When guidelines don’t guide…
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NV ASP
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Learning objectives

• Identify common infection misdiagnoses (e.g. UTI, cellulitis, and C. difficile)
• Review the impact of these misdiagnoses on antimicrobial stewardship efforts and clinical outcomes
• Discuss the non-provider’s role in minimizing misdiagnoses
Antimicrobial stewardship

- Simply stated,
  - It is the APPROPRIATE use of antimicrobials
- Appropriate use of antimicrobials leads to
  - Improved patient outcomes
  - Fewer resistant infections
  - Fewer nosocomial infections
  - Fewer adverse drug events

Empiric Therapy
(Select appropriate agent(s) and dose)

Narrow Therapy  Escalate Therapy
(Choose the most narrow spectrum agent that remains effective and is associated with minimal collateral damage)

Discontinue
Antimicrobial stewardship team

- The real deal is never perfect
- Our current stewardship model:
Common stewardship interventions

- Treatment guidelines/ clinical pathways
- IV to PO
- Dose optimization
- De-escalation
- Duration of therapy
- Allergy assessment
- Bug/drug mismatch

Empiric Therapy
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Discontinue
All the treatment guidelines and stewardship interventions in the world won’t help if the diagnosis is incorrect.

If the diagnosis is incorrect, the best you can hope to achieve with stewardship interventions is the lesser of two evils.
What are common infection misdiagnoses?

- **Viral pharyngitis** → Streptococcal pharyngitis
- **Cough** → Bronchitis
- **Diarrhea** → C. difficile infection
- **Asymptomatic bacteriuria** → Cystitis

- **Gout** → Septic arthritis
- **Acute respiratory distress syndrome** → Pneumonia
- **Aspiration pneumonitis** → Pneumonia
- **Venous stasis** → Cellulitis
What are common infection misdiagnoses?

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- **Aspiration pneumonitis** → Pneumonia
- **Venous stasis** → Cellulitis
“Cellulitis”
Cellulitis

- Cellulitis is a common infection of the skin and subcutaneous tissue
- The most common pathogens are *Streptococcus pyogenes* and *Staphylococcus aureus*
- Leads to 2.3 million emergency department visits and 650,000 hospital admissions each year
- Inpatient treatment often consists of an IV beta-lactam and/or IV vancomycin
- 30 to 90% of diagnoses are actually pseudocellulitis
Pseudocellulitis

- Non-infectious inflammatory dermatoses
- Similar characteristics to cellulitis
  - Erythema
  - Edema
  - Warmth
  - Tenderness
- Not treated with antibiotics
- Oftentimes other treatment is needed
Costs and Consequences Associated With Misdiagnosed Lower Extremity Cellulitis

Qing Yu Weng, MD; Adam B. Raff, MD, PhD; Jeffrey M. Cohen, MD; Nicole Gunasekera, BS; Jean-Phillip Okhovat, MD, MPH; Priyanka Vedak, MD; Cara Joyce, PhD; Daniela Kroshinsky, MD, MPH; Arash Mostaghimi, MD, MPA, MPH

- Cross-sectional study of patients admitted to a large-urban U.S. hospital via the ER with a diagnosis of cellulitis
  - 79 of 259 (31%) patients were misdiagnosed with cellulitis
  - 44 (17%) patients did not require hospitalization based on ultimate diagnosis

Extrapolated nationally
- 50,000 to 130,000 unnecessary hospitalizations per year
- $195 to 515 million in avoidable health care spending per year
- 9,000 unnecessary HAIs
- 1,000 to 5,000 additional C. difficile infections
- 2 to 6 additional cases of anaphylaxis per year
Outcomes of Early Dermatology Consultation for Inpatients Diagnosed With Cellulitis

Prospective cohort study of an early dermatology consult in patients with a diagnosis of cellulitis in the ER at a large-urban hospital

- 39 of 116 patients diagnosed with pseudocellulitis
  - 34 patients were started on antibiotics
  - Antibiotics were discontinued in 26 of the 34 misdiagnosed cases
  - Discharge was recommended for 20 patients
- No patient diagnosed with pseudocellulitis worsened after discharge based on phone and clinic 30-day follow-up
Prospective cohort study of an early dermatology consult in patients with a diagnosis of cellulitis in the ER at a large-urban hospital

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How do you tell the difference?

