MINDFUL PRACTICE

Personal Antibiotic Resistance

BY JON O. EBBERT, M.D., AND ERIC G. TANGALOS, M.D.

The Problem

A 42-year-old woman presents to you with a 5-day history of nonproductive cough, postnasal drainage, and sore throat. She denies fevers, shortness of breath, or headache. She received amoxicillin 2 weeks ago for similar symptoms, and although she improved, she feels that she has not completely recovered. On examination she is afebrile and her head and neck, lymph node, and lung exams are normal. You deliver your speech about antibiotic resistance and how important it is to use antibiotics only when absolutely necessary. She becomes quite irritated. You acquiesce by offering her a delayed antibiotic prescription for azithromycin. You inform her not to take it unless she develops fever, shortness of breath, or increased cough. You also ask her to inform the nurse if she starts the antibiotic. You once again berate yourself for "caving." You also wonder what the evidence is for her personally being resistant to amoxicillin because of the first course of antibiotics she received.

The Question

In patients receiving antibiotics in primary care, what is the evidence for personal antibiotic resistance, and how long does it last?

The Search

You open PubMed (www.pubmed.gov) and enter "antibiotic resistance" AND "primary care." You find a relevant study. (See box at right.)

Our Critique

This systematic review was well conceived and has broad application to primary care. The search was thorough, and methods of abstraction and quality assessment were standard. What is most striking about this study is that it provides overwhelming evidence for antibiotic resistance in our individual patients after antibiotic treatment, rather than within the abstract concept of "the community." Resistance can be transferred from commensal and pathogenic organisms so that even if the pathogen is eradicated, new pathogens can pick up resistance from the remaining nonpathogenic bacteria. This information should be provided to patients who, when ill, may not be concerned about antibiotic resistance at the population level but who may be more influenced by hearing about possible increased difficulty with their own treatment if they "really get sick."

Clinical Decision

The patient calls the next day to tell the nurse that she started the antibiotic because she was not getting any better. You work on your antibiotic speech to make it more convincing for the next patient.

DR. EBBERT *and* DR. TANGALOS *are with the Mayo Clinic in Rochester, Minn. They report having no conflicts of interest. To respond to this column or suggest topics for consideration, write to Dr. Ebbert and Dr. Tangalos at our editorial offices or e-mail them at imnews@elsevier.com.*

The Evidence

Costelloe C., et al. Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: Systematic review and meta-analysis. BMJ 2010;340:c2096.

► **Criteria for study inclusion:** Studies were eligible for inclusion if they investigated the relationship between antibiotics prescribed in primary care and antimicrobial resistance in bacteria sampled from any body site, were observational and experimental, and were analyzed at the level of the individual.

► **Study identification:** Investigators searched MEDLINE (1955 to May 2009), EMBASE (1980 to May 2009), Cochrane databases, and the ISI Web of Knowledge.

► **Data extraction and quality assessment:** Full articles were reviewed independently by two reviewers who extracted study data and assessed study quality.

► **Outcomes:** Outcomes included bacteria type, sampling location, antibiotics to which resistance was measured, and the method of measuring resistance. The outcome measure was the odds ratio (OR) of resistance among participants exposed to antibiotics, compared with those who were not exposed. ORs were tabulated by bacterium type and sampling location and by time since antibiotic exposure.

► **Results:** Twenty-four papers were included in the review, including 5 randomized controlled trials and 19 observational studies (2 prospective, 17 controlled observational or case-control). Twenty-two studies sampled bacteria from patients with urinary tract infection, upper respiratory infection, otitis media, chronic obstructive pulmonary disease, methicillin-resistant *Staphylococcus aureus* (MRSA), or trachoma; two studies were conducted in healthy adult volunteers. A wide variety of antibiotics were given 2-104 weeks before measurement of antibiotic resistance. For the five studies of urinary tract bacteria including more than 14,000 subjects, the ORs for resistance were 2.5 (95% CI: 1-2.9) within 2 months of antibiotic treatment and 1.33 (95% CI: 1.2-1.5) within 12 months. For the seven studies of respiratory tract infections including more than 2,600 patients, the ORs were 2.4 (95% CI: 1.4-3.9) within 2 months and 2.4 (95% CI: 1.3-4.5) within 12 months. Antibiotic resistance changed over time from 12.2 (95% CI: 6.8-22.1) at 1 week to 6.1 (95% CI: 2.8-13.4) at 1 month, 3.6 (95% CI: 2.2-6.0) at 2 months, and 2.2 (95% CI: 1.3-3.6) at 6 months. Longer durations and multiple courses were linked to higher resistance rates. One study found a link between MRSA and the prescription of an antibiotic in the previous 0-6 months (OR 3.1; 95% CI: 1.1-8.6).

