Antibiotic Stewardship

**Antibiotic use:** leads to resistance; must consider choice of antibiotic, dosing, when to use prophylaxis, and when to use ≥1 agent; use pressured by patient or family; estimated that 70% of patients given antibiotics during stay in medical centers (estimated that ≥50% of use inappropriate or unnecessary); unnecessary use can lead to, eg, adverse reactions, increased readmissions, increased costs of medical care, selection of pathogenic and drug-resistant organisms, and Clostridium difficile infection

**Antimicrobial stewardship:** system of informatics, data collection, individuals, policies, and procedures that promotes optimal selection, dosing, and duration of therapy for antibiotic agents throughout course of their use; limits inappropriate and excessive antimicrobial use; improves and optimizes therapy for individual patients, and thus improves clinical outcomes; **goals** — prevent or slow emergence of resistance; optimize use for patients; reduce adverse effects (including C difficile infection), morbidity, mortality, length of stay, and health care expenditures

**Guidelines:** published initially in 2007 (by Infectious Diseases Society of America and Society for Healthcare Epidemiology of America); advocate multidisciplinary team in medical center led by infectious diseases (ID) physician or ID-trained clinical pharmacist; other team members should include, eg, microbiologists, information systems specialists, infection control professional, hospital epidemiologists; **qualities of leading physician** — in speaker’s view, medical staff function; need not be ID physician; hospitalist, intensivist, internist can lead team; additional training in antimicrobial therapy useful but not necessary; time and availability; compensation from hospital; conceptualization, communication, and coercion; some facilities contract with outside ID physician and provide access to electronic medical records to discuss patients and antibiotics with pharmacist

**Levels of team function:** **patient** — improve antimicrobial therapy for individual patients, generally through prospective audit with intervention and feedback; team led by pharmacist or physician identifies patients on problematic antimicrobials or with problematic diagnoses, and reviews medications, culture results, and therapy; therapy often stopped or streamlined (documented on electronic chart that responsible medical provider contacted and advised; compliance voluntary); in speaker’s facility, 80% to 85% of medical providers comply; hospital — restrict or require preauthorization for certain antibiotics; payer or other system used by physicians to call for permission to use specific antibiotic; authors must be respected physicians or clinical pharmacists; preauthorization clearly changes or modulates antibiotic use; helpful during shortages; disadvantages include loss of autonomy and receipt of inaccurate or misleading information for decision making; **other measures** — guidelines or clinical pathways; electronic decision making in electronic records; **education** — not highly effective; requires patient-specific feedback and consolidation of information

**Molecular testing:** can distinguish methicillin-resistant *Staphylococcus aureus* (MRSA) from methicillin-susceptible *S aureus* (MSSA) from coagulase-negative staphylococci in 1 hr; can identify *Candida albicans* (easily treated with fluconazole); other strains of *Candida* need higher level of antifungal therapy; can distinguish vancomycin-resistant *Enterococcus* (VRE) from non-VRE in 1 hr; can identify 9 different respiratory viruses from simple nasopharyngeal swab in 1 hr (allows for deescalation of antibiotics); **procalcitonin testing** helps determine whether inflammation due to high-level bacterial agent; more useful than lactate testing, C-reactive protein testing, or erythrocyte sedimentation rate; high procalcitonin suggests higher likelihood of bacterial infection than viral infection; particularly helpful when evaluating patients for high-order upper respiratory infections (URIs; eg, differentiating pneumonia from other viral respiratory infection); useful for bacterial exacerbations of chronic obstructive pulmonary disease, pneumonia, and sepsis; likelihood ratios available; sensitivity and specificity ≥80%; not helpful if pretest suspicion of bacterial sepsis high because posttest probability based on likelihood ratio not much better than what clinician knew before test; if pretest likelihood low and test results negative, then bacterial entity unlikely; most helpful when pretest likelihood and clinical suspicion unclear; positive test then leads clinician to posttest probability that bacterial sepsis present; if test negative bacterial sepsis unlikely; perform test early (if negative, repeat 6 hr later; if still negative, antibiotic can be stopped in setting of intermediate to low pretest likelihood)

5. Discuss cardiovascular risk associated with macrolide antibiotics.

**Educational Objectives**

The goal of this program is to improve management of antimicrobial therapy and infectious diseases. After hearing and assimilating this program, the clinician will be better able to:

1. Define antimicrobial stewardship and list its goals.
2. Outline components of an effective antimicrobial stewardship program.
3. Describe the different types of influenza vaccine.
4. Review guidelines for pneumococcal and meningococcal vaccination in immunocompromised patients.

