1. Which type of Clostridium difficile infection (CDI) is the most common?
   - (A) Health care facility (HCF)-onset
   - (B) Community-onset, HCF associated
   - (C) Community-associated
   - (D) Indeterminate origin

2. All the following antimicrobial agents are frequent inducers of CDI, except:
   - (A) Ampicillin
   - (B) Cindamycin
   - (C) Macrolides
   - (D) Third-generation cephalosporins

3. C difficile colonization is associated with an increased risk for recurrent C difficile-associated diarrhea (CDAD).
   - (A) True
   - (B) False

4. Which of the following agents should not be used to treat CDAD?
   - (A) Metronidazole
   - (B) Vancomycin
   - (C) Probiotics
   - (D) Atropine

5. Approximately _______ of patients with CDAD relapse within 30 days after cessation of therapy.
   - (A) 20%
   - (B) 33%
   - (C) 40%
   - (D) 50%

6. Ceftriaxone fosamil is the only β-lactam antibiotic active against:
   - (A) Extended-spectrum β-lactamase-producing gram-negative bacteria
   - (B) Pseudomonas aeruginosa
   - (C) Acinetobacter baumannii
   - (D) Methicillin-resistant Staphylococcus aureus

7. The presence and degree of pyuria cannot be used to diagnose a catheter-associated urinary tract infection.
   - (A) True
   - (B) False

8. Which of the following statements about the use of spinosad for treating head lice is incorrect?
   - (A) More effective than permethrin
   - (B) Combing of nits not required
   - (C) Two or more applications required for full efficacy
   - (D) Approved in January 2011 for individuals ≥4 yr of age

9. In the United States, 60 cases of Cryptococcus neoformans were reported in humans between 2004 and July 1, 2010.
   - (A) neoformans
   - (B) laurentii
   - (C) albidus
   - (D) gattii

10. Treatment of influenza with oseltamivir is recommended in all the following groups, except:
    - (A) Patients <5 yr or ≥65 yr of age
    - (B) Healthy adolescents
    - (C) Individuals with chronic disease
    - (D) Pregnant or postpartum women

Correction to Audio-Digest Internal Medicine Volume 58, Issue 39: The 27th Annual Congress of Clinical Rheumatology was held May 12-15, 2011.

Answers to Audio-Digest Internal Medicine Volume 58, Issue 43: 1-D, 2-B, 3-C, 4-A, 5-D, 6-C, 7-D, 8-A, 9-A, 10-A

Attention Accreditation Participants
The cutoff date for logging credits is December 31. Test forms received after that date will be accredited to 2012. You should receive the current year’s history by the end of January 2012.

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Audio-Digest ’ INTERNAL MEDICINE
Volume 58, Issue 45
December 7, 2011

Infectious Disease Update
Refractory Clostridium Difficile Infection
Nasir Safdar, MD, Assistant Professor, Department of Medicine, Infectious Disease, University of Wisconsin School of Medicine and Public Health, Madison

Historical background: Clostridium difficile first described in 1935; emergence of clindamycin-associated colitis (condition due to toxin-producing clostridia) seen in 1970s; for many years thereafter, C difficile infection (CDI) thought easily treatable with metronidazole; however, outbreaks of virulent epidemic strain associated with high morbidity and mortality reported in last decade

Factors contributing to resurgence of C difficile-associated diarrhea (CDAD):
- virulence of C difficile; resistance of enteric bacteria; spread of toxin B1/NAP1 strain (for moderate to severe CDI)
- atropine and similar antimotility agents should be avoided; probiotics—trials of many probiotics showed high efficacy for prevention of AAD, but most effective probiotic undetermined due to high heterogeneity

Recurrent CDAD:
- ≥25% of patients improve without need for further therapy and change in or complete discontinuation (if possible) of triggering antibiotic; older randomized trial showed similar treatment success and relapse rates with metronidazole and oral vancomycin
- more recent study showed that vancomycin appears to be more effective than metronidazole against B1/NAP1 strain (for moderate to severe CDI); atropine and similar antimotility agents should be avoided; probiotics—trials of many probiotics showed high efficacy for prevention of AAD, but most effective probiotic undetermined due to high heterogeneity

Luminalin complex: x-ray of abdomen recommended in patients with moderate to severe CDI to rule out perforation or pseudomembranous colitis

Education Objectives
The goal of this program is to improve the management of infectious disease, including Clostridium difficile infection (CDI). After hearing and assimilating this program, the clinician will be better able to:
- Identify patients at greatest risk of developing C difficile-associated diarrhea.
- Choose the most effective medical agent for treatment of primary and recurrent CDI.
- Consider ceftriaxone fosamil for the treatment of skin and soft tissue infections and community-acquired pneumonia.
- Diagnose and manage catheter-associated urinary tract infections.
- +50% unable to mount protective antibody response (devel-op CDAD); 60% to 90% of patients with CDAD recover without recurrence; recurrence may occur when comorbidity or trigger responsible for infection persists

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5. Prescribe oseltamivir to appropriate risk groups for treatment of influenza.

