisms (e.g., amphetamine)
  - Drug Administration (e.g., amphotericin)
  - Pharmacologic Effects (e.g., Jarisch-Herxheimer Reaction)
  - Idiosyncratic Reactions (e.g., malignant hyperthermia)
  - Immune-Mediated/Hypersensitivity Reactions (e.g., most ABx)

Drugs Associated with Drug Fever

Timeline of Fever Onset

- Cardiac: 44, 7.8, 10, 111.1
- Antimicrobial: 41, 6, 0.5, 12.3
- Antineoplastic: 34, 18.3, 16, 15.9
- CNS: 40, 15.7, 7, 36.1
- Other: 19, 18.3, 7, 36.1

Fever Characteristics

- Fever is high
- Usually defervesce within 1-2 d of stopping the drug

Treatment

- Discontinue all potentially causative meds, together or sequentially
- In cases where benefit > risk in continuing, can try to pre-treat:
  - Corticosteroids
  - Antihistamines
  - But watch for S/Sx of progression of hypersensitivity
- Rechallenge will usually cause recurrence of fever within a few hours, confirming the diagnosis
  - If fever was accompanied by severe adverse effects, avoid rechallenge
  - Important to document suspected drug fever in the allergy section with as much detail of associated symptoms as possible
Cross-Reactivity of Antibiotics?

- Change to another class if possible (i.e. Beta-lactam to fluoroquinolone)
- No studies exist which address drug fever cross reactivity specifically – focus is on all symptoms of hypersensitivity


Drug Fever: Take Home Points

- Always consider it in the ddx for fever in the hospital
- Look for eos, temp-pulse dissociation, rash although remember these are present in <20% of cases
- Consider stopping the ABx or switching classes if you really suspect it
- Remember to document drug fever as an allergy!

VTE and Fever

- Seen in 5-15% of patients presenting with PE/DVT
- Characteristics:
  - Usually <38.3
  - Peaks on day of PE
  - Gradually subsides within 1 week


Central Fever

- Accounts for ~50% of fever in the Neuro-ICU
- Seen in patients with brain tumors, SAH, intraventricular hemorrhage
- Associated with vasospasm
- Appears within 72 hours of admission, persists for longer than infectious causes of fever
- No difference in height of fever

Hocker et al, JAMA Neurol 2013, 70:1499.

Can ARDS Itself Cause Fever?

- The fibroproliferative phase of ARDS can cause fever and leukocytosis that is indistinguishable from infection
- Open lung biopsy in 7/9 patients with late ARDS found fibroproliferative phase of diffuse alveolar damage and no evidence of infection
- So...probably, but would look very hard elsewhere and this is a diagnosis of exclusion


Case #5

65 y/o F in the ICU for a prolonged course after a Whipple procedure. Her course has included a VAP and UTI and she has received multiple courses of antibiotics. She has been spiking fevers for the last 3 days despite linezolid and meropenem. You get a call from the micro lab that 1/2 blood cultures (peripheral) is growing yeast.
The most appropriate next step is:
1. Start voriconazole
2. Start fluconazole
3. Start caspofungin

What is the ddx for “yeast in the blood”?
- Yeast in the blood almost always = candida
- Rarely it could be cryptococcus in the right host (e.g., HIV, transplant)

Back to the case...
- So you know it’s candidemia, so now what do you do?
- You need to do 3 things:
  1. Start caspofungin
  2. Evaluate for source → pull lines
  3. Eye exam

Why caspofungin and not fluconazole?
- What kinds of candida are there?
  - C albicans (50-65%)
  - C glabrata (~20%) – can be fluconazole resistant
  - C parapsilosis (6-17%)
  - C tropicalis (7-11%)
  - C krusei (2%)
  - C lusitaniae (<1%)
  - C dublinensis (<1%)

Caspofungin Basics
- Dosing:
  - 70mg IV x 1 then 50mg IV daily
  - No adjustment needed for renal failure or HD/CVVH
  - SEVERE hepatic disease: decrease maintenance dose to 35mg qday
    (*based on PK study of drug levels, not adverse effects)
- Drug-drug interactions:
  - Increase maintenance dose to 70mg when given with phenytoin,
    rifampin, carbamezepine, dexamethasone, nevirapine, or efavirenz
- Adverse effects: very well tolerated, can get elevation of LFTs

Back to the Case...
- The candida comes back as C glabrata...anything else to do?
  - Yes – ask the lab for fluconazole susceptibilities!
  - If it comes back sensitive to fluconazole → switch to fluconazole to finish the course.
Candida Susceptibilities

| Candida species | Fluconazole | Voriconazole | Posaconazole | Itraconazole | Amphotericin B | Candida
|-----------------|-------------|--------------|--------------|--------------|----------------|------
| Candida albicans | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s |
| Candida tropicalis | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s |
| Candida parapsilosis | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s |
| Candida glabrata | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s |
| Candida krusei | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s |
| Candida lusitaniae | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s |

NOTE: *1. Intermediate susceptibility, R. resistant, S. susceptible, SOD susceptibility dose-dependent.