- Characteristics of true bacterial cellulitis:
  - Asymmetry (unilateral involvement)
  - Painful erythematous rash
  - Ill-defined borders
  - Little scaling
  - Quickly enlarging
  - Does not resolve when leg is raised above the heart
  - Improves with antibiotics
- Anyone with sign and symptoms of sepsis should be treated as cellulitis until another cause is confirmed
“Cellulitis” case

• 58 y.o. male referred by the ER physician to the hospitalist for admission for cellulitis.
• HPI: Pain, swelling, and redness x 2 weeks; started on right 5th toe and now radiating to entire foot. Diagnosed with gout at urgent care, but returned to urgent care after no improvement; then prescribed clindamycin with no improvement.
• PMH: gout, DM
• ROS: denies fever, chills, and N/V
• Vitals WNL
• WBC 12K
“Cellulitis” case

- Diagnosed with “cellulitis” by the ER physician and hospitalist
- Oritavancin administered “to avoid an admission”
- Three days later
  - Patient returned with worsening right foot pain, swelling and redness but now has wrist pain
  - Lactic acid 2.2 but no fever or chills and labs WNL
  - ER physician and hospitalist diagnosed “cellulitis” and admitted the patient for observation
  - Started on ampicillin-sulbactam
“Cellulitis” case

• Infectious diseases consultant diagnosed gout
  • “…2 joints swollen, both classics sites for gout. He has no evidence to suggest infection with a normal white count and no fever.”
  • Infection unlikely since joints continue to swell while on antibiotics
  • Recommendation
    – Colchicine and indomethacin
    – Discharged home
• Patient has not been seen for “cellulitis” since being discharged over a month ago
“Cystitis”
Cystitis

- Generally, a self-limiting infection of the bladder
- *Escherichia coli* is the most common pathogen
- Goal of treatment is symptom relief
  - Progression to pyelonephritis and/or sepsis is very rare and treatment does not appear to prevent progression
- Uncomplicated cystitis can be diagnosed based on “classic” symptoms
  - Urinalysis and culture are not necessary to make the diagnosis or treat

<table>
<thead>
<tr>
<th>Classic symptoms</th>
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<tbody>
<tr>
<td>Dysuria</td>
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<tr>
<td>Urinary frequency</td>
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<tr>
<td>Urinary urgency</td>
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</tbody>
</table>
Asymptomatic bacteriuria

- Bacteria in the urine with no symptoms
- Relatively common
- Antibiotics are not recommended except in the following situations:
  - Pregnancy
  - Peri-operative period for urological procedures where mucosal bleeding is anticipated
Prospective, randomized study

- Treatment of ASB results in more symptomatic UTIs
  - 6 month follow-up: 7.6% vs 29.7%, p < 0.0001
- ASB may play a protective role in preventing recurrence
- ASB treatment results in higher prevalence of UTIs with antibiotic-resistant strains
Signs vs symptoms

- A sign is something that can be measured or observed
  - Objective data
- A symptom is something that cannot be measured by the caregiver
  - Subjective information

