2:15 – 3 pm

ID Primary Care Challenges for 2015 and Beyond

SPEAKER
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Presenter Disclosure Information

The following relationships exist related to this presentation:

- Christopher Carpenter, MD, FACP, FIDSA: Author of electronic chapters for Johns Hopkins ABX Guide.

Off-Label/Investigational Discussion

- In accordance with pmiCME policy, faculty have been asked to disclose discussion of unlabeled or unapproved use(s) of drugs or devices during the course of their presentations.

Learning Objectives

- Discuss the extent and magnitude of the growing threat of antimicrobial resistance and the need for antimicrobial stewardship
- Identify five things that physicians and patients should question as inappropriate and overused clinical infectious diseases practices
- Review the evolution of HIV diagnosis and management strategies in the United States
- Utilize clinical clues to help differentiate between acute bacterial and acute viral rhinosinusitis

Newer Antimicrobials 2010 - Present

- October 29, 2010: Ceftaroline (Teflaro) – Forest Laboratories – treatment of bacterial skin infections and bacterial pneumonia
- May 27, 2011: Fidaxomiccin (Dificid) – Optimer Pharmaceuticals – treatment of *Clostridium difficile* diarrhea
- December 28, 2012: Bedaquiline (Sirturo) – Johnson & Johnson – treatment of multi-drug resistant tuberculosis
- June 20, 2014: Tedizolid (Sivextro) – Cubist Pharmaceuticals – Treatment of acute bacterial skin and skin structure infections
- May 23, 2014: Dalbavancin (Dalvance) – Durata Therapeutics – Treatment of acute bacterial skin and skin structure infections
- August 6, 2014: Oritavancin (Orbactive) – The Medicines Company – Treatment of acute bacterial skin and skin structure infections
- December 19, 2014: Ceftolozane-azobactam (Zerbaxa) – Cubist Pharmaceuticals – Treatment of complicated UTIs and complicated intra-abdominal infections
- February 26, 2015: Ceftazidime-avibactam (Avycaz) – Actavis – Treatment of complicated UTIs and complicated intra-abdominal infections
- Good start, but…

High Yield Points

Antibiotic resistance is a serious and urgent threat requiring immediate action to avoid catastrophic consequences

Choosing Wisely Campaign

- An initiative of the American Board of Internal Medicine (ABIM) Foundation
- Response to the challenge put to U.S. medical specialty societies by Howard Brody in 2010 to identify five tests and treatments that were overused in their specialty and did not provide meaningful benefit for patients
- Infectious Disease Society of America (IDSA) Quality Improvement Committee directed the development of IDSA's *Choosing Wisely* list

www.choosingwisely.org

Choosing Wisely Campaign

- Goal to help choose care that is:
  - Supported by evidence
  - Not duplicative of other tests or procedures already received
  - Free from harm
  - Truly necessary
- The recommendations are meant as guidelines to spur conversation to determine an appropriate treatment plan together
- > 400 recommendations from > 50 societies
  - Several societies have more than 5 recommendations

www.choosingwisely.org

1. Don't treat asymptomatic bacteruria with antibiotics

- Asymptomatic bacteruria is the presence of a significant number of bacteria in the urine that occurs without symptoms such as burning or frequent urination
- Use of antibiotics to treat asymptomatic bacteruria is not clinically beneficial and dose not improve morbidity or mortality
  - Exceptions:
    - Pregnant patients
    - Patients undergoing prostate surgery or other invasive urologic surgery
    - Kidney or kidney-pancreas organ transplant recipients within the first year of transplant

www.choosingwisely.org; *Clin Infect Dis.* 2005 Mar 1;40(5);643-54; *Clin Infect Dis.* 2007 Nov 15;45(10A):1335-7

1. Don't treat asymptomatic bacteruria with antibiotics

- Major contributor to antibiotic overuse in patients
  - Costly
  - Can lead to *Clostridium difficile* infection
  - Can lead to the emergence of resistant pathogen
- Urinary catheters increase the risk of bacteruria
- Antibiotics do not, however, decrease the incidence of symptomatic catheter-associated urinary tract infection (CAUTI)
- Unless symptoms referable to the urinary tract or symptoms with no identifiable cause, catheter-associated asymptomatic bacteruria does not require screening or antibiotic therapy

www.choosingwisely.org; *Clin Infect Dis.* 2005 Mar 1;40(5);643-54; *Clin Infect Dis.* 2007 Nov 15;45(10A):1335-7

