Evaluating Combination Therapy in Community-Acquired Pneumonia

To the Editor:

It is unclear whether the study by Brown et al (May 2003) 

either "confirms the value of dual therapy," or that previous investigations have "verified" the benefits of combination therapy in community-acquired pneumonia (CAP). While the accompanying editorial points out that many of the studies of combination therapy in CAP are retrospective, another issue complicating interpretation of these studies is their observational study design. Observational studies are, by their nature, not randomized. Clinicians decisions to administer combinations of antimicrobials are not random events, but based on factors relevant to the individual patient. Therefore, many factors other than antimicrobial therapy could have accounted for the results. Large numbers of patients do not mitigate the issues with lack of randomization, and increasing sample size does not strengthen the conclusions of the study. A trial on hormone replacement therapy (HRT) in women illustrates the issues with observational data. Numerous observational trials showed a benefit of HRT, but recent randomized placebo-controlled trials did not validate such benefits, and indeed, showed potential worse outcomes in women receiving HRT.

Administration of multiple antimicrobials for CAP also could result in potential worse outcomes in the form of increased drug-related adverse events. The study by Brown et al does not report on adverse events of combination compared to monotherapy. These data are necessary in order to balance the potential benefits with the potential for increased adverse events of combination therapy.

Several prospective trials have not shown a benefit of combination therapy in CAP. The use of combination therapy in these prospective trials has been discretionary, which results in the same biases due to lack of randomization. These results raise the question, however, of whether there is a true benefit of combination therapy in CAP. Observational, retrospective trials raise interesting hypotheses about the potential benefits of combination therapy in CAP, but do not provide us with definitive answers. We need randomized, prospective blinded trials comparing the safety and efficacy of monotherapy to combination therapy in CAP to answer these important questions. It is unclear whether the data at this time support recommendations of combination therapy for all patients with CAP.

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Bird-Years as Well as Pack-Years

To the Editor:

Although pulmonary physicians can make a difference for their patients, it is not often that they can cure their diseases. Asthma, COPD, and most interstitial lung diseases are chronic conditions that patients often have to endure for a lifetime. Patients usually have to be satisfied that their pulmonary symptoms can be "controlled" but not totally alleviated with the help of their pulmonologist.

It should excite us as pulmonologists that we can actually "cure" a disease that is potentially lethal. There is one such curable interstitial lung disease whose diagnosis does not even depend on sophisticated testing but is simply established by taking an adequate medical history. Failure to ask certain easy-to-answer questions can have catastrophic consequences to the point that the patient may acquire end-stage pulmonary fibrosis and respiratory failure.

The disease is hypersensitivity pneumonitis, and the questions involve exposure to organic aerosols, especially exposure to birds. Because the risk of hypersensitivity pneumonitis depends on the patient's immune response and the degree and duration of exposure, we determine the patient's "bird-years." Simply put, bird-years are determined by the number of birds and the years of bird exposure, as is done for pack-years of cigarette smoking. For example, if a person has four birds for 5 years or one bird for 20 years, they would both have accumulated 20 bird-years. Obviously not all bird exposures are identical. Cleaning of bird cages and walking through enclosed cages as pigeon breeders do would imply extremely high exposure to bird bioaerosols. Questions about whether the patient "owns pets" are not specific enough, as many patients do not consider birds as pets. Questions also need to be posed concerning exposure to water sources including humidifiers, hot tubs, and moldy environments.

Hypersensitivity pneumonitis can present as acute illness with rapid onset of fever, chills, dyspnea, and alveolar infiltrates on the chest radiograph. The disease may also present subacutely and resemble chronic bronchitis. Finally there is a chronic form of the disease in which dyspnea, lung restriction, and pulmonary fibrosis develop insidiously.

The combination of restriction on pulmonary function tests, interstitial lung disease observed on high-resolution CT scans, and positive precipitins to avian or mold antigens strongly suggests the presence of hypersensitivity pneumonitis. BAL shows an average of 60% lymphocytes, with up to 90% in acute cases. However, without eliciting the appropriate medical