**Faculty Disclosure**

In adherence to ACCME Standards for Commercial Support, Audio-Digest requires all faculty and members of the planning committee to disclose relevant financial relationships within the past 12 months that might create any personal conflicts of interest. Any identified conflicts were resolved to ensure that this educational activity promotes quality in health care and not a proprietary business or commercial interest. For this program, Dr. Ohl and the planning committee reported nothing to disclose.
Outcomes of antimicrobial stewardship: difficult to measure or evaluate effects on antibiotic resistance; decrease in antibiotic consumption; reductions in expenditures and length of stay in hospital or intensive care unit; decrease in \textit{C difficile} infection; studies in multiunit area showed that when antimicrobial stewardship carefully performed, antibiotic resistance improved.

**Clinical entities that can be affected by antibiotic stewardship:** 
- \textit{pneumonia} — abnormalities on chest x-ray not always sign of pneumonia; important to make correct diagnosis; \textit{cellulitis} — often treated with multiple antibiotics; first-generation cephalosporin (eg, ceffazolin) or nafcillin effective for routine cellulitis, ie, redness without gross purulence (rarely MRSA); \textit{urinary tract infections (UTIs)} — discuss symptoms with patient to distinguish between symptomatic and asymptomatic bacteriuria; in elderly patients in nursing homes with indwelling catheters or ileal conduits, neither pyuria, abnormal urinalysis, or positive urine culture predictive of UTI; 50% of women and 40% of men $>$70 yr of age in nursing homes have bacteria in urine (nearly 100% if patient has indwelling catheter); asymptomatic bacteriuria rarely associated with abnormal mental status; if patients do not have evidence of pyelonephritis (source of cytokines for abnormal mental status, fever, and abnormal white blood cell count) then abnormal mental status not due to UTI; ciprofloxacin commonly causes exacerbations of delirium and dementia.

**Deescalating antibiotics:** assess patient at 72 hr; define infection anatomically, microbiologically, and pathophysiologically; if patient does not have infection, then stop antibiotics at 72 hr; if infection identified, then streamline therapy (provide guideline-based duration of therapy for that defined infection).

**Infectious Disease Update**

**Influenza vaccines:** less effective in elderly (especially infirm elderly), but still protective against death and secondary pneumonia; \textit{cocooning} — strategy to protect elderly by reducing exposure through immunization of children in school and young adults in workplace; \textit{inactivated influenza vaccine trivalent (IIV3)} — 70% to 90% efficacy in healthy young individuals (lower in elderly and those with comorbidity, but still protective against death and comorbidity-related complications); available in multidose vial or as single dose (preservative free); thimerosal-free vaccines and latex-free syringe tip caps available; 2013-2014 U.S. vaccine to contain A/California/2009 H1N1 (“swine flu”) virus, H3N2 virus, and B virus; \textit{quadivalent vaccine} — contains additional B virus; likely to be used next year; \textit{high-dose vaccine} — slightly more immunogenic for elderly patients (unknown whether more protective); associated with higher incidence of local pain and swelling; higher cost; speaker advises reserving for more infirm geriatric patients; \textit{intra-dermal trivalent vaccine} — approved for individuals 18 to 64 yr of age; uses smaller needle, but still associated with increased complaints of redness and soreness at site; higher cost; \textit{intranasal vaccine} — quadrivalent vaccine; approved for healthy, nonpregnant individuals 2 to 49 yr of age; 2 sprays in each nostril; not indicated for patients with asthma and immunocompromised patients; acceptable for health care workers who care for immunocompromised patients (except bone marrow transplantation patients); no reported cases of transmission from health care worker to immunocompromised patient; produced in eggs (consider patients with egg allergy); vaccines not manufactured in eggs — FLUCELVAX; FluBlok (approved for patients 18-49 yr of age); higher cost; \textit{influenza prophylaxis for adults} — recommended for high-risk individuals (eg, immunocompromised or elderly patients, patients with chronic medical conditions, pregnant women) with close contact with individuals with known or highly suspected influenza; give for 2 wk; includes nursing home outbreaks.

