Risk Factors Should Guide Pneumonia Therapy

Recommendations focus on using clinical judgment and giving antibiotics before culture results are back.

BY MARY ELLEN SCHNEIDER
New York Bureau

DALLAS — Selection of an antibiotic for the treatment of community-acquired pneumonia should be based on the severity of the illness, coverage of common pathogens, and presence of factors that increase the risk for aspiration and/or infection with antibiotic-resistant organisms, Dr. Horace M. DeLisser said at the annual meeting of the National Medical Association.

Physicians shouldn't wait for culture results before treating. Instead, they should rely on the history to identify risk factors that will require modifying the treatment plan, said Dr. DeLisser of the pulmonary, allergy, and critical care division of the University of Pennsylvania, Philadelphia.

To determine whether the patient should be treated on an inpatient or outpatient basis, physicians can use the pneumonia severity index, a widely utilized and rigorously studied prediction rule, he said.

The index is based on 20 parameters that are commonly available at presentation, including demographic information, exam findings, and lab and imaging results. Each parameter is assigned a specific point value that allows physicians to stratify patients into five risk classes.

Classes 1-3 are low risk, class 4 is moderate risk, and class 5 is high risk. Generally, patients in risk classes 1 and 2 are treated on an outpatient basis, those in risk classes 4 and 5 are treated as inpatients, and those in class 3 may be treated as outpatients or admitted briefly, Dr. DeLisser said. "Your clinical judgment should always be used, particularly if there are other psychosocial or emotion factors," he said.

Dr. DeLisser advised physicians not to wait for the culture to come back. Between 40% and 60% of patients will have no pathogens identified, and for inpatients, early administration of antibiotics decreases mortality, he said. Instead, physicians should take into account the modified risk factors for infections, such as residence in a nursing home, underlying disease, and recent antibiotic therapy.

Several organizations in the United States, Europe, and Asia have developed guidelines for the treatment of community-acquired pneumonia. The following treatment recommendations are based on guidelines developed by the American Thoracic Society (www.thoracic.org/sections/publications/statements/pages/mtpi/commacq1-25.html).

► In otherwise healthy adults who do not have modifying risk factors, use an advanced-generation macrolide, such as azithromycin or clarithromycin. Another option for this group is treatment with doxycycline.

► For outpatients with comorbid disease or modifying risk factors, use a respiratory fluoroquinolone alone, or β-lactam plus an advanced-generation macrolide.

► For otherwise healthy inpatients who are not in the ICU, use an intravenous respiratory fluoroquinolone alone or intravenous azithromycin alone.

► For inpatients with comorbid disease or modifying risk factors, use intravenous respiratory fluoroquinolones alone or a combination of intravenous azithromycin plus intravenous β-lactam.

► Patients in the ICU who do not have risk factors for *Pseudomonas aeruginosa* infection can be treated with intravenous β-lactam plus either intravenous azithromycin or intravenous respiratory fluoroquinolone.

► Those patients at risk for *P. aeruginosa* infection can be treated with intravenous antipseudomonal β-lactam plus intravenous antipseudomonal fluoroquinolone. Another option is treatment with intravenous antipseudomonal β-lactam plus intravenous aminoglycoside plus either intravenous azithromycin or intravenous nonpseudomonal fluoroquinolone.

Most patients will become clinically stable within 3-7 days. Treatment is recommended for a minimum of 5-7 days and for at least 48 hours after reaching clinical stability, Dr. DeLisser said. Longer treatment—between 10 and 14 days—may be required for patients with infections caused by *Staphylococcus aureus*, *P. aeruginosa*, or Legionella species.

Patients can be discharged once their vital signs have been stable for a 24-hour period, they are able to take oral antibiotics, they can maintain adequate nutrition and hydration on their own, their mental status is back to baseline, and they have no other active clinical or psychosocial issues.

If the pneumonia does not resolve, consider microbial resistance to the initial antimicrobial regimen, suppurative complications like an abscess or empyema, or subsequent development of nosocomial pneumonia, Dr. DeLisser said. ■

Low-Dose, Whole-Virion Vaccine For Avian Flu Looks Promising

BY ROBERT FINN
San Francisco Bureau

A whole-virion vaccine for the H5N1 avian influenza virus produces acceptable levels of immunity even at low doses, researchers found in a preliminary study.

