Updates in infectious diseases

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Conflict of interest disclosure

• No conflicts of interest
Off label drug use disclosure

• This presentation will provide evidence of antimicrobial use outside of the Food and Drug Administration (FDA) approved indication for the following medications:
  o Tobramycin inhalation
  o Ceftazidime
  o Amikacin
  o Colistin
  o Aztreonam lysine for inhalation
### FDA-approved medications in 2016

<table>
<thead>
<tr>
<th>Medication</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obiltoxaximab</td>
<td>Treatment of inhalation anthrax</td>
</tr>
<tr>
<td>Emtricitabine and tenofovir alefenamide</td>
<td>Treatment of HIV-1 infection</td>
</tr>
<tr>
<td>Sofobuvir and velpatasvir</td>
<td>Treatment of Hepatitis C</td>
</tr>
<tr>
<td>Dronabinol oral solution</td>
<td>Treatment of anorexia associated with AIDS</td>
</tr>
<tr>
<td>Emtricitabine, rilpivirine, and tenofovir alefenamide</td>
<td>Treatment of HIV-1 infection</td>
</tr>
<tr>
<td>Cholera vaccine, live, oral</td>
<td>Immunization against Cholera</td>
</tr>
<tr>
<td>Tenofovir alefenamide</td>
<td>Treatment of chronic hepatitis B</td>
</tr>
<tr>
<td>Elbasvir and grazoprevir</td>
<td>Treatment of HCV genotypes 1 and 4</td>
</tr>
<tr>
<td>Bezlotoxumab</td>
<td>Treatment of recurrent <em>Clostridium difficile</em> in patients receiving antibacterial therapy</td>
</tr>
</tbody>
</table>

*Note: *Clostridium difficile* is the scientific name for the bacterium responsible for *Clostridium difficile* infection.
Updated clinical practice guidelines

<table>
<thead>
<tr>
<th>Disease Category</th>
<th>Guideline Title(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stewardship</td>
<td>• Implementing an Antibiotic Stewardship Program: Guidelines by the IDSA and the SHEA</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>• Official ATS/CDC/IDSA Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis</td>
</tr>
<tr>
<td></td>
<td>• Official ATS/CDC/IDSA Clinical Practice Guidelines: Diagnosis of Tuberculosis in Adults and Children</td>
</tr>
<tr>
<td>Fungal Infections</td>
<td>• Clinical Practice Guidelines for The Management of Candidiasis</td>
</tr>
<tr>
<td></td>
<td>• Practice Guidelines for the Diagnosis and Management of Aspergillosis: 2016 Update by the IDSA</td>
</tr>
<tr>
<td></td>
<td>• Clinical Practice Guidelines for the Treatment of Coccidioidomycosis</td>
</tr>
<tr>
<td>Parasites</td>
<td>• Diagnosis and Treatment of Leishmaniasis: Clinical Practice Guidelines by the IDSA and the ASTMH</td>
</tr>
</tbody>
</table>
Objectives

- Discuss recently approved antimicrobial agents
- Summarize newly published infectious diseases guidelines on hospital-acquired and ventilator-associated pneumonia
- Review evidence for aerosolized administration for select antibiotics in the management of multi-drug resistant gram-negative pneumonia
Question #1

• Which of the following do you think most accurately represents current trends in infectious diseases pharmacotherapy?
  a. An abundant pipeline of agents with stable antimicrobial resistance rates
  b. A depleted armamentarium of agents with increasing rates of antimicrobials resistance
  c. A stable pipeline of agents with decreasing rates of antimicrobial resistance
  d. A limitless supply of agents with increasing antimicrobial resistance rates
# World Health Organization Rankings