2. Avoid prescribing antibiotics for upper respiratory infections

- Majority of acute upper respiratory infections (URIs) are viral in etiology
- Use of antibiotic treatment for acute URIs is ineffective, inappropriate and potentially harmful
- Proven infection with Group A Streptococcal disease (Strep throat) and pertussis (whooping cough) should be treated with antibiotic therapy

www.choosingwisely.org; *Clin Infect Dis.* 2012 Apr;54(8);e72-112; *Am Fam Physician.* 2012 Nov 1;86(9):817-22

2. Avoid prescribing antibiotics for upper respiratory infections

- Symptomatic treatment for URIs should be directed to maximize relief of the most prominent symptom(s)
- Discuss consequences of misusing antibiotics in viral infections with your patients
  - Increase costs
  - Antimicrobial resistance
  - Other adverse effects (e.g., *C. difficile* infection)

www.choosingwisely.org; *Clin Infect Dis.* 2012 Apr;54(8);e72-112; *Am Fam Physician.* 2012 Nov 1;86(9):817-22

3. Don't use antibiotic therapy for stasis dermatitis of lower extremities

- Stasis dermatitis is commonly treated with antibiotic therapy
  - Result of misdiagnosis or lack of awareness of the pathophysiology of the disease
- Standard treatment of stasis dermatitis is leg elevation and compression
  - Accelerates improvements by promoting drainage of edema and inflammatory substances
  - A short course of topical corticosteroids may also reduce symptoms (≤ 2 weeks)
- Routine use of oral antibiotics does not improve healing rates and may result in unnecessary hospitalization, increased health care costs, and potential for patient harm

www.choosingwisely.org; *Clin Infect Dis.* 2014 Jul 15;59(2);147-59; *Am Fam Physician.* 2010 Apr 15;81(8):989-96

4. Avoid testing for *Clostridium difficile* in the absence of diarrhea

- Testing for *C. difficile* or its toxins should be performed only on diarrheal (unformed) stool
  - Unless ileus due to *C. difficile* is suspected
- Because *C. difficile* carriage is increased in patients on antibiotic therapy, and in patients in the hospital, only diarrheal stools warrant testing
- In the absence of diarrhea, the presence of *C. difficile* indicates carriage and should not be treated and therefore, not tested

www.choosingwisely.org; *Infect Control Hosp Epidemiol.* 2010 May;31(5);431-55; *Am J Gastroenterol.* 2013 Apr;108(4):478-98

5. Avoid prophylactic antibiotics for the treatment of mitral valve prolapse

- Antibiotic prophylaxis is no longer indicated in patients with mitral valve prolapse for prevention of infective endocarditis
- The risk of antibiotic-associated adverse effects exceeds the benefit (if any) from prophylactic therapy
- Limited use of prophylaxis will likely reduce the unwanted selection of antibiotic-resistant strains and their unintended consequences such as *C. difficile* infection

www.choosingwisely.org; *J Am Coll Cardiol.* 2008 Aug 19;52(8);676-85; *Clin Med Res.* 2009 Sep;7(3):63-8

High Yield Points

1. Don't treat asymptomatic bacteruria with antibiotics
2. Avoid prescribing antibiotics for URIs
3. Don't use antibiotics for stasis dermatitis
4. Avoid *C. difficile* testing in the absence of diarrhea
5. Avoid prophylactic antibiotics for mitral valve prolapse

HIV/AIDS Epidemiology

- Over 1.2 million persons are currently living with HIV infection in the United States
  - Prevalence includes 156,000 people who have not been diagnosed – 14% of all patients with HIV infection
  - Incidence is stable at approximately 50,000 new cases per year
    - Incidence was highest among individuals aged 25-34 (31%) followed by individuals aged 13-24 (26%)

MMWR 2015;64:657-62; CDC *HIV Surveillance Supplemental Report* 2012;17(No. 4); http://www.cdc.gov/hiv/statistics/surveillance/incidence.html accessed August 2015

HIV/AIDS Screening and Treatment

- Benefits of detection and early intervention:
  - Early identification and antiretroviral treatment (ART) associated with a markedly reduced risk for progression to AIDS, AIDS-related events, and death in individuals with immunologically advanced diseases (CD4 < 200)
  - Initiating ART earlier (CD4 > 200, including CD4 > 500) also associated with reduced risk for AIDS-related events and death
  - Use of ART is associated with a substantially decreased risk for transmission from HIV-positive persons to uninfected partners – Treatment as Prevention

Ann Intern Med. 2013; 159:51-60; MMWR 2015;64:657-62; NEJM DOI: 10.1056/NEJMoa1506816

HIV/AIDS Treatment – When to Start

START Study:

- Randomly assigned HIV-positive adults with CD4 > 500 to start ART immediately or defer it until CD4 < 350 or AIDS developed
- Primary endpoint: Serious AIDS-related or serious non-AIDS-related event, including death
- Initiation of ART in HIV-positive patients with a CD4 > 500 provided net benefit over deferring therapy in patients until the CD4 count had declined < 350