<table>
<thead>
<tr>
<th>Sign</th>
<th>Symptom</th>
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</thead>
<tbody>
<tr>
<td>Leukocyte esterase</td>
<td>Dysuria</td>
</tr>
<tr>
<td>Pyuria</td>
<td>Flank pain</td>
</tr>
<tr>
<td>Nitrite positive</td>
<td>Suprapubic tenderness</td>
</tr>
<tr>
<td>Color of urine</td>
<td>Urinary urgency</td>
</tr>
<tr>
<td>Fever</td>
<td>Urinary frequency</td>
</tr>
<tr>
<td>Sign/symptom that may be present</td>
<td>Cystitis</td>
</tr>
<tr>
<td>---------------------------------</td>
<td>----------</td>
</tr>
<tr>
<td>Abnormal urine color</td>
<td>X</td>
</tr>
<tr>
<td>Cloudy urine character</td>
<td>X</td>
</tr>
<tr>
<td>Elevated urine pH</td>
<td>X</td>
</tr>
<tr>
<td>Nitrite positive</td>
<td>X</td>
</tr>
<tr>
<td>Presence of leukocyte esterase</td>
<td>X</td>
</tr>
<tr>
<td>Pyuria</td>
<td>X</td>
</tr>
<tr>
<td>Presence of bacteria in urine</td>
<td>X</td>
</tr>
<tr>
<td>Foul urine odor</td>
<td>X</td>
</tr>
<tr>
<td>Symptoms of dysuria, urinary frequency or urgency, new onset hematuria, suprapubic pain</td>
<td>X</td>
</tr>
</tbody>
</table>

¹: Transplant patients.
Altered mental status

• UTI can cause mental status changes in the elderly population

• However, if altered mentation is the only symptom (no dysuria, frequency, urgency, or suprapubic discomfort) it is usually secondary to another cause
  • Common causes of altered mental status: medications, blood pressure, electrolyte abnormalities

Sustained reduction in inappropriate treatment of asymptomatic bacteriuria in a long-term care facility through an educational intervention

Trina F. Zabarsky, RN, a Ajay K. Sethi, PhD, b and Curtis J. Donskey, MD a, c
Cleveland, Ohio

- Education of nursing staff to discourage the collection of urine cultures in the absence of symptoms and providers to not treat ASB
- The rate of ASB treatment did not change
- However, the number of patients identified with ASB decreased because fewer cultures were obtained (1.7 to 0.6 per 1,000 patient days, p = 0.002)
- Total antimicrobial days of therapy were reduced (167.7 to 117.4 per 1,000 patient days, p = 0.001)
- The role of nurses as the first line of defense cannot be underestimated
By making reflex urine culture criteria more strict
- Fewer cultures were obtained resulting in fewer patients being identified with ASB
- The rate ASB treatment did not change
- The number of antibiotic courses decreased
• By making reflex urine culture criteria more strict
  • Fewer cultures were obtained resulting in fewer patients being identified with ASB
  • The rate ASB treatment did not change
  • The number of antibiotic courses decreased

Again, the key seems to be preventing the urine culture from being obtained in the first place
Engage the patient

Antibiotics usually don’t help when there are no UTI symptoms
• It does not prevent UTIs
• It does not help bladder control
• It does not help memory problems or balance

Antibiotics for urinary tract infections in older people
When you need them—and when you don’t
“UTI” case

- 84 y.o. female with acute mental status changes at Skilled Nursing
- PMH: Alzheimer’s dementia (unable to communicate), recurrent UTIs, colonized with ESBL-producing *Klebsiella sp.*
- VS: WNL
- Diagnosed with UTI and empirically started on IM ertapenem

<table>
<thead>
<tr>
<th>Urinalysis</th>
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<tbody>
<tr>
<td>Leukocyte esterase</td>
<td>Positive</td>
</tr>
<tr>
<td>Nitrite</td>
<td>Negative</td>
</tr>
<tr>
<td>WBC/hpf</td>
<td>2 to 5</td>
</tr>
<tr>
<td>Blood</td>
<td>Negative</td>
</tr>
<tr>
<td>Bacteria</td>
<td>Negative</td>
</tr>
</tbody>
</table>
“UTI” case

- Upon further review found to have been started on oxybutynin 10 mg ER two days prior to mental status changes
- New assessment and plan:
  - Medication-induced mental status changes
    - Decrease oxybutynin dose to 5 mg
    - Discontinue ertapenem
- Mental status returned to baseline
“C. difficile infection”
Clostridium difficile infection

