Clinical Pearls of Antimicrobial Stewardship and Infection Prevention & Control

Presented by:
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Objectives

At the completion of this activity, the participant will be able to:

- Describe the intent of the Centers for Medicare & Medicaid Services (CMS) Mega Rule as it relates to the Infection Prevention and Control Program (IPCP)
- List the Centers for Disease Control (CDC) Core Elements for an effective Antimicrobial Stewardship Program (ASP)
- Explain the role of a robust Immunization Program
- Identify collateral damage of antimicrobial use including adverse drug events, drug interactions and clostridium difficile
- Describe the role of probiotics, cranberry and ascorbic acid
• Dr. Milito has no disclosures to report

The CMS Perspective

• Nursing home residents are at risk for adverse outcomes or collateral damage associated with the inappropriate use of antibiotics that may include but are not limited to the following:
  ▫ Increased adverse drug events and drug interactions (e.g., allergic rash, anaphylaxis, or death)
  ▫ Serious diarrheal infections from C. difficile
  ▫ Disruption of normal flora (e.g., this can result in overgrowth of Candida such as oral thrush)
The CMS Perspective ( Continued )

- Infection Prevention and Control Program (IPCP) includes an Antibiotic Stewardship Program (ASP)
  - ASP is not a stand-alone program
- Antibiotic resistance has emerged as a national healthcare concern
- Even appropriate use of antibiotics can contribute to antibiotic resistance

Case

- An effective Infection Prevention and Control Program (IPCP) includes an Antimicrobial Stewardship Program (ASP) and Immunizations.

- True or False
Preventing Spread of Illness Related to Multi-Drug Resistant Organisms (MDROS)

- Methicillin Resistant Staphylococcus Aureus (MRSA)
- Vancomycin Resistant Enterococci (VRE)
- Clostridium difficile
- Pseudomonas aeruginosa
- Extended Spectrum Beta Lactamase (ESBL)
- Carbapenem Resistant Enterobacteriaceae (CRE)

Regulatory Support

- §483.80

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<th>F880</th>
<th>Infection Prevention &amp; Control</th>
<th>483.80(a)(1)(2)(4)(e)(f)</th>
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<td>F881</td>
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<td>Influenza and Pneumococcal Immunizations</td>
<td>483.80(d)(1)(2)</td>
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CMS Mega Rule
Phase 2
Effective Date: November 28, 2017
Infection Prevention & Control Program (IPCP)

Components of an IPCP
- Policies & Procedures
- Program oversight
- Infection Preventionist (IP)
- Surveillance
- Education
- Antibiotic Review
- Immunization Program
Individual Risk Factors for Developing an Infection

- Medications: corticosteroids and chemotherapy
- Compromised host defenses: decreased or absent cough reflex – aspiration pneumonia
- Thinning skin - pressure injuries
- Decreased tear production - conjunctivitis
- Vascular insufficiency – wounds
- Coexisting Chronic diseases (Diabetes, Arthritis, Cancer, COPD, Anemia)

Individual Risk Factors for Developing an Infection (Continued)

- Decreased cognition
- Impaired response to infection (cell mediated responses)
- Bedfast
- Invasive devices
- Increased frequency of toxicity – decreased liver and kidney function
- Complications from invasive diagnostic procedures and skin/bloodstream/infections
Institutional Risk Factors for Developing an Infection

- Pathogen exposure (handrails & equipment)
- Common air circulation
- Decorative water displays
- Direct/Indirect contact with others
- Hospital admission or emergency department visit
- Improper hand hygiene, glove use, or food handling

Standard Precautions

- Applicable to:
  - Hand hygiene and the use and disposal of gloves
  - Safe injection practices
  - Use of personal protective equipment
  - Resident placement
  - Care of environment, textiles, laundry, equipment
  - Infectious waste: sharps, biohazard waste bags

Reference: SHEA/Epic Guideline Infection prevention and control in the long-term care facility. Infect control Hosp Epidemiology 29 (9); pg. 803
Transmission Based Precautions

- **Contact Precautions**: gloving and gowning, private room preferred, cohorting acceptable
  - Reusable items cleaned and disinfected
  - Soap and water hand washing – no hand sanitizer
  - C. difficile
- **Droplet Precautions**: mask when within 3 feet of a resident infected with a disease spread by droplets (influenza, pertussis, meningococcal disease, private room preferred cohorting acceptable)
- **Airborne Precautions**: used when diseases are spread by fine particles spread by air current (Varicella Zoster, Tuberculosis, measles), includes use of a test-fitted N-95 respirator, eye protection, private room required

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CMS Mega Rule
Phase 2
Effective Date: November 28, 2017
Antimicrobial Stewardship Program (ASP)