Antivirals Blunted Flu Complications

BY BRUCE JANCIN

FROM THE ANNUAL EUROPEAN CONGRESS OF CLINICAL MICROBIOLOGY AND INFECTIOUS DISEASES

VIENNA — It's well established that timely prescription of the neuraminidase inhibitors can reduce the duration of seasonal influenza symptoms; now there's good evidence that the drugs are effective in reducing influenza-related complications, too.

The benefit was substantially greater in high-risk patients than in previously healthy patients.

DR. FALAGAS

A meta-analysis of 11 placebo-controlled randomized trials—10 of them double blind—demonstrated that treatment with oseltamivir (Tamiflu) or zanamivir (Relenza) reduced the overall rate of flu-related complications by 26% in otherwise healthy patients with confirmed seasonal influenza, Dr. Matthew Falagas reported at the meeting.

The magnitude of benefit was substantially greater in high-risk patients than in those who were previously healthy. In the four trials totaling 475 high-risk patients, the rate of flu-related pneumonia, bronchitis, sinusitis, pharyngitis, and other complications was 8% in neuraminidase inhibitor–treated patients compared with 25% with placebo—for a 63% relative risk reduction, said Dr. Falagas, director of the Alfa Institute of Biomedical Sciences, Athens.

In the six trials totaling nearly 2,000 subjects in which administration of antibiotics was an end point, treatment with a neuraminidase inhibitor conferred a 23% reduction in the use of antibiotic therapy, he continued.

The overall reduction in flu-related complications in the group receiving antivirals was driven by a highly significant 50% decrease in the rate of acute otitis media. Indeed, the number of patients who needed to be treated (NNT) with a neuraminidase inhibitor to prevent one additional case of acute otitis media was 18.

There were consistent albeit weaker trends for lower rates of pneumonia, sinusitis, and the other flu-related complications in neuraminidase inhibitor–treated patients, none of which achieved significance. For example, the incidence of pneumonia in the placebo group was just 2%, and it was estimated that roughly 330 patients would need to be treated with a neuraminidase inhibitor to prevent one additional case of pneumonia.

Only four trials included mortality as a study end point. There were no deaths.

The 11-trial meta-analysis involved 5,315 randomized patients. Three of the trials were done in children; the rest were done in adults and adolescents. The magnitude of risk reduction with neuraminidase inhibitor therapy was similar in children and adults, and with oseltamivir compared with zanamivir.

Whether these meta-analysis results apply to 2009 H1N1 influenza–related complications as well is anybody's guess, in Dr. Falagas's view, because there are as yet no good randomized controlled trials of neuraminidase inhibitors in patients infected with H1N1 flu.

He deemed the safety profile of the drugs to be acceptable. There were no significant differences between the neuraminidase inhibitors and placebo in the rates or severity of any adverse events. Although the rate of nausea/vomiting was 13% in the neuraminidase inhibitor–treated patients, vs. 6.4% with placebo, this trend fell shy of significance. There was a 30% reduction in diarrhea with the neuraminidase inhibitors, but again this was not significant. Of note, none of the trials recorded neuropsychiatric adverse events. ■

VITALS

Major Finding: In the four trials totaling 475 high-risk patients, the rate of flu-related pneumonia, bronchitis, sinusitis, pharyngitis, and other complications was 8% in neuraminidase inhibitor–treated patients, compared with 25% with placebo.

Data Source: A meta-analysis of 11 placebo-controlled randomized trials of oseltamivir or zanamivir.

Disclosures: The meta-analysis was supported by the nonprofit Alfa Institute of Biomedical Sciences. Dr. Falagas reported having no financial conflicts.