Are Wide-Spectrum Antibiotics Overused in Mild Pneumonia?

ARTICLES BY
KATE JOHNSON
Montreal Bureau

MONTREAL — European and North American experts continue to disagree about the management of mild community-acquired pneumonia, with the debate centering on the overuse of wide-spectrum antibiotics.

New guidelines released jointly by the Infectious Diseases Society of America and the American Thoracic Society recommend that empiric treatment of mild CAP in previously healthy individuals should include a macrolide to cover not only the most common pathogen (*Streptococcus pneumoniae*) but also atypical pathogens (Clin. Infect. Dis. 2007;44 [suppl. 2]:S29-72). In contrast, European guidelines do not target atypical pathogens, recommending β-lactams as the only treatment of choice (Eur. Respir. J. 2005;26:1138-80).

"If and when we get rapid diagnostic tests [to identify specific pathogens], this is a moot point, but right now all we can do is base our treatment decisions on an empiric approach," Dr. Thomas File, professor of internal medicine and head of infectious diseases at Northeastern Ohio Universities, Rootstown, said at an international conference on community-acquired pneumonia.

European and North American experts agree that roughly 40% of mild CAP may be caused by atypical pathogens, but Europeans are prepared to ignore these pathogens in their choice of empiric therapy because these infections are usually self-resolving, said Dr. Jean-Claude Pechère, a professor of medicine at the University of Geneva.

"In this way, we can avoid a lot of antibiotic overuse," he said in an interview. "In the context of increasing resistance, it's a big public health issue."

Although many atypical CAP infections are self-resolving, the evidence shows that antibiotics can speed recovery, Dr. File said at the conference, sponsored by the International Society of Chemotherapy. "People get sick, and people are off work or school. If, by treating them, we can help them resolve their illness quicker, then we think it's worthwhile," he said in an interview. "If you tell a patient, 'I am going to reduce your fatigue and malaise by 6 days,' that's important. It may not affect mortality at all, but if it can significantly reduce morbidity, I would argue that's a significant benefit."

However, new evidence suggests coverage of atypical pathogens also may improve mortality, at least in hospitalized patients, Dr. File said. An analysis of more than 2,000 patients found that, compared with those treated only for typical pathogens, those treated with atypical coverage had decreased time to clinical stability (3.2 vs. 3.7 days), decreased length of hospital stay (6.1 vs. 7.1 days), decreased total mortality (7.0% vs. 11.1%), and decreased CAP-related mortality (3.8% vs. 6.4%) (Am. J. Respir. Crit. Care Med. 2007 [Epub doi:10.1164/rccm.200603-350OC]).

"The significant global presence of atypical pathogens and the better outcomes associated with antimicrobial regimens with atypical coverage support empiric therapy for all hospitalized patients with CAP with a regimen that covers atypical pathogens," the authors concluded.

The atypical pathogens responsible for mild CAP include *Mycoplasma pneumoniae* and *Chlamydia pneumoniae*. Dr. Pechère and Dr. File agreed that the third atypical pathogen, *Legionella,* without question should be treated immediately and aggressively, because it is associated with a high mortality rate.

According to Dr. Pechère, the North American guidelines "promote overuse" of antibiotics. But Dr. File sees it differently. The IDSA/ATS guidelines underscore the necessity of a chest x-ray in the diagnosis of CAP, thus ensuring that only radiographically confirmed cases are treated. "If the decision is based on a positive chest x-ray, then we feel all those patients warrant antimicrobial therapy—because it's unlikely that they've got viral bronchitis if they've got true infiltrate."

But this is not the scenario in Europe, he said, where x-ray confirmation is not required for the diagnosis of CAP. "The overuse of antibiotics in respiratory infection is not from overtreating pneumonia, it's from overtreating viral infections, which are much more common than pneumonia. The Europeans may be overtreating a lot of viral bronchitis." ■

Management of Flu Can Curb Pneumonia

MONTREAL — Influenza vaccines and antiviral drugs greatly reduce the incidence of and mortality associated with community-acquired pneumonia, but they are grossly underutilized, according to Dr. Grant Stiver, professor of medicine at the University of British Columbia, Vancouver.

"We are not optimizing the management of influenza by far, in my opinion—largely because of costs and political unwillingness to put out money," he said at an international conference on community-acquired pneumonia (CAP), calling on attendees to take a stand. "We are the ones that influence policy and set the track, and we need to do a better job at campaigning for improved resources to reduce the morbidity and mortality due to influenza because it's quite clear now that we're just not doing enough."