18-month moratorium – financial penalties
The Antibiotic Stewardship Program in Relation to Pharmacy Services

- The assessment, monitoring, and communication of antibiotic use shall occur by a licensed pharmacist.
- A pharmacist must perform a medication regimen review (MRR) at least monthly, including review of the medical record and identify any irregularities, including unnecessary drugs.
- *This review must include a review of the resident’s medical chart*

CMS Mega Rule
Phase 1 – November 28, 2016

§483.45(d) Unnecessary Drugs

- Each resident’s drug regimen must be free from unnecessary drugs. An unnecessary drug is any drug when used-
  - (1) In excessive dose (including duplicate drug therapy; or
  - (2) for excessive duration; or
  - (3) without adequate monitoring; or
  - (4) without adequate indication for its use; or
  - (5) in the presence of adverse consequences which indicate the dose should be reduced or discontinued; or
  - (6) any combinations of the above
Antimicrobial Stewardship

- Steward:  
  *Verb*  
  1. Manage or look after

- Stewardship:  
  *Noun*  
  1. the conducting, supervising, or managing of something; especially: the careful and responsible management of something entrusted to one’s care.

- Antimicrobials – bacteria, viruses, fungi, and parasites

ASP Presidential Executive Order

Combating Antibiotic-Resistant Bacteria

- Issued by President Obama on September 18, 2014
- Establishes national and governmental recognition of one of the greatest global threats to human kind
  - Antibiotic misuse is now an official national security priority
- Established a National Task Force in charge of combating antibiotic-resistant bacteria
  - Multi-departmental effort
  - Developed a 5-Year National Action Plan
ASP
Why should we be involved?
• 23,000 residents die each year as a direct result of an antibiotic resistant infection in nursing homes.
• Up to 70% of nursing home residents receive antibiotics annually
• Roughly 20-50% of antibiotics are prescribed inappropriately
• Nearly 50% of antibiotics prescribed in nursing homes may be given longer than necessary

Case - We will build upon this as we proceed through the presentation
• Ciprofloxacin 500 mg PO every 12 hours
The CDC Core Elements for Nursing Homes
Summary of Core Elements for Antibiotic Stewardship in Nursing Homes

Leadership commitment
Demonstrate support and commitment to safe and appropriate antibiotic use in your facility

Accountability
Identify physician, nursing and pharmacy leads responsible for promoting and overseeing antibiotic stewardship activities in your facility

Drug expertise
Establish access to consultant pharmacists or other individuals with experience or training in antibiotic stewardship for your facility

Action
Implement at least one policy or practice to improve antibiotic use

Tracking
Monitor at least one process measure of antibiotic use and at least one outcome from antibiotic use in your facility

Reporting
Provide regular feedback on antibiotic use and resistance to prescribing clinicians, nursing staff and other relevant staff

Education
Provide resources to clinicians, nursing staff, residents and families about antibiotic resistance and opportunities for improving antibiotic use
Checklist for Core Elements of Antibiotic Stewardship in Nursing Homes

- The following checklist is a companion to the Core Elements of Antibiotic Stewardship in Nursing Homes. The CDC recommends that all nursing homes take steps to implement antibiotic stewardship activities. Before getting started, use this checklist as a baseline assessment of policies and procedures that are in place. Then use the checklist to review progress in expanding stewardship activities on a regular basis (e.g., annually). Over time, implement activities for each element in a step-wise fashion.

Checklist for Core Elements of Antibiotic Stewardship in Nursing Homes (Continued)

<table>
<thead>
<tr>
<th>LEADERSHIP SUPPORT</th>
<th>ESTABLISHED AT FACILITY</th>
</tr>
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<tbody>
<tr>
<td>1. Can your facility demonstrate leadership support for antibiotic stewardship through one or more of the following actions?</td>
<td>□ Yes □ No</td>
</tr>
<tr>
<td>□ Written statement of leadership support to improve antibiotic use</td>
<td></td>
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<tr>
<td>□ Antibiotic stewardship duties included in medical director position description</td>
<td></td>
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<tr>
<td>□ Antibiotic stewardship duties included in director of nursing position description</td>
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<tr>
<td>□ Leadership monitors whether antibiotic stewardship policies are followed</td>
<td></td>
</tr>
<tr>
<td>□ Antimicrobial use and resistance data is reviewed in quality assurance meetings</td>
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<tr>
<th>ACCOUNTABILITY</th>
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<tr>
<td>2. Has your facility identified a lead(s) for antibiotic stewardship activities?</td>
</tr>
<tr>
<td>□ Medical director</td>
</tr>
<tr>
<td>□ Director or assistant director of nursing services</td>
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<tr>
<td>□ Consultant pharmacist</td>
</tr>
<tr>
<td>□ Other</td>
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<tr>
<th>DRUG EXPERTISE</th>
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</thead>
<tbody>
<tr>
<td>3. Does your facility have access to individuals with antibiotic stewardship expertise?</td>
</tr>
<tr>
<td>□ Consultant pharmacist has staff trained in antibiotic stewardship</td>
</tr>
<tr>
<td>□ Part of care plan at inpatient hospital</td>
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<tr>
<td>□ External infectious disease/antibiotic stewardship consultants</td>
</tr>
<tr>
<td>□ Other</td>
</tr>
</tbody>
</table>
Checklist for Core Elements of Antibiotic Stewardship in Nursing Homes (Continued)