NEJM DOI: 10.1056/NEJMoa1506816 published online on July 20, 2015 at NEJM.org

Primary Care Guidelines for the Management of Persons Infected with HIV

- Guidelines developed by the HIV Medicine Association of the IDSA
- Over 70 recommendations
- Covers several areas of HIV primary care:
  - Initial evaluation and immediate follow-up
  - HIV disease testing, measurement of CD4 count and HIV RNA levels, resistance testing
  - Additional laboratory tests (monitoring and screening)
  - Behavioral interventions
  - Special considerations for women, children, and adolescents
  - Metabolic comorbidities associated with HIV and ART
  - Adherence optimization

Clin Infect Dis. 2014;58(1):e1-34

Primary Care Guidelines for the Management of Persons Infected with HIV

- Adherence optimization
  - *All patients should be evaluated for depression and substance abuse, and if present, a management plan that addresses these problems should be developed and implemented in collaboration with appropriate providers (strong recommendation, moderate quality evidence)*
    - Long-term effectiveness of ART is dependent on durable suppression of viral replication
    - Primary reason for treatment failure is suboptimal adherence to treatment regimens
    - Critical to effectively engage and retain patients in care
    - These two comorbid conditions have been found to be important barriers to consistent adherence to ART and HIV care

Clin Infect Dis. 2014;58(1):e1-34

Primary Care Guidelines for the Management of Persons Infected with HIV

- Metabolic comorbidities associated with HIV
  - *Fasting blood glucose and/or hemoglobin A1c should be obtained prior to and within 1-3 months after starting ART; patients with diabetes should be monitored in accordance with the American Diabetes Association Guidelines (strong, moderate)*
  - *Fasting lipid levels should be obtained prior to and within 1-3 months after starting ART; patients with abnormal lipid levels should be managed according to National Cholesterol Education Program Guidelines (strong, moderate)*
  - Many antiretroviral drugs, HIV infection itself, and host factors are associated with insulin resistance and increased cholesterol and triglyceride levels

Clin Infect Dis. 2014;58(1):e1-34

Primary Care Guidelines for the Management of Persons Infected with HIV

- Metabolic comorbidities associated with HIV and ART, continued
  - *Baseline bone densitometry (DXA) screening for osteoporosis in HIV-infected individuals should be performed in postmenopausal women and men aged >50 years (strong, moderate)*
    - Tenofovir may cause renal phosphate wasting and, especially in combination with vitamin D deficiency, may result in osteopenia, osteoporosis and osteomalacia
    - If the DXA demonstrates osteopenia or if the patient has a history of fragility or fracture, intervention with vitamin D, calcium, and a bisphosphonate or other medical therapy may be warranted

Clin Infect Dis. 2014;58(1):e1-34

High Yield Points

1. Nearly 15% of all people with HIV infection in the United States are undiagnosed
2. Of the approximately 50,000 new cases of HIV infection annually, 26% are aged 13-24 years
3. All patients with HIV infection should be considered for antiretroviral therapy
4. Common complications of HIV infection and antiretroviral treatment include diabetes mellitus, dyslipidemia, and osteopenia

Acute Rhinosinusitis – Bacterial vs Viral

- Which clinical presentations best identify patients with acute bacterial vs viral rhinosinusitis? Any of the following 3 are recommended –

1. Onset with persistent symptoms or signs compatible with acute rhinosinusitis, lasting for ≥ 10 days without any evidence of clinical improvement (strong, low-moderate)

Clin Infect Dis. 2012;54(8):e1-41

Acute Rhinosinusitis – Bacterial vs Viral

- Which clinical presentations best identify patients with acute bacterial vs viral rhinosinusitis? Any of the following 3 are recommended –

  2. Onset with severe symptoms or signs of high fever (≥ 39ºC) and purulent nasal discharge or facial pain lasting for at least 3-4 consecutive days at the beginning of illness (strong, low-moderate), or

Clin Infect Dis. 2012;54(8):e1-41

Acute Rhinosinusitis – Bacterial vs Viral

- Which clinical presentations best identify patients with acute bacterial vs viral rhinosinusitis? Any of the following 3 are recommended –

  3. Onset with worsening symptoms or signs characterized by the new onset of fever, headache, or increase in nasal discharge following a typical viral upper respiratory infection (URI) that lasted 5-6 days and were initially improving ("double-sickening") (strong, low-moderate)