<table>
<thead>
<tr>
<th>Critically important antimicrobial classes</th>
<th>Example drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aminoglycosides</td>
<td>Amikacin</td>
</tr>
<tr>
<td>Ansamycins</td>
<td>Rifampin</td>
</tr>
<tr>
<td>Carbapenems and other penems</td>
<td>Meropenem</td>
</tr>
<tr>
<td>Cephalosporins (3&lt;sup&gt;rd&lt;/sup&gt; and 4&lt;sup&gt;th&lt;/sup&gt; generation)</td>
<td>Cefepime</td>
</tr>
<tr>
<td>Phosphonic acid derivatives</td>
<td>Fosfomycin</td>
</tr>
<tr>
<td>Glycopeptides</td>
<td>Vancomycin</td>
</tr>
<tr>
<td>Lipopeptides</td>
<td>Daptomycin</td>
</tr>
<tr>
<td>Macrolides and ketolides</td>
<td>Azithromycin</td>
</tr>
<tr>
<td>Oxazolidinones</td>
<td>Linezolid</td>
</tr>
<tr>
<td>Penicillins (natural, synthetic, antipseudomonal)</td>
<td>Piperacillin</td>
</tr>
<tr>
<td>Polymyxins</td>
<td>Colistin</td>
</tr>
<tr>
<td>Quinolones</td>
<td>Ciprofloxacin</td>
</tr>
</tbody>
</table>
Recently FDA approved antimicrobials

- Cephalosporin/β-Lactamase Inhibitor combinations
  - Ceftazidime/avibactam (2015)
  - Ceftolozane/tazobactam (2015)
- New oxazolidinone
  - Tedizolid phosphate (2014)
- New anti-mold azole antifungal
  - Isavuconazonium sulfate (2015)
Cephalosporins

• Mechanism of Action
  o Inhibition of bacterial cell wall synthesis
    • Inhibit enzymes (penicillin binding proteins) that create the cross-linkage between the peptide chains preventing peptidoglycan development.
  • Penicillin binding proteins
    o PBP-1: Cell elongation
    o PBP-2: Cell elongation, shape and size
    o PBP-3: Wall formation (cross-linkage), cell division
  o Activation of endogenous autolytic system
Cephalosporins

<table>
<thead>
<tr>
<th>Generation (example medication)</th>
<th>Gram (+) activity</th>
<th>Gram (-) activity</th>
<th>Nuances</th>
</tr>
</thead>
<tbody>
<tr>
<td>First generation (cefazolin)</td>
<td>+++</td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>Second generation (cefoxitin)</td>
<td>+++</td>
<td>+++</td>
<td>Cephamycins active against anaerobes</td>
</tr>
<tr>
<td>Third Generation (ceftriaxone)</td>
<td>++</td>
<td>+++</td>
<td>Ceftazidime active against <em>P. aeruginosa</em></td>
</tr>
<tr>
<td>Fourth generation (cefepime)</td>
<td>++++</td>
<td>+++++</td>
<td></td>
</tr>
<tr>
<td>Fifth generation (ceftaroline)</td>
<td>+++</td>
<td>+++</td>
<td>Active against MRSA Variable anaerobe</td>
</tr>
<tr>
<td>Newer (ceftazidime/avibactam, ceftolozane/tazobactam)</td>
<td>++</td>
<td>++++</td>
<td>Designed for MDR Enterobacteriaceae*</td>
</tr>
</tbody>
</table>


*Stenootrophomonas maltophilia and Acinetobacter spp have resistance to Newer cephalosporin combinations
# Resistance overview

<table>
<thead>
<tr>
<th>Enzyme</th>
<th>Activity</th>
<th>Drugs Hydrolyzed</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESBL</td>
<td>ESBL</td>
<td>First-generation to third-generation cephalosporins (variable against cephamycins and cefepime), aztreonam, older BBLIs</td>
</tr>
<tr>
<td>AmpC</td>
<td>Cephalosporinase</td>
<td>First-generation to third-generation cephalosporins, older BBLIs, carbapenems</td>
</tr>
<tr>
<td>KPC</td>
<td>Carbapenemase</td>
<td>First-generation to fourth-generation cephalosporins, aztreonam, older BBLIs, carbapenems</td>
</tr>
<tr>
<td>NDM</td>
<td>Carbapenemase</td>
<td>First-generation to fourth-generation cephalosporins, older BBLIs, carbapenems</td>
</tr>
<tr>
<td>OXA-48 group</td>
<td>Carbapenemase</td>
<td>First-generation to fourth-generation cephalosporins, carbapenems; however, may have variable or diminished hydrolysis of third-generation or fourth-generation cephalosporins</td>
</tr>
</tbody>
</table>
### Resistance overview reformatted