**Tracking: Monitoring Antibiotic Prescribing, Use, and Resistance**

7. Does your facility monitor one or more measures of antibiotic use?  
   - Yes  
   - No
   
   If yes, indicate which of the following are being tracked (select all that apply):
   - Adherence to clinical assessment documentation (signs/symptoms, vital signs, physical exam findings)
   - Adherence to prescribing documentation (dose, duration, indication)
   - Adherence to facility-specific treatment recommendations
   - Performs point prevalence surveys of antibiotic use
   - Monitors rates of new antibiotic starts/1,000 resident-days
   - Monitors antibiotic days of therapy/1,000 resident-days
   - Other:

8. Does your facility monitor one or more outcomes of antibiotic use?  
   - Yes  
   - No
   
   If yes, indicate which of the following are being tracked (select all that apply):
   - Monitors rates of C. difficile infection
   - Monitors rates of antibiotic-resistant organisms
   - Monitors rates of adverse drug events due to antibiotics
   - Other:

Reference: The Core elements of antibiotic stewardship for nursing homes. Checklist: CDC Cs256096A
Checklist for Core Elements of Antibiotic Stewardship in Nursing Homes (Continued)

**Reporting Information to Staff on Improving Antibiotic Use and Resistance**

9. Does your facility provide facility-specific reports on antibiotic use and outcomes with clinical providers and nursing staff?
   - Yes
   - No
   - If yes, indicate which of the following are being tracked (select all that apply):
     - Measures of antibiotic use at the facility
     - Measures of outcomes related to antibiotic use (i.e., C. difficile rates)
     - Report of facility antibiotic susceptibility patterns (within last 18 months)
     - Personalized feedback on antibiotic prescribing practices (to clinical providers)
     - Other:

**Education**

10. Does your facility provide educational resources and materials about antibiotic resistance and opportunity for improving antibiotic use?
   - Yes
   - No
   - If yes, indicate which of the following are being tracked (select all that apply):
     - Clinical providers (e.g., MDs, NPs, PAs, PharmDx)
     - Nursing staff (e.g., RNs, LPNs, CNAAs)
     - Residents and families
     - Other:

Reference: The Core elements of antibiotic stewardship for nursing homes. Checklist. CDC Cs256066-A

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Case

- Ciprofloxacin 500 mg PO every 12 hours. What is needed for this order?
  A. Duration
  B. Diagnosis
  C. 7-day reassessment
  D. All of the above
Antibiogram

• What is an antibiogram?
  ▫ A table that contains susceptibility information that defines a specified period of time

• Why is it important?
  ▫ Raise awareness of antimicrobial resistance
  ▫ Helps to determine optimal empiric therapy
  ▫ Provides opportunities to evaluate antibiotic usage
Antibiogram

- Who should be involved?
  - Members of the microbiology staff
  - Pharmacists
  - Physicians
  - Others

Challenges

- Challenges in obtaining an antibiogram:
  - Lab participation
  - Education of staff
  - Inaccurate due to small isolate number
## Antibiogram – Things to Consider

- What is the % of MRSA isolates?
- What is the E. Coli susceptibility to the quinolones?
- What is the Pseudomonas susceptibility to the quinolones?
- Are the carbapenems holding strong?
FDA Warning for Quinolones

Fluoroquinolone Warning

- The U.S. Food and Drug Administration approved safety labeling changes for fluoroquinolones to enhance warnings about their association with disabling and potentially permanent side effects and to limit their use in patients with less serious bacterial infections.
- FDA safety review found that both oral and injectable fluoroquinolones are associated with disabling side effects involving tendons, muscles, joints, nerves and the central nervous system. These side effects can occur hours to weeks after exposure to fluoroquinolones and may potentially be permanent.
- FDA-approved fluoroquinolones include: levofloxacin (Levaquin), ciprofloxacin (Cipro), ciprofloxacin extended-release tablets, moxifloxacin (Avelox), ofloxacin and gemifloxacin (Factive)
- The labeling changes include an updated Boxed Warning and revisions to the Warnings and Precautions section of the label about the risk of disabling and potentially irreversible adverse reactions that can occur together.
- Reserve fluoroquinolones for patients who do not have other available treatment options for acute bacterial sinusitis, acute bacterial exacerbation of chronic bronchitis and uncomplicated urinary tract infections.