Developed at the Sinovac Biotech Co. in Beijing, the vaccine appears to be effective when delivered in two 10-mcg doses 28 days apart. A different whole-virion vaccine required two 90-mcg doses, and a split-virion vaccine required two 30-mcg doses.

Supplies of a higher-dose, split-virion vaccine would be limited to about 225 million people, far lower than worldwide demand in a pandemic.

Given current manufacturing constraints, supplies of that split-virion vaccine would be limited to about 225 million people, far lower than worldwide demand in the event of an avian flu pandemic. A much greater number of people could be treated if the new dosage-sparing vaccine is found effective in larger clinical trials.

Dr. Jiangtao Lin of the Chinese-Japanese Friendship Hospital, Beijing, and colleagues reported on a placebo-controlled, double-blind, phase I trial of 120 volunteers aged 18-60 years. The participants were given either two injections of placebo or two injections of an inactivated, whole-virion influenza A (H5N1) vaccine at four doses between 1.25 mcg and 10 mcg. Aluminum hydroxide was added as an adjuvant, a practice previously shown to reduce the dosage needed to produce immunogenicity.

All four doses produced immune responses, but the 10-mcg dose produced 78% seropositivity, which was significantly higher than that produced by the other doses (Lancet 2006 Sept. 7 [Epub DOI:10.1016/S0140-6736(06)69294-5]).

No serious adverse events were reported at any dose level up to 56 days after the first injection. Local and systemic reactions were all rated as mild and transient. Pain at the injection site in the deltoid muscle was more frequently reported in the vaccine groups than in the placebo group, but there were no significant differences in systemic reactions, the most common of which were fever, headache, myalgia, and nausea.

In an editorial, Dr. Iain Stephenson, of the Leicester (England) Royal Infirmary, noted that vaccination will be central to any response to an avian flu pandemic (Lancet 2006 Sept. 7 [Epub DOI:10.1016/ S0140-6736(06)69340-9]). The 1918 influenza pandemic—also derived from an avian virus—caused up to 50 million deaths.

Dr. Stephenson said that the dose-sparing approach described by Dr. Lin could be crucial for obtaining a global supply of the vaccine.

He also noted that earlier whole-virion vaccines were associated with febrile reactions, especially in children. Although larger clinical trials will certainly be necessary before widespread immunization, Dr. Stephenson suggested that a modest amount of reactogenicity might be acceptable in the face of the threat of a worldwide pandemic.

The authors of the study acknowledged that funding came from the Sinovac Biotech Co., which had a role in both study design and monitoring. They said the company had no role in data collection or in the writing of the report. ■

Empiric Antibiotic Choice Overshadows Blood Cultures In Averting Pneumonia Deaths

BY TIMOTHY F. KIRN
Sacramento Bureau

SEATTLE — Of the recommended measures taken in hospital treatment of pneumonia, only the administration of the proper, empiric antibiotic appears to make any difference in patient mortality. Culturing blood does not. And prompt antibiotic treatment does not, according to a study from the Mayo Clinic presented at the annual research meeting of Academy Health.

To explore the actual impact of the three principles of care that are thought to have the most influence in pneumonia treatment, the Mayo Clinic researchers analyzed data from a random selection of patients admitted with a diagnosis of pneumonia to the clinic's Rochester, Minn., facility between July 2004 and June 2005, a total of 395 patients. They excluded those who received comfort care only, those transferred from other institutions, and those who did not receive antibiotic treatment within 36 hours.

Since some patients were treated with adherence to all three of those principles—and some only one, two, or none—the patients could be compared for outcome, said Monica VanSuch, of the clinic's division of health care policy and research, in a poster presentation.

The study found that when patients were not treated with the type of antibiotic that guidelines suggest for empiric treatment, they were more likely to have a longer hospital stay (relative risk 1.71) and a decreased chance of survival (relative risk 3.26). They also tended to be less likely to be readmitted after discharge, though that finding was not statistically significant.

Whether the patient received an antibiotic within 4 hours, or within 8 hours, of admission did not make a difference in any of the outcomes. Neither did blood culturing.

The finding that the promptness of antibiotic treatment did not impact outcome is surprising, and might reflect a bias of the study instead of truth, Ms. VanSuch said in an interview. Only a small group of the patients did not receive the proper, empiric antibiotic (35 of the 395 patients), and the importance of that proper antibiotic might be so great that it overwhelmed the influence of prompt treatment in the analysis. ■