Faculty Disclosure
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patients who consumed probiotic drink containing L casei Shirota were 81% less likely to get CDI compared to those who did not consume such probiotic, proven effective in primary prevention of CDI

New treatments for C difficile: in development — monoclonal antibodies (mAb) against a common epitope of C. difficile toxin A (currently in phase III trials); currently available for other indications — IVIG for head lice; new TRI-SEA (Tripterygium Glycosides) for treatment of acute pancreatitis; Fosamil part of prodrug (converted to active anti-infective agent and exposure to C difficile required for infection

Infectious Disease Review: January 2010 to March 2011

Lisinat Abidin, MD, Associate Clinical Professor, University of Wisconsin School of Medicine and Public Health, and Vice Chief, Inpatient Medical Services and Hospital Epidemiologist, San Francisco General Hospital

Cefadroxil fosam: fosamidal part of prodrug (converted to active cefadroxil fosamid) binds to penicillin-binding proteins (PBPs) in cell membrane unlike other β-lactam antibiotics, binds to and inhibits modified PBP 2a found in methicillin-resistant Staphylococcus aureus (MRSA); not active against extended-spectrum β-lactamase-producing bacteria and some other resistant organisms, such as Pseudomonas aeruginosa; binds to and inhibits modified PBP 2a found in methicillin-resistant Staphylococcus aureus (MRSA); uses for skin and soft tissue infections and community-acquired pneumonia; fosamid is approved to be fairly effective against resistant S aureus organisms in vitro

Pertussis outbreaks: number of pertussis reported in California peaked at 95,280 in 2014; must be treated since 1945 in many other parts of United States (US); highest age-specific rate in Hispanic-Americans aged 20-24 years; potential for transmission of unvaccinated or inadequately vaccinated children (≥2010 randomized study reviewed effectiveness of pertussis vaccine for children aged ≥2010). Internal Medicine Today 2010

Newer family of antibiotics, binds to and inhibits modified PBP 2a found in methicillin-resistant Staphylococcus aureus (MRSA); not active against extended-spectrum β-lactam antibiotics, binds to and inhibits modified PBP 2a found in methicillin-resistant Staphylococcus aureus (MRSA); uses for skin and soft tissue infections and community-acquired pneumonia; fosamid is approved to be fairly effective against resistant S aureus organisms in vitro

Preventing surgical-site infections in nasal carriers of Clostridium difficile — monoclonal antibodies to toxins A and B; fidaxomycin (currently in phase III trials); currently available for other indications — eg, arthritis, peptic ulcer disease. Update: detection of Clostridium difficile in stool samples; developed in public-private partnership; both sensitive and rapid:

Suggested Reading


Preventive diarrheal disease: often fatal disease of pistachios (bird); affects autonomic nerves of upper and middle di-}
S. aureus infection 3.4% in treatment group vs 7.7% in placebo; children <5 yr of age (especially <2 yr), elderly, those with severe disease, and patients with chronic liver disease, immunosuppression; pregnant or postpartum women; and individuals with extensive drug-resistant tuberculosis (TB): defined as resistance to isoniazid plus rifampin plus fluoroquinolone plus injectable second-line drugs

Dr. Safdar was recorded at Internal Medicine 2010, held December 1-2, 2010, in Wisconsin Dells, WI, and presented by the University of Wisconsin School of Medicine and Public Health and the Interstate Postgraduate Medicine Association. Dr. Winston was recorded at a recent trial found lower rates of relapse in patients without B1/NAP1 strain to be main advantage of oral fidaxomicin (vs vancomycin) for treatment of C. difficile; first in new class of macrolide antibiotics that inhibit RNA polymerase; has narrow spectrum; achieves high stool levels; approved by FDA for C. difficile-associated urinary tract infection in adults who are at high risk for failure with alternative antibiotics (cured in this group); applications—consider pertussis in patients with prolonged cough illness; consider tetanus; diptheria-pertussis: vaccination for all adults who are not previously immunized (recommends different test than second sample with same test)

Test of cure: almost never required because patients carry toxico- genic C. difficile; if infection is possibly recurring, blood testing recom- mended in patients with recurrence, because episode may be different from prior episodes

Helping patients tolerate metronidazole: probiotics may help mitigate nausea and other adverse effects; limit duration of therapy (10-14 days)

Once-daily methicillin for treatment of C. difficile: not recommended for colonization of patients: most tests confined to semiformal, loose, or watery stools, so labora- tory often automatically reports results from patients with as-ymptomatic colonization (because they have formed stool); instrument that distinguishes between epidemic and non-epidemic strains exists, but used only in research (not clinically available)