Reference: FDA Drug Safety Communication: FDA updates warnings for oral and injectable fluoroquinolone antibiotics due to disabling side effects. FDA.gov
Case

- Which of the following is correct regarding the use of Ciprofloxacin 500 mg PO every 12 hours x 10 days (UTI)

A. Ciprofloxacin is not a good empiric choice to treat uncomplicated UTI based on the antibiogram.

B. 3-5 days is an appropriate duration for uncomplicated UTI treatment.

C. Ciprofloxacin is renally cleared.

CMS Mega Rule
Phase 3
Effective Date: November 28, 2019
Infection Preventionist (IP)
Infection Preventionist (IP)

- Leader of the IPCP
- Qualified by education, training, experience, certification
- A member of the facility’s quality assurance and performance improvement (QAPI) committee
- Report infection data, analyze information, implement and monitor the plan

A Robust Immunization Program is Necessary
Healthy People 2020

The Department of Health and Human Services has introduced this initiative to improve overall health and disease prevention in the United States, with specific goals to meet by the year 2020.

For Healthy People 2020, there are numerous categories of goals related to various disease and public health programs, including immunization and infectious diseases.

Goal vaccination rates for those 65 years of age or older by the year 2020 are:

- Influenza: 90%
- Pneumococcal: 90%
- Zoster: 30%

* There is no goal related to reduction in pertussis in the elderly population


Immunizations

- The administration of pneumococcal and influenza vaccine, in accordance with national recommendations; facilities must follow the CDC and ACIP recommendations for vaccines
- As necessary, determine if the facility developed influenza and pneumococcal vaccine policies and procedures, including the identification and tracking/monitoring of all facility residents’ vaccination status

Reference: CMS-20054 (5/2017)
Assessment Question #4

Case

- Part of a robust immunization program includes:
  A. Prevnar 13 should be given after Pneumovax 23 in a pneumococcal naive 66 year old.
  B. Shingrix is administered as one IM injection
  C. All of the above
  D. None of the above

Collateral Damage
Collateral Damage

- *Clostridium difficile*
- Drug-drug Interactions
- Adverse drug reactions

Clostridium Difficile
• **What** is *C. difficile* infection (CDI)?
• **Why** is it important?
• **How** can we treat it and prevent it?

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**Clostridium Difficile**

- Gram-positive, anaerobic spore-forming, toxin-producing bacterium
- Most common infectious cause of health-care associated diarrhea in developed countries
- Associated with increased length of hospital stay, health care costs, morbidity and mortality

**Risk Factors**
- Antimicrobial agents (most common)
- Advanced age
- Hospitalization or residence in a long-term care facility
- Cytotoxic chemotherapy
- Immunosuppressive treatment
- Acid suppressing medications
Most Common CDI Causing Antimicrobial Agents

- Clindamycin
- Ampicillin/Amoxicillin
- 2nd or 3rd generation cephalosporins
- Fluoroquinolones


Clostridium Difficile Symptoms

- Profuse watery or green mucoid, foul smelling diarrhea
- Cramping abdominal pain
- In the most severe cases, patients can have life-threatening pseudomembranous colitis, toxic megacolon, bowel perforation, and death
- Antibiotic associated CDI usually begins 4-10 days after starting antibiotic therapy

Reference: Emily Hell, PharmD, BCPS-AQ ID (2016). C. Difficile; Antimicrobial Stewardship in LTPAC
Clostridium Difficile

- 250,000 INFECTIONS PER YEAR
- 14,000 DEATHS
- 1,000,000,000 IN EXCESS MEDICAL COSTS PER YEAR

THREAT LEVEL URGENT

Reference: Emily Heil, PharmD, BCPS-AQ ID (2016). C. Difficile; Antimicrobial Stewardship in LTPAC

Testing and Diagnosis

- Molecular Test – PCR Assay Testing
  - *Clostridium difficile* DNA Toxin Assay for toxin B gene has sensitivity and specificity of 95%
  - Remember that the test is picking up the toxin gene, **does not** distinguish between colonization and infection
- Glutamate Dehydrogenase (GDH) Antigen Test
  - Rapid test (<1 hour), high sensitivity (negative result effectively rules out CDI) but non-specific to antigen so must be combined with toxin detection or PCR
- Toxin AB Enzyme Immunoassay (EIA)
  - Detects the presence of toxins A & B, lower sensitivity and specificity than the PCR based testing