**New approaches for pneumococcal vaccination in immunocompromised adults:** Advisory Committee on Immunization Practices recommends pneumococcal 13-valent conjugate vaccine (Prevnar 13) and polyvalent pneumococcal vaccine (Pneumovax 23); patients with immunocompromise, functional or anatomic asplenia, cerebrospinal fluid leak, or cochlear implants who have not received either vaccine should receive Prevnar 13 followed by Pneumovax 23 at least 8 wk later; if patient previously received Pneumovax 23 but not Prevnar 13, then give Prevnar 13 $\geq$ 1 yr after Pneumovax 23 dose; give Pneumovax 23 every 5 yr until age 65 yr, then give once after 65 yr of age; unknown whether Prevnar 13 better for preventing pneumonia (trial underway); unknown whether Prevnar 13 (used in children for last 2-3 yr) has same effect on 13-valent serotypes that are covered by children and adults (use of Prevnar 7 resulted in fewer infections with 7 strains in adults due to herd immunity).

**Meningococcal vaccines in immunocompromised patients:** patients infected with HIV at marginally increased risk for meningococcal infection, compared to patients with asplenia or other protein deficiencies; no recommendations based on HIV infection alone; risk for meningococcal infection increased in adolescence and early adulthood (particularly during high school and college years); all adolescents should be immunized with meningococcal vaccine; immunize travelers to sub-Saharan Africa or to Mecca during Hajj, undergraduate college students (particularly those living in dormitories) up to 22 yr of age, military recruits, asplenic patients, and patients with complement deficiencies; vaccinate adolescents at age 11 or 12 yr (give booster before college or if other risk present); HIV-infected adolescents respond to vaccines well (giving 2 doses increases response and duration of immunity); patients with complement deficiencies or functional or anatomic asplenia should be given 2 doses 2 mo apart; other patients with risk factors should be given 1 dose.

**Antibiotics associated with increased risk for ventricular dysrhythmias and sudden death:** erythromycin and clarithromycin (particularly in patients with QT problems); \textit{azithromycin} — large study in Tennessee looked at Medicaid database of patients in wide age range who received azithromycin or other antibiotic; nearly all indications for azithromycin were URIs; study found 47 additional cardiovascular deaths per million patients who received azithromycin (statistically significant); among death or cardiovascular death cases, more patients on azithromycin, compared to no antibiotic, amoxicillin, or nonmacrolide antibiotic; $\approx$40 million patients receive prescription for azithromycin per year; another study looking at healthier group of patients in Denmark showed no difference in 5-day mortality between azithromycin and penicillin (control group smaller and subjects healthier); azithromycin increases risk for cardiovascular death presumably due to torsades de pointes; assess...
whether antibiotic needed by patient; in patients with heart disease, consider using different antibiotic; azithromycin may be acceptable in patients with heart disease who require macrolide antibiotic as long as patient does not have prolonged QT interval, not on other medication that prolongs QT, and does not have history of ventricular dysrhythmias; guidelines suggest using ceftriaxone with azithromycin in patients who present with community-acquired pneumonia (consider fluoroquinolone, eg, levofloxacin or amoxicillin, or dropping macrolide antibiotic)

Severe valve dysfunction with endocarditis and large vegetation on echocardiography; prospective randomized trial looked at conventional medical therapy (surgery performed only when complications developed during medical treatment) vs early surgery in patients with severe valve dysfunction and large vegetation; found that group who received early surgery had fewer complications (statistically significant); fewer in-hospital deaths or embolic events alone in early surgery group, compared to conventional surgery group (1 vs 9); 0 embolic events alone in early surgery group; early surgery prevented stroke; early surgery should be performed on patients with valve dysfunction and evidence of large vegetation; important to collaborate with surgeons; standard of care evolving; consider transferring patient to center where surgeons comfortable performing early surgery on patients with valve dysfunction and large vegetation

