

# Low-Dose Steroids Cut Mortality in Septic Shock

BY BRUCE JANCIN  
Denver Bureau

LISBON — After decades of controversy, a consensus has emerged that corticosteroids provide major benefits in patients with severe sepsis or septic shock, Dr. Djillali Annane said at the 12th International Congress on Infectious Diseases.

The benefits, as demonstrated in multiple randomized placebo-controlled trials, are improved 28-day mortality, shorter shock duration, improved hemodynamics, reduced organ dysfunction, and less systemic inflammation.

It should be emphasized that these benefits accrue only with low-dose corticosteroids administered for at least 5 days, and only in the sizable patient subsets having adrenal insufficiency or refractory septic shock, said Dr. Annane of the University of Versailles, France.

Much of the lengthy controversy in this field was the result of great heterogeneity in clinical trials, particularly those before 1992. For example, steroids for septic shock

fell into disfavor in the 1980s and 1990s because multiple trials before 1992 showed no benefit because the negative studies used short-course, high-dose corticosteroids, Dr. Annane explained.

Today, with the benefit of hindsight, no evidence supports the use of such therapy, he said at the congress, which was sponsored by the International Society for Infectious Diseases.

Dr. Annane was first author of a 2006 Cochrane Collaboration systematic review of corticosteroids for treatment of severe sepsis and septic shock (Cochrane Library ISSN 1464-780X).

In 15 randomized trials of more than 2,000 children and adults included in the analysis, steroid therapy didn't change 28-day all-cause mortality. But the results varied according to dosing strategy. In nine trials of replacement-dose corticosteroids—

the equivalent of hydrocortisone at 200-300 mg/day intravenously for 5 days or longer—there was a highly significant 20% reduction in the relative risk of 28-day mortality,

**The benefits accrue only in patients with adrenal insufficiency or refractory septic shock.**

DR. ANNANE

Several new trials have been published since completion of the Cochrane review. An updated analysis incorporating these studies shows a significant 12% reduction in all-cause mortality with steroid therapy when all trials are considered. For only those involving low-dose therapy for at least 5 days, the relative risk reduction in mortality is now an even more robust 23%.

The Cochrane review found no significant increase in rates of superinfection, GI

bleeding, or hyperglycemia linked to steroid therapy, but Dr. Annane found those trial results inconsistent with real-world practice. These adverse events are common with steroids, he cautioned, adding that only patients likely to obtain therapeutic benefit should be exposed to such risks.

That's why American College of Critical Care Medicine guidelines, which were coauthored by Dr. Annane, recommend low-dose steroids only in septic shock that is refractory or accompanied by adrenal insufficiency, as defined by an increase in cortisol of 9 mcg/dL or less in response to a corticotropin test (Crit. Care Med. 2004;32:1928-48).

The rationale behind low-dose steroid therapy in septic shock is that systemic inflammation is a hallmark of sepsis. Inflammatory cytokines suppress the hypothalamic-adrenal-pituitary axis, resulting in adrenal insufficiency in about half of septic shock patients. Steroids induce immune modulation through numerous cellular mechanisms of action. Indications for steroids in septic shock may soon rise. ■



## 'Switch Therapy' Is Deemed Safe in Elderly Patients With Pneumonia

BY JANE SALODOF  
MACNEIL  
Southwest Bureau

SAN DIEGO — Advanced age by itself should not be a barrier to switching a patient with community-acquired pneumonia from intravenous to oral antimicrobial therapy soon after the patient shows clinical improvement, Dr. Paulo Rossi said in a poster presentation at the International Conference of the American Thoracic Society.

An observational study of 2,648 adult patients at 40 hospitals in 13 countries showed that, regardless of age, about two-thirds were discharged within 24 hours of meeting the criteria for "switch therapy." Of 372 patients aged 85 years or older, 65% were discharged in this early time frame, as were

68% of 1,161 patients aged 65-84 years and 72% of 1,115 patients aged 18-64 years. No deaths occurred in the youngest group after switch therapy, and mortality was low in the older groups: 9 deaths (1.6%) of the 554 switch-therapy patients in the 65-84 age group and 2 deaths (1.2%) of the 164 patients in the oldest cohort.

The study shows that frail elderly patients with community-acquired pneumonia (CAP) can handle switch therapy, said Dr. Rossi of S. Maria della Misericordia Hospital in Udine, Italy.