Reference: Emily Heil, PharmD, BCPS-AQ ID (2016). C. Difficile; Antimicrobial Stewardship in LTPAC
Testing Guidelines

• Perform testing for
  ▫ New diarrhea (>= 3 unformed stools in 24 h)
  ▫ Clearly worsening diarrhea in those with chronic GI conditions
  ▫ Suspected ileus due to *C. difficile*

• Only test unformed diarrheal stool (i.e., stool that takes the shape of the container), unless patient has ileus

Testing Guidelines (Continued)

• **DO NOT** test if
  ▫ Diarrhea due to tube feeds, laxatives or other bowel regimen
  ▫ Sepsis or leukocytosis without GI symptoms or signs

• DO NOT repeat testing as a test of cure
  ▫ Molecular tests can remain positive for weeks after treatment
## Medical Management

### Treatment Recommendations

<table>
<thead>
<tr>
<th>Clinical Definition</th>
<th>Clinical Data</th>
<th>Recommended Treatment a</th>
<th>Strength of Recommendation/Quality of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial episode, non-severe</td>
<td>Leukocytosis with a white blood cell count of ≤15 000 cells/mL and a serum creatinine level &lt;1.5 mg/dL</td>
<td>• VAN 125 mg given 4 times daily for 10 days, OR • FDX 200 mg given twice daily for 10 days</td>
<td>Strong/High Strong/High Weak/ High</td>
</tr>
<tr>
<td>Initial episode, severe b</td>
<td>Leukocytosis with a white blood cell count of ≥15 000 cells/mL or a serum creatinine level &gt;1.5 mg/dL</td>
<td>• VAN 125 mg 4 times per day by mouth for 10 days, OR • FDX 200 mg given twice daily for 10 days</td>
<td>Strong/High Strong/High</td>
</tr>
<tr>
<td>Initial episode, fulminant</td>
<td>Hypotension or shock, ileus, megacolon</td>
<td>• VAN 500 mg 4 times per day by mouth or by nasogastric tube. If ileus, consider adding rectal instillation of VAN. Intravenously administered Metronidazole (500 mg every 8 hours) should be administered together with oral or rectal VAN, particularly if ileus is present.</td>
<td>Strong/Moderate (oral VAN); Weak/Low (rectal VAN); Strong/Moderate (intravenous metronidazole)</td>
</tr>
</tbody>
</table>

Reference: Clinical Practice Guidelines for *Clostridium difficile* Infection • CDC 2018
Treatment Recommendations (Continued)

<table>
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<th>Recommended Treatment</th>
<th>Strength of Recommendation/Quality of Evidence</th>
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</thead>
</table>
| First recurrence                     | - - -         | • VAN 125 mg given 4 times daily for 10 days if metronidazole was used for the initial episode, OR  
|                                      |               | • Use a prolonged tapered and pulsed VAN regimen if a standard regimen was used for the initial episode (e.g., 125 mg 4 times per day for 10–14 days, 2 times per day for a week, once per day for a week, and then every 2 or 3 days for 2–8 weeks), OR  
|                                      |               | • FDX 200 mg given twice daily for 10 days if VAN was used for the initial episode | Weak/Low  
|                                      |               |                        | Weak/Low  
|                                      |               |                        | Weak/Moderate |
| Second or subsequent recurrence      | - - -         | • VAN in a tapered and pulsed regimen, OR  
|                                      |               | • VAN 125 mg 4 times per day by mouth for 10 days followed by rifaximin 400 mg 3 times daily for 20 days, OR  
|                                      |               | • FDX 200 mg given twice daily for 10 days, OR  
|                                      |               | • Fecal microbiota transplantation c | Weak/Low  
|                                      |               |                        | Weak/Low  
|                                      |               |                        | Weak/Low  
|                                      |               |                        | Strong/Moderate |

Abbreviations: FDX, fidaxomicin; VAN, vancomycin.

*All randomized trials have compared 10-day treatment courses, but some patients (particularly those treated with metronidazole) may have delayed response to treatment and clinicians should consider extending treatment duration to 14 days in those circumstances.

*The criteria proposed for defining severe or fulminant Clostridium difficile infection (CDI) are based on expert opinion. These may need to be reviewed in the future upon publication of pro-spectively validated severity scores for patients with CDI.

*The opinion of the panel is that appropriate antibiotic treatments for at least 2 recurrences (i.e., 3 CDI episodes) should be tried prior to offering fecal microbiota transplantation.