- Toxin-mediated diarrheal illness
  - ≥ 3 unformed stools in 24 hours
- Occurs when toxin-producing Clostridium difficile colonizes and proliferates
- Mild to severe-life threatening disease
- Antibiotic use is the biggest risk factor
- Clinical diagnosis with laboratory confirmation
- Some laboratory tests only detect the organism and will not identify the presence of toxin production
Non-\textit{C. difficile} diarrhea

- Diarrhea in hospitalized patients is common
  - \textit{C. difficile} is usually not the cause (less the 30\% of cases, more often 5 to 10\%)
  - More common causes
    - Medication-induced
    - Tube feedings
- \textit{C. diff} colonization
  - 3 to 26\% of adult acute care inpatients
  - 5 to 7\% among elderly patients
Overdiagnosis of *Clostridium difficile* Infection in the Molecular Test Era

Christopher R. Polage, MD, MAS. Clare E. Gyorke, BS, Michael A. Kennedy, BS, Jhansi L. Leslie, BS, David L. Chin, PhD, Susan Wang, BS, Hien H. Nguyen, MD, MAS, Bin Huang, MD, PhD, Yi-Wei Tang, MD, PhD, Lenora W. Lee, MD, Kyoungmi Kim, PhD, Sandra Taylor, PhD, Patrick S. Romano, MD, MPH, Edward A. Panacek, MD, MPH, Parker B. Goodell, BS, MPH, Jay V. Solnick, MD, PhD, and Stuart H. Cohen, MD

- Meridian Tox A/B toxin testing alone vs molecular testing alone to diagnose CDI
- Single-center, prospective, observational cohort study
“Clinicians can improve laboratory test relevance by only testing patients likely to have *C. difficile* infection.”

**Recommendations**

- Do not routinely test stool from a patient who has received a laxative in the preceding 48 hours
- Develop and implement stool rejection criteria
- Utilize a two-step testing algorithm if the above measures cannot be implemented
“C. difficile infection” case

• 70 y.o. male with recent hospitalization for heart failure and COPD now admitted for dizziness x 3 days, malaise, and diarrhea (3 stools per day x 2 days)
  • Vitals: WNL except O2 sat 95% on 4L
  • PE: positive bowel sounds, soft, nontender, nondistended
  • WBC 7.7
  • Diagnosed with acute hypoxemic respiratory failure secondary to COPD and/or CHF; diarrhea r/o C. difficile
  • No treatment started
“C. difficile infection” case

- Day 2:
  - Oral vancomycin initiated
  - Patient now having formed stool
- Day 3:
  - Formed stool
  - Hospitalist discontinued vancomycin after the pharmacist documented in the medical record that this was likely colonization
  - Isolation discontinued
- Day 4: Discharged home without treatment and was not readmitted

<table>
<thead>
<tr>
<th>Test</th>
<th>Interpretation</th>
</tr>
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<tbody>
<tr>
<td>C. difficile PCR</td>
<td>POSITIVE</td>
</tr>
<tr>
<td>027-NAP1-B1</td>
<td>POSITIVE</td>
</tr>
<tr>
<td>C. difficile Toxin A&amp;B</td>
<td>NEGATIVE</td>
</tr>
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</table>
The non-provider’s role

• Patient and nursing education are equally as important as, if not more important than, provider education
• Optimize laboratory resources
  • Change urine reflex criteria
  • Two-step *C. difficile* testing algorithm
  • Specimen-rejection criteria
• Develop and implement diagnosis algorithms
  • Clinical decision support
• Collect and analyze data to provide feedback to providers
Conclusion

• Non-infections are commonly misdiagnosed as infectious
  • Misdiagnoses have a negative impact on clinical outcomes, healthcare costs, and antibiotic use
• Providers play an incredibly important role ensuring the diagnosis is correct
• There are roles for non-providers to minimize incorrect infection diagnoses
References