- C albicans or C tropicalis:
  - Fluconazole resistance very rare: C albicans ~1-2%, C tropicalis ~4%
  - Fluconazole is drug of choice

Pappas, CID 2009.

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- C parapsilosis:
  - Caspofungin MICs are in general higher, although clinical significance unclear
  - Fluconazole is drug of choice (~4% fluconazole resistance seen)

Pappas, CID 2009.

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- C glabrata:
  - Fluconazole resistance is ~15% nationally, voriconazole resistance ~10%
  - Caspofungin is drug of choice to start, then narrow to fluconazole based on sensitivities (consider voriconazole oral step-down alternative if sensitive)

Pappas, CID 2009.

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| Candida albicans | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s |
| Candida tropicalis | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s |
| Candida parapsilosis | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s |
| Candida glabrata | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s |
| Candida krusei | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s |
| Candida lusitaniae | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s |

NOTE: *1. Intermediate susceptibility, R. resistant, S. susceptible, SOD susceptibility dose-dependent.

- C krusei:
  - Intrinsic fluconazole resistance

Pappas, CID 2009.

Candida Susceptibilities

| Candida species | Fluconazole | Voriconazole | Posaconazole | Itraconazole | Amphotericin B | Candida
|-----------------|-------------|--------------|--------------|--------------|----------------|------
| Candida albicans | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s |
| Candida tropicalis | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s |
| Candida parapsilosis | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s |
| Candida glabrata | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s |
| Candida krusei | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s |
| Candida lusitaniae | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s | 5 s 5 s |

NOTE: *1. Intermediate susceptibility, R. resistant, S. susceptible, SOD susceptibility dose-dependent.

- C lusitaniae:
  - Can be amphotericin resistant

Pappas, CID 2009.

IDSA guidelines:

- If no metastatic foci of infection, treat for 2 weeks from date of 1st negative culture (so be sure to get surveillance cx)
  - This is based on the results of several prospective, randomized trials in which treatment for 2 weeks was associated with few complications and relapses

Pappas, CID 2009.
Pull the line!

• Remove catheters if possible:
  • Often difficult to tell in an individual patient if catheter or GI is the source
  • Exception: C parapsilosis is often catheter-associated
  • Removal is associated with more rapid clearance of blood cultures and decreased mortality
  • Note that this data is less compelling in neutropenic patients, so recommendation to remove catheters is less strong in this population

Get an Eye Exam

• Rule out chorioretinitis (seen in ~10%) or endophthalmitis (seen in 1-2%)

• This is not an emergency (unless having visual symptoms)

• In fact, may increase your sensitivity by waiting ~1 week after starting therapy

Why does this matter?

• Intravitreal injections (ampho)

• Longer duration of therapy (4-6 weeks)

• Choose an agent with good eye penetration
  • Azoles (voriconazole>fluconazole)
  • Ampo + 5-FC
  • NOT echinocandins (have poor ocular penetration)

Candidemia: Take Home Points

1. Start an echinocandin empirically
  • Check surveillance cx in 48hr
  • Get susceptibilities if it’s C glabrata and change to fluc if sensitive
  • Change to fluc if it’s a susceptible species (albicans, tropicalis, parapsilosis)
  • Treat for 2 weeks from the date of the 1st negative culture

2. Pull the line

3. Eye exam
  • If positive, use vori if sensitive
  • Duration of therapy 4-6 weeks for eye involvement

What is the role of procalcitonin in the ICU?

• Diagnosis of sepsis vs. non-infectious SIRS
  • Meta-analysis of 18 studies suggests low diagnostic accuracy (sensitivity/specificity of ~ 70%)

• Aid in antibiotic discontinuation
  • Meta-analysis of 14 RCTs investigating PCT algorithms for antibiotic therapy decisions
    • Reduced antibiotic exposure by 20-37%
    • No mortality difference
    • Decrease LOS in some studies, not in others


Fever in the ICU: Fever of Too Many Origins?

Horowitz, NEJM 2013, 368:3.
Thank you!