Testing Guidelines

- **Discontinue** the offending antimicrobial, if possible
- **Do not** administer antiperistaltic agents (e.g., loperamide)
- **Discontinue** proton pump inhibitors (PPIs), if possible
- **Discontinue** bowel regimens!
Other Treatment Related Issues

• Use of Probiotics
  ▪ The routine use of probiotics for the prevention of *C. difficile* or as an adjunct treatment for *C. difficile* is not recommended due to inadequate data along with safety concerns in immunocompromised populations

Reference: Emily Heil, PharmD, BCPS-AQ ID (2016). C. Difficile; Antimicrobial Stewardship in LTPAC

Novel Therapies: Fecal Microbiota Transplantation (FMT)

• The process of taking stool from a healthy donor and placing it into the GI tract of a patient
• Goal is to restore the healthy gut microbiota by replenishing the intestinal ecosystem of the patient with the microbiota of the healthy donor
• Increasingly popular in the clinical arena and the public media
• Introduction of detrimental microbes during fecal transplantation is a concern

Reference: Emily Heil, PharmD, BCPS-AQ ID (2016). C. Difficile; Antimicrobial Stewardship in LTPAC
Novel Therapies: Bezlotoxumab (BEZ) (Continued)

- Monoclonal antibody
- Safe and effective in preventing CDI recurrence
- High cost

Infection Prevention

- Wash your hands with soap and water!
  - Alcohol based hand sanitizers do not kill *C. difficile* spores
- Enteric pathogen isolation
  - Contact isolation with gowns and gloves
  - Handwashing required before and after resident visit
- Bleach-based room cleaning

Reference: Emily Heil, PharmD, BCPS-AQ ID (2016). *C. Difficile*; Antimicrobial Stewardship in LTPAC
Case

- Antimicrobials that can contribute to C. diff are:
  - A. Clindamycin
  - B. Ceftriaxone
  - C. Quinolones
  - D. All of the above

Significant Drug-Drug Interactions
Azole Antifungals and Warfarin Interactions

- High severity drug interaction
- Azole antifungals increase the effect of warfarin
  - Fluconazole
  - Itraconazole
  - Ketoconazole
  - Miconazole
  - Posaconazole
- Monitor INR
- Prescriber may lower the dose of warfarin when the antifungal is initiated

Reference: Emily Heil, PharmD, BCPS-AQ ID (2016). C. Difficile; Antimicrobial Stewardship in LTPAC

Cephalosporins and Warfarin Interactions

- Second and third generation cephalosporins might increase the effect of warfarin
- High severity interactions
  - Cefotetan
- Moderate severity interaction
  - Cefazolin
  - Cefoxitin
  - Ceftriaxone
- Monitor INR when therapy is started or stopped

Reference: Emily Heil, PharmD, BCPS-AQ ID (2016). C. Difficile; Antimicrobial Stewardship in LTPAC
Fluoroquinolones and Warfarin Interactions

- May increase the response to warfarin
- High severity interactions
  - Ciprofloxacin
  - Levofloxacin
  - Moxifloxacin
  - Norfloxacin
  - Ofloxacin
- Monitor INR when any fluoroquinolone is started or stopped

Reference: Emily Heil, PharmD, BCPS-AQ ID (2016). C. Difficile; Antimicrobial Stewardship in LTPAC

Macrolide Antibiotics and Warfarin Interactions

- May increase the response to warfarin
- High severity interactions
  - Azithromycin
  - Clarithromycin
  - Erythromycin
- Monitor INR when any macrolide is started or stopped

Reference: Emily Heil, PharmD, BCPS-AQ ID (2016). C. Difficile; Antimicrobial Stewardship in LTPAC
Penicillin Antibiotics and Warfarin Interactions

- May increase the response to warfarin
- High doses of IV penicillins
- Moderate severity drug interactions
  - Amoxicillin, Amoxicillin/Clavulanate
  - Ampicillin, Ampicillin/Sulbactam
  - Penicillin G, Penicillin G Benzathine, Penicillin G Procaine
  - Piperacillin, Piperacillin/Tazobactam
  - Ticarcillin/Clavulanate

Tetracyclines and Warfarin Interactions

- May increase the response to warfarin
- Moderate severity interactions
  - Demelocycline
  - Doxycycline
  - Minocycline
  - Tetracycline (Monitor INR when tetracycline is started or stopped)
Trimethoprim/Sulfamethoxazole (TMP/SMX) Interactions

- TMP/SMX
  - Frequently prescribed for Urinary Tract Infections (UTIs)
  - Over 20 Million prescriptions per year in the U.S.
  - May increase the effect of warfarin
  - R and S isomer activity

Reference: Emily Heil, PharmD, BCPS-AQ ID (2016). C. Difficile; Antimicrobial Stewardship in LTPAC