<table>
<thead>
<tr>
<th>Antibiotic generation</th>
<th>ESBL producer</th>
<th>AmpC producer</th>
<th>Carbapenemase producing GNB</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>KPC</td>
</tr>
<tr>
<td>First</td>
<td>R</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>Second</td>
<td>S</td>
<td>R</td>
<td>V/R</td>
</tr>
<tr>
<td>Third</td>
<td>R</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>Fourth</td>
<td>V</td>
<td>S</td>
<td>R</td>
</tr>
<tr>
<td>Fifth</td>
<td>R</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>Ceftolozane-tazobactam</td>
<td>S</td>
<td>V/R</td>
<td>R</td>
</tr>
<tr>
<td>Ceftazidime-avibactam</td>
<td>S</td>
<td>S</td>
<td>S</td>
</tr>
</tbody>
</table>
B-Lactamase inhibitor difference

Clavulanic acid

Tazobactam

Sulbactam

Avibactam
Avibactam

• Bridged diazabicyclo-octane β-lactamase inhibitor
• Designed specifically to inhibit class C enzymes and KPC carbapenemases
  o Carbamyl group vs. acyl group

Ceftazidime/avibactam

- FDA indication(s):
  - Treatment of complicated urinary tract infections
  - Treatment of complicated intra-abdominal infections

- Dosing
  - Intravenous: 2.5 grams every 8 hours
    - Ceftazidime 2 grams + Avibactam 500 mg
    - Infusion over 2 hours
  - Adjustments needed for renal impairment
  - Duration of therapy:
    - cUTI: 7 to 14 days
    - cIAI: 5 to 14 days (with metronidazole)
Ceftazidime/avibactam for cIAI

- Prospective, randomized (1:1), multicenter (global), double-blind, double-dummy, comparative study
- Noninferiority: pre-specified margin of -10%
- Centers: 136, Countries: 20, Patients: 1058
- Study duration: 3/2012 to 4/2014
- Comparator groups:
  - Ceftazidime-avibactam 2.5 grams IV every 8 hours + metronidazole 500mg IV every 8 hours
  - Meropenem 1 gram IV every 8 hours
Ceftazidime/avibactam for cIAI

Modified intention to treat

Clinical cure

<table>
<thead>
<tr>
<th>CFZ-AVI</th>
<th>MPM</th>
</tr>
</thead>
<tbody>
<tr>
<td>81.6</td>
<td>85.1</td>
</tr>
</tbody>
</table>

Clinically evaluable

Clinical cure

<table>
<thead>
<tr>
<th>CFZ-AVI</th>
<th>MPM</th>
</tr>
</thead>
<tbody>
<tr>
<td>91.7</td>
<td>92.5</td>
</tr>
</tbody>
</table>
Ceftazidime/avibactam for cUTI

- Prospective, randomized (1:1), multicenter (global), double-blind, double-dummy, parallel-group study
- Noninferiority: pre-specified margin of -10%
- Centers: 160, Countries: 25, Patients: 1033
- Study duration: 10/2012 to 8/2014
- Comparator groups:
  - Ceftazidime-avibactam 2.5 grams IV every 8 hours + metronidazole 500mg IV every 8 hours
  - Doripenem 500 mg IV every 8 hours
Ceftazidime/avibactam for cUTI

Patient-associated symptomatic resolution at day 5

0 20 40 60 80 100

70.2 66.2

Microbiologic eradication**

0 20 40 60 80 100

77.4 71

Composite clinical and microbiological endpoint**

0 20 40 60 80 100

71.2 64.5

CFZ-AVI DORI
Ceftazidime/avibactam

- Side effect profile
  - CNS abnormalities
    - Headache, dizziness, anxiety, insomnia
  - Cardiovascular issues
    - Chest pain, Hypertension
  - Gastrointestinal disturbances
    - Nausea, Vomiting, diarrhea, constipation, abd. Pain
  - Hepatic transaminase increases
  - Allergic reactions/cross-reactivity
Advanced cephalosporin(s) summary

• Two, new intravenous agents are FDA-approved to treat cUTI and cIAI infections
• Structural modifications and addition of B-Lactamase inhibitor permit activity against drug-resistant GNB (particularly *P. aeruginosa*)
• Avibactam is a novel B-lactamase inhibitor restoring activity against very drug-resistant organisms
• Side effects were similar to other cephalosporins without unintended reactions
Clinical case scenario

A 62-year-old diabetic male presents to your clinic with an erythematous 3 cm long ulcer on the heel of her left foot causing excruciating pain (10/10) with every step.