He and his coinvestigators reviewed records of CAP patients who were entered into the Community-Acquired Pneumonia Organization database from June 2001 to May 2005. The database includes hospitals in the United States, and the study coordinator was based at the University of Louisville (Ky.).

The study relied on American Thoracic Society guidelines for time to switch therapy. Patients had to meet four criteria to be considered candidates for a switch: improvement in cough and shortness of breath; at least 8 hours without a fever; leukocytosis reduced by at least 10% from the previous day; and "tolerating oral intake with adequate gastrointestinal absorption." The investigators con-

sidered patients to be candidates for hospital discharge after they met the above criteria for oral therapy, a diagnostic work-up was completed, any comorbidity was treated, and social needs were met. Any discharge within 24 hours of the patient's meeting the criteria for switch therapy was considered an early discharge.

Of the oldest patients, 90% were classified as being at high risk—a much larger proportion than in any other age group. Nonetheless, 51.6% met the criteria for switch therapy on or before the 6th day of hospitalization. In the middle group of patients, aged 65-84 years, 54.2% passed this goal by the 5th day. In the youngest group, 57.1% were ready to switch on or before the 4th day.

The proportions of patients who met the criteria for switch therapy declined with age, going from 71% of the youngest group to 63% of the middle group to 56% of the oldest group. However, the proportion of patients who were switched was similar across groups: 80% of the under-65 patients, 76% of the middle group, and 78% of those aged 85 and up.

After therapy was switched, the oldest patients were the least likely to require reestablishment of intravenous antibiotics. Just 2 (1.2%) of the 164 patients in the oldest group had to be switched back, compared with 20 (3.6%) of the 554 patients in the middle group and 46 (7.4%) of the 621 patients in the youngest group. ■

## Telephone Outreach Boosts Pneumococcal Shot Rates

CHICAGO — Telephone outreach is relatively inexpensive and successful at raising pneumococcal vaccination rates, Dr. Adrienne Mims said at the annual meeting of the American Geriatrics Society.

Dr. Mims presented data from an outpatient study conducted in five managed care clinics that compared a telephone intervention with a control condition. A total of 2,395 healthy patients over the age of 65 years and 3,711 patients aged 18 years and older with diabetes, coronary artery disease, or congestive heart failure were randomized to either the telephone-intervention group or the control group.

These populations are targeted for universal immunization, according to practice guidelines. There were 3,053 patients in each of arm of the study, which was funded by the Centers for Disease Control and Prevention.

Patients in the intervention arm were sent a letter explaining the study and received up to four calls during daytime and evening hours from outreach nurses who explained the shot was free, available at a nurse visit, and could be scheduled if desired. The nurses also asked why the patient had not been immunized, then gave information tailored to the reason mentioned by the participant. Most commonly, patients said "they didn't know or the doctor

didn't tell me," said Dr. Mims of Kaiser Permanente, Atlanta.

At the 6-month follow-up, 489 patients (16%) in the intervention group were vaccinated, compared with 211 (7%) in the control group. Overall, patients who received the telephone intervention were 2.3 times more likely to be vaccinated than were patients in the control group, reported Dr. Mims and associates.

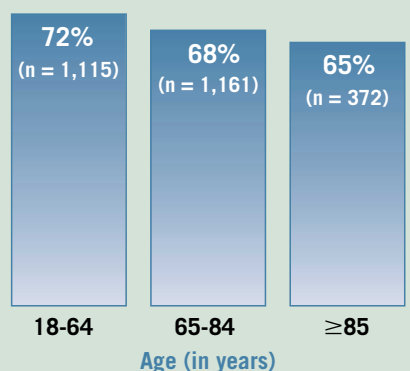
The elderly were more likely to be vaccinated than were younger, chronically ill patients (17% vs. 16%), but immunization rates improved significantly in both populations. Most patients received their pneumococcal vaccine within 3 months of the outreach.

The cost of the phone calls was \$41,520, or \$147 per additional patient vaccinated, compared with the cost of an office visit or of hospitalization for treating pneumococcal disease, which averages about \$5,000.

Kaiser Permanente in Atlanta had previously tried several initiatives to improve pneumococcal immunization rates, such as patient outreach letters and clinic posters. Those efforts significantly improved immunization rates, to 60% in seniors and about 40%-45% in younger, chronically ill patients. But the target set by the Healthy People 2010 initiative of the Department of Health and Human Services is 90%.

—Patrice Wendling

### CAP Patients Released <1 Day After Switch to Oral Antibiotics



Source: Dr. Rossi