Trimethoprim/Sulfamethoxazole (TMP/SMX) Interactions

- Warfarin
  - High severity of drug interaction, even with short courses of therapy
  - Avoid use if possible
  - Some prescribers lower the dose of warfarin by 25%-50%
    - Monitor INR when Trimethoprim/Sulfamethoxazole is started or stopped

Reference: Emily Heil, PharmD, BCPS-AQ ID (2016). C. Difficile; Antimicrobial Stewardship in LTPAC
Trimethoprim/Sulfamethoxazole (TMP/SMX) Interactions with ACE Inhibitors (ACEI’s) and Angiotension II Receptor Blockers (ARBs)

- TMP/SMX can reduce the excretion of potassium
- 80% of resident taking TMP/SMX have an increase in serum potassium
  - This increase in potassium can place a resident at risk for hyperkalemia when also taking an ACEI or ARB
  - May lead to an unnecessary hospitalization or death


Antimicrobials that Inhibit the Effect of Warfarin

- Dicloxacillin
- Griseofulvin
- Nafcillin
- Oxacillin
- Rifampin
- Rifabutin

- Monitor INR when started or stopped

Reference: Emily Heil, PharmD, BCPS-AQ ID (2016). C. Difficile; Antimicrobial Stewardship in LTPAC.
Other Oral Anticoagulants that May Interact with Antimicrobials

1. **Apixaban**
   - Reduce dose by 50% with strong inhibitors: itraconazole, ketoconazole, ritonavir, clarithromycin

2. **Dabigatran**
   - Reduce dose to of Dabigatran to 75mg BID with ketoconazole

3. **Rivaroxaban**
   - Avoid ketoconazole, itraconazole, posaconazole; use with caution with clarithromycin and fluconazole
   - Use erythromycin with caution in residents with mild to moderate renal impairment.

What Should Facility Staff Do When an Antimicrobial is Prescribed in the Presence of Warfarin?

1. **When taking a phone order for an antimicrobial, remind the prescriber when the resident is taking warfarin**
2. **Before the prescriber hangs up, ask if there is an order to monitor the INR**
3. **Never remove an antimicrobial from an emergency kit without checking if the resident is also taking warfarin**
What Should Facility Staff Do When an Antimicrobial is Prescribed in the Presence of Warfarin?

- Vigilantly monitor the resident for signs of bruising or bleeding Q shift
- Report INRs to the prescriber immediately if above or below the target INR
- Only use antimicrobials for the minimum duration of therapy based on the infection type, its severity, and the condition of the resident

Reference: Emily Heil, PharmD, BCPS-AQ ID (2016). C. Difficile; Antimicrobial Stewardship in LTPAC

Case

- Patient takes Ciprofloxacin 500 mg PO every 12 hours x 10 days (UTI) and is taking Warfarin 2.5 mg PO daily.

Which of the following is true:

A. Order more frequent INR
B. Hold warfarin x 2 days
C. Ciprofloxacin can potentiate the INR
D. All of the above
Adverse Drug Reactions

Risks of Using Unnecessary Antimicrobials

- Drug-induced diarrhea – *Clostridium difficile*
- Nausea
- Drug-drug interactions
- Renal toxicity
- Increased Antimicrobial Resistance
- Anaphylactic and other allergic reactions
- Cardiotoxicity via QT prolongation [Macrolides/Quinolones]
- Blood Dyscrasias
- Rash, Skin Reactions, Stevens-Johnson Syndrome
- Musculoskeletal toxicity (tendonitis/tendon rupture) [Quinolones]
Case

Ciprofloxacin 500 mg PO every 12 hours x 10 days. CrCl = 25 ml/min
A. Keep dose the same
B. Decrease dose to 250 mg
C. Extend the interval to 18 hours
D. B & C

A Few More “Pearls”
Cranberry

Cranberry?

- 2009 Guidelines state insufficient evidence to recommend for prophylaxis in catheterized patients
- 2012: Cochrane review of 24 studies (4472 patients) concluded:
  - Juice does not appear to have a benefit
  - Cranberry tablets/capsules appeared to trend towards prevention of UTI but was not significant possibly due to lack of potency
- 2012 and 2016 RCTs in Female Nursing Home Residents:
  - 2012: 80 residents → possible dose-dependent (max PAC dose 108 mg) decrease in *E. coli* bacteriuria but findings not significant
  - 2016: 185 women (low recurrence risk) → No difference in bacteriuria + pyuria vs. placebo

Cranberry: Summary

- Potential mechanism: Proanthocyanidins (PAC) help reduce bacterial adhesion (dose-dependent) → Mostly studies with *E. coli*