Dose of clindamycin and risk of developing C. difficile: no dose-dependent effect; lowest dose possible recommended for treating skin and soft tissue infections; if higher dose indicated, IV rather than oral route advised; use of clindamycin is limited to patients who cannot tolerate other agents

Ground or tap water as source of community-associated C. difficile: anti-infectives ubiquitous in ground and tap water; rates of community-associated C. difficile low because both anti-infective agent and exposure to C. difficile required for infection

Infectious Disease Review: January 2010 to March 2011

Lisa Winston, MD; Associate Clinical Professor, University of California, San Francisco, and Vice Chief, Inpatient Medical Services and Hospital Epidemiologist, San Francisco General Hospital

Ceftaroline fosamil: fosamil portion of prod (converted to active form in liver) to inhibit porins; binds to penicillin-binding proteins (PBPs) in cell membrane unlike other β-lactam antibiotics, binds to and inhibits modified PBP 2a found in methicillin-resistant Staphylococcus aureus (MRSA) patients and syringes; 50,000 persons exposed to unsafe practice notified (largest pharmacovigilance study); 50,000 persons exposed to unsafe practice notified (largest pharmacovigilance study)
Refractory Clostridium Difficile Infection

Nasir Safdar, MD, Assistant Professor, Department of Medicine, Infectious Disease, University of Wisconsin School of Medicine and Public Health, Madison

Historical background: Clostridium difficile first described in 1935; emergence of clindamycin-associated colitis (condition due to toxin-producing clostridia) seen in 1970s; for many years thereafter, C. difficile infection (CDI) thought easily treatable with metronidazole; however, outbreaks of virulent epidemic strain associated with high morbidity and mortality reported in last decade

Mechanism of CDAD: presence of toxin in intestine induces array of inflammatory cascade reactions that result in multiple disruptions of epithelial barrier, neutrophil infiltration, and, subsequently, PMN inflammatory response. New epidemic strain (BI/NAP1) of C. difficile; contains additional toxin (‘binary toxin’); deletions in negative regulatory genes allow increased production of toxins A and B (produces more toxin than non-epidemic strain); has greater propensity for resistance to fluoroquinolones; associated with higher incidence of sepsis, leukopenia, coagulopathy, and death

Treatment of CDAD: ~25% of patients improve without further therapy in change in or complete discontinuation of (possibly) triggering antibiotic; older randomized trial showed similar treatment success and relapse rates with metronidazole and oral vancomycin; more recent study showed that vancomycin appears to be more effective than metronidazole against BI/NAP1 strain (for moderate to severe CDI); atorvastatin and similar anti-microbial agents should be avoided; probiotics—trials of many probiotics showed high efficacy for prevention of AAD, but most effective probiotic undetermined due to high heterogeneity

Fulminant colitis: x-ray of abdomen recommended in patients with moderate to severe CDI to rule out impending or present toxic megacolon; positive finding indicates need for immediate operation to prevent complications from perforation; mortality rate of 30% to 40%

Risk factors for CDI: healthcare facility (HCF)-onset—develops >48 hr after admission to HCF; community-onset but HCF-associated—constitutes majority of cases; symptom onset occurs briefly after discharge from HCF; community-associated—rare; no history of discharge from HCF in preceding 12 wk; (if discharge within 4-12 wk, C. difficile is categorized as community-onset)

Prevalence: has risen dramatically since 1990s; highest in patients >65 yr of age (800 cases per 100,000, vs 140 cases per 100,000 in overall population); infection emerging in populations previously thought to be at low risk

Proportion of population with positive toxin assay for C. difficile: healthy neonates—vast majority (but generally asymptomatic); healthy adults—only 1% to 2%; hospitalized patients—3% to 18%; patients with antibiotic-associated diarrhea (AAD)—10% to 25%; patients with pseudomembranous colitis (PMC)—95% to 100%

Risk factors for CDAD: >65 yr of age; antimicrobial exposure; gastrointestinal (GE) surgery; tube feeding; use of proton pump inhibitors and histamine-2 receptor antagonists; comorbidities (especially organ transplantation and renal failure); use of cancer chemotherapeutic agents; length of stay in hospital single greatest risk factor for exposure to C. difficile

Antimicrobial agents that induce CDI: clindamycin, vancomycin, third-generation cephalosporins, fluoroquinolones; infrequent inducers—macrolides and sulfonamides

C. difficile colonization is associated with increased risk for recurrent C. difficile-associated diarrhea (CDAD)

Mechanisms of CDAD:

(A) Health care facility (HCF)-onset (B) Community-onset, HCF associated (C) Indeterminate origin

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INFECTION DISSEASE UPDATE

INFECTIOUS DISEASE UPDATE

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