Until now, influenza prevention has focused on so-called high-risk groups, but there is no reason why the net shouldn't be widened to include everyone, Dr. Stiver said. During the 2003-2004 influenza season, half of the 153 influenza-associated deaths among children in the United States were in those with no high-risk conditions (N. Engl. J. Med. 2005;353:2559-67).

"These were your normal children or grandchildren," he said, adding that 70% of the deaths resulted from respiratory infection, and 47% of these were from confirmed CAP. "Pneumonia is a scary thing for the public, but influenza is not. Influenza is something that the public can trivialize until it's a member of their family that dies from pneumonia. So if we show we can actually prevent pneumonia with the optimization of influenza vaccine and antivirals, we can probably get better public acceptance."

Dr. Stiver suggested putting more pressure on target groups such as health care workers. "We should make vaccination a condition of employment for health care workers, and if they don't want it, they can't work in a health care institution." And essential service workers designated as first priority for antiviral prophylaxis in the event of a pandemic should be denied the drugs if they were not vaccinated, he said at the meeting, sponsored by the International Society of Chemotherapy. ■

Pneumococcal Vaccine Could Aid Pandemic Preparedness

MONTREAL — U.S. plans for an influenza virus pandemic should include a strong recommendation for bacterial pneumonia vaccination, as this measure has been shown to reduce influenza mortality by up to 50%, said Dr. Keith Klugman.

"In the U.S. pandemic plan, there is little mention of bacterial vaccines. I believe their role is significant and has not been considered up until now," he said at an international conference on community-acquired pneumonia.

Although the influenza virus alone can be fatal, the risk of death is greater with secondary pneumococcal infection, said Dr. Klugman, professor of infectious diseases and the William H. Foege Chair of Global Health at Emory University, Atlanta.

"The combination of bacterial superinfection and influenza is highly fatal. It's a huge problem, and it's not a small part of influenza mortality and morbidity," he said in an interview.

Evidence that pneumococcal infection played a major role in the 1918 influenza pandemic "is substantial, but seems to have been forgotten," Dr. Klugman recently wrote in a letter to the editor (Science 2007;316:49-50), citing historical evidence of culturable pneumococci in the blood of at least half of the survivors and victims of influenza (Br. Med. J. 1919;1:3-5; JAMA 1918;71:1735).

A randomized, controlled trial by Dr. Klugman and his colleagues has shown that, in children, vaccination against the pneumococcal bacteria results in a 31% decrease in pneumonias associated with respiratory viruses (Nat. Med. 2004;10:811-3). "Because of the vaccine, they are not getting the superinfection that brings them to the hospital," he said at the meeting, sponsored by the International Society of Chemotherapy. "People have known for years that there can be bacterial superinfections with influenza, but they just didn't realize how common they were."

The 23-valent pneumococcal polysaccharide vaccine (PPV 23) is recommended in adults older than 65 years, but giving the 7-valent pneumococcal conjugate vaccine (PCV 7) to children is more protective against bacterial pneumonia in adults, Dr. Klugman said.

Data from the Centers for Disease Control and Prevention show that adult infections with the 7 pneumococcal strains covered in the children's vaccine have decreased, while infections from the other 16 strains covered by the adult vaccine have increased. "The burden of disease in adults has been impacted more by giving the conjugate vaccine to children than by giving the 23-valent vaccine to adults," he said.

This has led some investigators to ask whether adults might benefit by being immunized using the children's conjugate vaccine. (See box.)

A new study (Lancet 2007;369:1179-86) has shown that vaccinating children protects adults against all (not just bacteremic) pneumococcal pneumonia, he said. ■

Should Adults Get the Kids' Vaccine?

Is there a role for giving the children's conjugate vaccine to adults?

In a recent study (Vaccine 2007;25:4029-37), immunogenicity in elderly patients (aged 70-79 years) given the children's dose of conjugate vaccine was "nothing to get overly excited about," Dr. Klugman said.

A study presented at the 2006 International Symposium on Pneumococci and Pneumococcal Diseases by Dr. Andrés de Roux of the Universitat Autònoma de Barcelona and colleagues suggested that the administration of the children's conjugate vaccine to elderly patients within 1 year of giving them the polysaccharide vaccine could actually suppress immunity. "It seems the adult vaccine interferes with the response to the conjugate, which … means we can't simply give the conjugate to people who have previously had the [PPV 23]. … It seems that certainly the conjugate needs to be given before the 23-valent," Dr. Klugman said.

A new conjugate vaccine that covers more strains than the current one will eventually replace the PPV 23 for adults, he predicted.