Other infectious diseases: tickborne diseases — work up patients with known tick bite and fever for new pathogen after ruling out Rocky Mountain spotted fever, erlichiosis, and other known tickborne diseases; Heartland virus (new tickborne virus) causes erlichiosis-like fever; Rickettsia parkeri found in ticks; Middle East respiratory syndrome—nearly 100 cases reported over past year; epicenter in Saudi Arabia and surrounding countries; brought to United Kingdom, Italy, and France by travelers to Saudi Arabia or Qatar; more severe with quicker onset than severe acute respiratory syndrome; 91 cases and 46 deaths reported (mortality >50%)

Acknowledgments
Dr. Ohl spoke in Myrtle Beach, SC, at the 42nd Annual Emery C. Miller Medical Symposium, presented July 29 to August 2, 2013, by Wake Forest School of Medicine and Northwest Area Health Education Center (AHEC). Visit northwesternace.org for information about upcoming courses. The Audio-Digest Foundation thanks Dr. Ohl and the sponsors for their cooperation in the production of this program.

Suggested Reading

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Estimated time to complete the educational process:
- Review Educational Objectives on page 1: 5 minutes
- Take pretest: 10 minutes
- Listen to audio program: 60 minutes
- Review written summary and suggested readings: 35 minutes
- Take posttest: 10 minutes

Audio-Digest Family Practice 61:46
ANTIBIOTIC STEWARDSHIP/INFECTIOUS DISEASE UPDATE

To test online, go to www.audiodigest.org and sign in to online services.
To submit a test form by mail or fax, complete Pretest section before listening and Posttest section after listening.

1. What is(are) the goal(s) of antimicrobial stewardship?
   (A) Prevent or slow emergence of resistance
   (B) Optimize use of antibiotics for patients
   (C) Reduce adverse effects of antibiotics
   (D) All the above

2. According to guidelines, multidisciplinary teams for antimicrobial stewardship should be led by:
   (A) Infectious diseases physicians
   (B) Infection-control professionals
   (C) Microbiologists
   (D) Hospital epidemiologists

3. Which of the following appears most effective in changing or modulating antibiotic use?
   (A) Restricting or requiring preauthorization for use of certain antibiotics
   (B) Providing educational materials for hospital staff and patients
   (C) Building electronic decision making into electronic records
   (D) Reviewing guidelines and clinical pathways for antibiotic use

4. Choose the correct statement about procalcitonin testing.
   (A) High procalcitonin level suggests higher likelihood of viral infection, compared to bacterial infection
   (B) Particularly helpful when evaluating patients for high-order upper respiratory infections
   (C) Sensitivity and specificity ≈60%
   (D) Most helpful when pretest likelihood of bacterial sepsis high

5. Which of the following outcomes of antimicrobial stewardship is most difficult to measure?
   (A) Antibiotic consumption
   (B) Clostridium difficile infection
   (C) Antibiotic resistance
   (D) Hospital expenditures

6. Intra-nasal influenza vaccine is contraindicated in all the following, except:
   (A) Patients with asthma
   (B) Pregnant women
   (C) School-aged children
   (D) Immune-compromised patients

7. Immunocompromised patients who have not received pneumococcal vaccines should receive the pneumococcal 13-valent conjugate vaccine (Prevnar 13) followed by the polyvalent pneumococcal vaccine (Pneumovax 23) ______ later.
   (A) 2 wk
   (B) 4 wk
   (C) 6 wk
   (D) 8 wk

8. Which of the following groups should be immunized with the meningococcal vaccine?
   (A) All adolescents 11 to 12 yr of age and in high school
   (B) Undergraduate college students living in dormitories
   (C) Military recruits
   (D) All the above

9. Azithromycin is acceptable in patients with heart disease who have prolonged QT intervals and history of ventricular dysrhythmias.
   (A) True
   (B) False

10. Choose the correct statement about Middle East respiratory syndrome.
    (A) Epicenter in Saudi Arabia and surrounding countries
    (B) Mortality rate ≥75%
    (C) Slower onset than severe acute respiratory syndrome
    (D) Caused by Heartland virus

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The cutoff date for logging 2013 credits is December 31. Test forms received after that date will be accrued to 2014.

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Answers to Audio-Digest Family Practice Volume 61, Issue 44: 1-D, 2-C, 3-A, 4-C, 5-B, 6-D, 7-B, 8-A, 9-A, 10-C