- Continued mixed results
  - Studies use various doses of PAC and formulations (juice versus capsules with standardized PAC)
  - Often dose of PAC may be too low
  - Study outcomes are all different and thus difficult to compare and group together
    - Incidence of recurrent UTI, incidence of pyuria+bacteriuria, UTI definitions are variable, younger populations of pre-menopausal women versus LTCF

- Needs
  - Active “ingredient”?
  - Further study in high-risk recurrent UTI patients using a high enough dose and duration
  - Strict UTI definition (clinical versus micro) in LTCFs


Ascorbic Acid
Ascorbic Acid (Vitamin C)

- Possible mechanism: decrease urinary pH
- Only two studies have been reported with contradictory results
- 1996 study in 38 spinal cord injury patients taking 500 mg 4x daily → only 13 completed study and no significant decrease in urine pH was observed
- 2007 study in 100 pregnant women taking a multivitamin with 100 mg ascorbic acid reported less UTI symptoms versus those taking multivitamin without ascorbic acid
  - Very low dose, unclear if urine cultures were done
- Cannot recommend ascorbic acid for prevention of UTI

Case

- This resident develops C. difficile. The provider orders a probiotic and metronidazole.
  A. Probiotics have been shown to be effective in treating C. difficile
  B. Metronidazole is a good choice for the initial treatment of mild-moderate C. difficile
  C. Droplet precautions should be started
  D. None of the above
Summary of Clinical Pearls

Clinical Pearls

1. Implement one policy, monitor one process, and measure one outcome as per the CDC Core Elements
2. Nitrofurantoin is a good choice to treat *E. coli* and can be used if CrCl is 30 ml/min and above
3. Prevnar13© is given first in residents who are 65 and older and pneumococcal naïve
4. Do not repeat testing as a test of cure for CDI
5. TMP/SMX can contribute to hyperkalemia
6. Fluoroquinolones should not be used for uncomplicated infections due to resistance, side effects, and adverse events
7. Cranberry does not appear to have a benefit for preventing UTI’s
8. Ascorbic acid can not be recommended for prevention of UTI
9. Probiotics may help to prevent a second recurrence of CDI
10. Pharmacists are the drug experts!
Thank You!!

Resources
Antimicrobial Stewardship in LTPAC

The American Society of Consultant Pharmacists (ASCP) in conjunction with the Society for Healthcare Epidemiology of America (SHEA) and the Infectious Diseases Society of America (IDSA) is offering an antimicrobial stewardship program (SIDP) for pharmacists. This three-phase program will be available in Summer 2017 and includes webinars and practical implementation sections. A Certificate of Achievement will be awarded to participants who successfully complete all three program components.

Learn more at ascp.com/amsstoollkit.

Visit ascp.com/whatsnew for the latest updates!

Schwanitz Senior Symposium

Up to 37 hours of practice-based CE credit!

No Travel Required!
Antibiotic Stewardship Program in Long-Term Care Virtual Workshop

Improving the use of antibiotics to protect residents and reduce the threat of antibiotic resistance is a top priority in long-term and post-acute care. AADNS has partnered with the American Society of Consultant Pharmacists (ASCP) to offer an online virtual workshop to help facilities comply with F881 infection control regulations related to antibiotic stewardship in the CMS Long-Term Care Final Rule. Using the CDC’s Core Elements of Antibiotic Stewardship for Nursing Homes as a guide, this workshop provides practical guidance on how to initiate, grow, and sustain an antibiotic stewardship program that will become an integral part of your facility’s Infection Control and Prevention Program. This course includes sample antibiotic protocols and helpful worksheets.

Following this course, you will:
- Be able to develop a plan of action to help your facility comply with this new regulation
- Understand how to improve the use of antibiotics to protect residents and reduce the threat of antibiotic resistance
- Know how to create a commitment statement, policies and procedures, assessment forms, and clinical staff education resources

This course qualifies for six hours of nursing and pharmacy CE.

Pricing
- Members: $399
- Non-Members: $798

If you are a pharmacist or a member of ASCP, please visit their website to purchase this product.

Antibiotic Stewardship Program in Long-Term Care Virtual Workshop

• Regulatory Compliance and Commitment
  - F881 Antibiotic Stewardship Program (ASP)
  - CDC Core Elements
  - Commitment Statement
• Facility Gap Analysis and ASP Committee Duties
  - Baseline Assessment
  - Role Description
  - Standardized Assessment
  - P&P for ASP
• Advancing ASP Quality assurance/Performance Improvement (QAPI)
  - Governance
  - Systematic Analysis and Systemic Action
• Consultant Pharmacist, Infection Preventionist: Roles in ASP
  - Paradigm Shift in Roles
  - Medication Regimen Review