**PMH:** Obesity (BMI=48), HTN, Dyslipidemia, Peripheral neuropathy, Depression, Recurrent *Clostridium difficile* infections

**Current medications:** lisinopril 20mg/day, metoprolol ER 100mg/day, Atorvastatin 80mg/day, sertraline 100mg/day, Aspirin 81mg/day, pregabalin 150mg twice daily, duloxetine 60mg/day, vancomycin 125mg orally twice daily

**Allergy:** Sulfamethoxazole – rash and throat swelling

**Vitals:** Temp: 101.3°F, HR: 100 beats/min, RR: 26 breaths/min

**Laboratory values:** WNL except Serum Creatinine: 1.6mg/dL
Question #2

• Wound culture results: MRSA

<table>
<thead>
<tr>
<th>Staphylococcus Aureus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vancomycin S</td>
</tr>
<tr>
<td>TMP-SMX S</td>
</tr>
<tr>
<td>Minocycline R</td>
</tr>
</tbody>
</table>

• Which antibiotic is the most appropriate to prescribe as empiric outpatient antimicrobial therapy?
  a. Vancomycin 15mg/kg intravenously every 12 hours
  b. Daptomycin 4mg/kg intravenously daily
  c. Linezolid 600mg by mouth twice daily
  d. Clindamycin 450mg by mouth four times daily
  e. None of the above - I’d like more options please
Tedizolid Phosphate

• Second Generation Oxazolidinone
  o Mechanism of action: inhibition of protein synthesis
    • Binding 23S RNA component of the 50S ribosome unit
  • Dosing
    o 200mg once daily orally or intravenously
  • FDA indication: Treatment of adults with acute bacterial skin and skin structure infections by susceptible gram-positive organisms
Tedizolid phosphate: structured for success

<table>
<thead>
<tr>
<th>Chemical Structure</th>
<th>Clinical Property</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydroxymethyl side chain combined with Para-oriented D-ring structure</td>
<td>Increased potency toward organisms</td>
</tr>
<tr>
<td>Phosphorylated side chain</td>
<td>Masks hydroxymethyl group from interactions with monoamine oxidase</td>
</tr>
</tbody>
</table>
Tedizolid phosphate for ABSSSI

- Prospective, randomized (1:1), multicenter (global), double-blind
- Noninferiority: pre-specified margin of -10%
- Centers: 58, Countries: 9, Patients: 666
- Study duration: 9/2011 to 1/2013
- Comparator groups:
  - Tedizolid 200mg IV once daily for 6 days
  - Linezolid 600mg IV twice daily for 10 days
  - Optional oral step-down
Tedizolid phosphate for ABSSSI

Early clinical response

End of treatment response

48-72hrs

- Tedizolid: 85%
- Linezolid: 83%

day 11

- Tedizolid: 87%
- Linezolid: 88%
Tedizolid phosphate for ABSSSI

• Similar to linezolid across variety of study endpoints regardless of formulation
  o Early response with sustained success

• Well tolerated
  o Major side effects were gastrointestinal

• Further research is needed to determine utility in other disease states
  o Current ongoing trials for pneumonia
### Tedizolid: new and improved

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Linezolid</th>
<th>Tedizolid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Greater antimicrobial potency</td>
<td>✖</td>
<td>✔</td>
</tr>
<tr>
<td>Longer half-life (once daily dosing)</td>
<td>✖</td>
<td>✔</td>
</tr>
<tr>
<td>Greater plasma protein binding</td>
<td>✖</td>
<td>✔</td>
</tr>
<tr>
<td>Interaction with tyramine or pseudoephedrine support</td>
<td>✔</td>
<td>✖</td>
</tr>
<tr>
<td>Hematologic adverse reactions</td>
<td>✔</td>
<td>?</td>
</tr>
</tbody>
</table>
Tedizolid phosphate: hematology toxicity

- Male patient in eighth decade of life
- Pulmonary infection: *Mycobacterium avium intracellulare* and *Mycobacterium kansasii*
  - Susceptible agents: ethambutol, clarithromycin, amikacin, trimethoprim/sulfamethoxazole, oxazolidinones
- Historic therapy complications:
  - Clarithromycin: gastrointestinal intolerance
  - Trimethoprim/sulfamethoxazole: renal toxicity
- Regimen: Ethambutol + Oxazolidinones
  - Linezolid x 38 days, then tedizolid
Tedizolid phosphate: hematology toxicity
Tedizolid phosphate summary