Clin Infect Dis. 2012;54(8):e1-41

Acute Rhinosinusitis – Bacterial vs Viral

- Any one of three of the following clinical presentations are recommended for identifying patients with acute bacterial vs viral rhinosinusitis
  1. Persistent and not improving (≥ 10 days)
  2. Severe (high fever (≥ 39ºC) and purulent nasal discharge or facial pain lasting for at least 3-4 consecutive days), or
  3. Worsening (new onset of fever, headache, or increase in nasal discharge following a typical URI) ("double-sickening")

Clin Infect Dis. 2012;54(8):e1-41

Acute Bacterial Rhinosinusitis (ABRS) – Therapy

- Empiric antimicrobial therapy should be initiated as soon as the clinical diagnosis of acute bacterial rhinosinusitis is established (strong, moderate)
  - Amoxicillin-clavulanate is recommended as empiric antimicrobial therapy for ABRS in children (strong, moderate) and adults (weak, low)
  - High-dose (2 grams orally twice a day or 90 mg/kg/day twice daily) is recommended in adults and children with ABRS (weak, moderate):
    - From regions with high rates (≥10%) of invasive penicillin non-susceptible *Streptococcus pneumoniae*
    - Those with severe infection (systemic toxicity with fever ≥39ºF, threat of suppurative complications)
    - Attendance at daycare
    - Age <2 or >65 years
    - Antibiotic use within the past month
    - immunocompromised

Clin Infect Dis. 2012;54(8):e1-41

ABRS – Therapy

- Alternatives to amoxicillin-clavulanate:
  - Second line agents should be considered for the empiric treatment of ABRS in adults and children with a history of penicillin allergy
  - Adults:
    - Respiratory fluoroquinolones (levofloxacin, moxifloxacin) (weak, moderate)
    - Doxycycline (weak, low)
  - Children:
    - Levofloxacin (type I hypersensitivity to penicillin)
    - Clindamycin plus a third-generation oral cephalosporin (cefixime or cefpodoxime) (non-type I hypersensitivity to penicillin) (weak, low)

Clin Infect Dis. 2012;54(8):e1-41

ABRS – Therapy

- Antibiotics not recommended as alternatives to amoxicillin-clavulanate:
  - Macrolides (clarithromycin, azithromycin) are not recommended for empiric therapy
    - High rates of resistance among *S. pneumoniae* (~30%) (strong, moderate)
  - Trimethoprim-sulfamethoxazole (TMP-SMX) is not recommended for empiric therapy
    - High rates of resistance among *S. pneumoniae* and *Haemophilus influenzae* (~30%-40%) (strong, moderate)
    - Empiric coverage of Staphylococcus aureus (especially methicillin-resistant S. aureus – MRSA) is not recommended (strong, moderate)

Clin Infect Dis. 2012;54(8):e1-41

ABRS – Therapy

- Duration of therapy for adults:
  - Uncomplicated ABRS: 5-7 days (weak, low-moderate)
- Duration of therapy for children:
  - 10-14 days
- Recommended adjunctive therapy:
  - Saline irrigation of the nasal sinuses with physiologic or hypertonic saline (weak, low-moderate)
  - Intranasal corticosteroids – primarily in patients with a history of allergic rhinitis (weak, moderate)
- Not recommended:
  - Neither topical nor oral decongestants and/or antihistamines are recommended (strong, low-moderate)

Clin Infect Dis. 2012;54(8):e1-41

ABRS – The Non-responsive Patient

- When to consider a change in antimicrobial therapy:
  - Symptoms worsen after 48-72 hours of initial empiric therapy or fail to improve despite 3-5 day (strong, moderate)
  - Re-evaluate for (strong, low):
    - possibility of a resistant pathogen
    - A non-infectious etiology
    - A structural abnormality
    - Other causes
- If the patient has failed both first-line and second-line agents, cultures should be obtained
  - Direct sinus aspiration (strong, moderate)
  - Endoscopically-guided cultures of the middle meatus may be an alternative in adults (weak, moderate)
  - Nasopharyngeal cultures are unreliable and are not recommended (strong, high)

Clin Infect Dis. 2012;54(8):e1-41

ABRS – The Non-responsive Patient

- If suppurative complications such as orbital or intracranial extension of infection is suspected in patients with ABRS, contrast-enhanced CT is recommended rather than MRI (weak, low)
- Specialist referral for consultation (otolaryngologist, allergist, infectious disease specialist)
  - Seriously ill
  - Immunocompromised
  - Continued deterioration despite extended courses of antimicrobial therapy
  - Recurrent bouts with clearing between episodes

Clin Infect Dis. 2012;54(8):e1-41

High Yield Points

Any of the following clinical presentations are recommended for identifying patients with acute bacterial (vs viral) rhinosinusitis:

Persistent & non improving (≥10 days);

Severe (≥3-4 days)

Worsening or "double sickening" (≥3-4 days)