- A second generation oxazolidinone currently approved for acute skin and skin structure infections
- Structural modifications show benefit
  - Increased spectrum of activity
  - Favorable pharmacokinetics
  - Tolerability without evidence of hematologic toxicities
  - Decreased likelihood of drug-drug MAOI interactions
- Future investigations will determine the role of tedizolid in the treatment of other infections
  - Bacteremia and pneumonia
Isavuconazonium sulfate

• FDA indication:
  o Treatment of invasive aspergillosis
  o Treatment of invasive mucormycosis

• Dosing:
  o Loading: Isavuconazole 200mg every 8 hours x 2 days
  o Maintenance: Isavuconazole 200mg once daily
    • Isavuconazonium sulfate 186mg = Isavuconazole 100mg
Isavuconazonium sulfate

• Regularly accumulating evidentiary support
  o SECURE
  o VITAL

• Favorable pharmacodynamics/pharmacokinetics

• Drug-Drug interactions

• Side Effect profile
Clinical practice guidelines by the IDSA and the ATS on Management of Adults with Hospital-acquired and Ventilator-associated pneumonia

Question #3

According to the 2016 ATS/IDSA Guidelines for management of HAP and VAP, when is inhaled antimicrobial therapy recommended?

A. As monotherapy for respiratory culture positive for *P. aeruginosa* that has resistance only to fluoroquinolones
B. As an adjunct to systemic therapy during VAP with a nasal swab positive for MRSA
C. As an adjunct to systemic antibiotics for patients with VAP due to GNB that are susceptible only to aminoglycosides or polymyxins
D. It is not recommended in any clinical scenario
Keys from 2005 guidelines

- HCAP
- Lower respiratory tract cultures
- Early, appropriate, broad-spectrum therapy
- Appropriate duration of therapy
- Prevention
Keys from 2016 guidelines

• GRADE methodology of evidence evaluation
• HCAP concept removed
• Lower respiratory tract cultures
• Early, appropriate, broad-spectrum therapy
• Short course duration of therapy
HAP/VAP Guidelines 2016

- Recommendation assessment: GRADE Methodology
  - Systematic review of literature
- Diagnostics
  - Clinical criteria
- Management
  - Based on MDR risk factors and local antibiogram data
  - De-escalation whenever possible
    - Procalcitonin can assist discontinuation decision
  - Uniform duration of therapy: 7 days
HAP/VAP Guidelines 2016

• Risk factors for multidrug resistant organisms
  • Intravenous antibiotic use within previous 90 days
  • Septic Shock
  • ARDS preceding VAP
  • More than 4 days in the hospital prior to VAP
  • Acute renal replacement therapy before VAP
HAP/VAP Guidelines 2016

• Risk factors **NOT** associated with MDR organisms
  - Re-intubation
  - Immunosuppression
  - Chronic respiratory failure
  - Tracheostomy
  - Diabetes mellitus
  - Recent use of corticosteroids
Aerosolized Antimicrobials in 2005

• Aerosolized may have value as adjunctive therapy in patients with VAP due to some MDR pathogens
  o Few agents
  o Limited evidence of efficacy
  o Potential for resistance
  o Bronchospasms
• Further investigation is warranted
## Aerosolized Antimicrobials in 2016

<table>
<thead>
<tr>
<th>Clinical Scenario</th>
<th>Recommendation</th>
<th>Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital-Acquired/Ventilator-associated</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• <em>Acinetobacter spp.</em> sensitive only to polymyxins</td>
<td>A systemic polymyxin should be combined with inhaled colistin</td>
<td>Weak recommendation, very low quality evidence</td>
</tr>
<tr>
<td>• Any carbapenem-resistant gram-negative pathogen sensitive only to polymyxins</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ventilator-associated pneumonia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Any gram-negative bacilli susceptible only to aminoglycosides or polymyxins</td>
<td>A combination of inhaled and systemic antibiotics should be administered</td>
<td>Weak recommendation, very low quality evidence</td>
</tr>
<tr>
<td>• Any patients not responding to intravenous antibiotics alone regardless of organism susceptibility profile</td>
<td>Adjunctive inhaled antibiotic therapy can be added as a last resort</td>
<td>Weak recommendation, very low quality evidence</td>
</tr>
</tbody>
</table>
Advantages of inhaled antimicrobials

- Rapid onset of action
- High, sustained lung tissue concentrations
- Attenuation of cytokines and pulmonary inflammation
- Minimized systemically related toxicities
Disadvantages of inhaled antimicrobials

• Historically derived misconceptions
• Variable site of action concentrations
• Drug-specific device requirements
• Adverse effects
• Unintended consequences and costs
# FDA approved antimicrobials for inhalation

<table>
<thead>
<tr>
<th>Medications</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aztreonam lysine for inhalation</td>
<td>Improve respiratory symptoms in cystic fibrosis (CF) patients with <em>P. aeruginosa</em></td>
</tr>
<tr>
<td>Tobramycin for inhalation</td>
<td>Management of cystic fibrosis patients with <em>P. aeruginosa</em></td>
</tr>
<tr>
<td>Pentamidine isethionate</td>
<td>Treatment of pneumonia due to <em>Pneumocystis jiroveci</em></td>
</tr>
<tr>
<td>Ribavirin for inhalation</td>
<td>Treatment of hospitalized infants and young children with severe lower respiratory tract infections due to respiratory syncytial virus</td>
</tr>
</tbody>
</table>
Ceftazidime

• Experimental models demonstrate adequate lung disposition and bacterial kill
• Pilot study: 40 patients
  o Inhaled Ceftazidime + inhaled amikacin
  o Ceftazidime 24hr CI + single daily dose IV amikacin
• Poorer outcomes for inhaled therapy
• Lack of adverse effects
• Lack of resistance from inhaled administration
Amikacin

• Preclinical evaluation
• Experimental models: Inhaled vs. systemic therapy
  o Increased lung disposition
  o Enhanced bacterial kill
• Inhaled amikacin combined with fosfomycin (5:2)
  o Enhanced potency of amikacin against 62 amikacin non-susceptible gram-negative pathogen
  o Better killing than each agent individually
• Aerosolized liposomal amikacin is currently undergoing investigation
**Tobramycin**

- “Stronger” clinical evidence against difficult to treat gram-negative bacilli causing VAP

- Promising inhaled combination
  - Fosfomycin:tobramycin in a 4:1 ratio

- Minimal adverse effects vs. systemic therapy
Aztreonam lysine

• Lysine

• Minimal particle size

• Non-CF bronchiectasis failure

• Lacks investigation in hospital-acquired or ventilator-associated pneumonia
Colistin

• Effective lung sterilization

• Retrospective studies: controversial results

• Prospective randomized controlled trials: lack of clinical benefit

• Metaanalysis: Benefit when aerosolized colistin was used as adjunctive treatment of VAP
Colistin

• Variable dosing
  o Colistin: 500,000 to 2 million IU every 8 to 12 hours
  o Colistin (as colistimethate): 75mg every 12 hours
    • Colistin base activity

• Common adverse effect: Bronchostriction
  o May also cause cough, airway irritation
Vancomycin

• MRSA decolonization
  o Variable dosing: 40 to 200mg inhaled 3-4 times daily
  o Variable duration: 3 days to 6 months

• Lacks investigation in hospital-acquired or ventilator-associated pneumonia
  o Ongoing clinical trials

• Adverse effects
  o Chest tightness,
  o Inhaled vancomycin–induced allergic reaction
  o Occupational asthma
Summary

• Agents undergoing investigation for initial and expended indications have a focus on treating drug-resistant organisms
• Avibactam is a novel non-β-lactam β-lactamase inhibitor with expanded activity
• Second generation oxazolidinones demonstrate improved pharmacokinetics and safety profile
• Antifungal therapy requires coverage for invasive mucormycosis
Summary

• New guidelines: www.id society.org
  o Clinical Infectious Diseases publications
  o Focus on adapting from previous guidelines and question & answer format

• Unique antimicrobial administration techniques and formations are undergoing investigation and expansion outside cystic fibrosis indication
  o Obvious knowledge gap and need for further rigorous prospective investigation
Updates in Infectious diseases for acute care practitioners

Jason Barreto, PharmD, BCPS (AQ-ID)
Assistant Professor in Pharmacy, Mayo Clinic
College of Medicine
9 February 2016