Feature Article

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11 Myths about Pneumonia in Emergency Medicine

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(Note: Dr. Martin has no proprietary interest in any specific medication or pharmaceutical concern - Ed.)

1. PNEUMONIA IS A RADIOLOGIC DIAGNOSIS

Clinical exam cannot reliably confirm the presence or absence of pneumonia, so the literature requires the presence of a new or worsening infiltrate to substantiate the diagnosis. This may be the best current gold standard, but it is not good enough. Experienced radiologists agree on the presence of an infiltrate only 80% of the time (1,2). Elderly patients, in particular, may not mount enough of a leukocytic response to manifest an infiltrate. This is particularly a problem in that elderly patients are less likely to present with signs suggestive of pneumonia. They will more often present with change in functional status, decreased mentation, increased falls or loss of appetite (3). Only 30% of elderly patients with pneumonia have a fever. Elderly patients are precisely those most likely to die from pneumonia, and these are the patients in whom neither the clinical evaluation nor the x-ray may detect pneumonia. Younger patients without co-morbidities can sometimes be diagnosed without x ray, as is often the case in out-patient offices. There is evidence to suggest that the need for x-ray can be screened by vital-sign abnormalities (4). However, in the patient with clinical presentation suggestive of pneumonia, there is inconsistent correlation between clinical findings and radiographic infiltrates. Of note, if present, certain x-ray findings (multilobar infiltrates, effusion) are associated with higher mortality.

2. MORTALITY RATES OF PNEUMONIA ARE IMPROVING

Mortality rates for pneumonia were reported as being 20-40% before the discovery of antibiotics. There was dramatic improvement with the use of antibiotics, but the death rate has actually been climbing for the past 20 years (5). This probably reflects an increased pool of susceptible elderly patients. The surge in mortality has been primarily in those patients over the age of 75. Changing patterns of bacterial resistance may be a factor, though there is little direct evidence to support this. Newer, stronger, broader spectrum antibiotics do not appear to be the complete answer to improving our care of pneumonia patients.

3. FOR HOSPITALIZED PATIENTS, ANTIBIOTICS SHOULD BE GIVEN WITHIN 8 HOURS OF PRESENTATION

The 1997 Pneumonia Outcomes Research Team (PORT) study of process of care in pneumonia of over 15,000 elderly patients concluded, "antibiotic administration within 8 hours of hospital arrival was associated with significantly lower 30-day mortality" (6). Unfortunately, this statement has been quoted extensively in subsequent articles and is used in numerous quality assurance studies. The Keystone Peer Review Organization, for instance, grades all hospitals in Pennsylvania on whether or not pneumonia patients receive antibiotics within 8 hours. While the PORT study did, in fact, show increasing

mortality when antibiotics were administered after eight hours, it also showed progressively lower mortality when antibiotics were administered sooner. It was really only when antibiotics were administered within 2 hours that there was a sharply improved outcome.

There are two phase changes in pneumonia. The first is that from healthy lung to infected lung, which can be effectively treated. The second phase change is from localized parenchymal disease to systemic inflammatory response. This transition needs to be prevented, as treatment is not very effective. As many as 80% of pneumonia patients in septic shock will die (7). There should be a door-to-needle time with antibiotics, ideally less than two hours. No patient should leave the ED with the diagnosis of pneumonia without having received the initial dose of antibiotic. There is evidence to suggest that administration of antibiotics in the ED not only decreases mortality but also results in decreased length-of-stay, with resultant cost savings (8). Predictors for delayed antibiotic administration include patients presenting without fever and respiratory signs, but also direct admissions. Patients who bypass the ED often do not get time-appropriate treatment (9).

4. BLOOD CULTURES ARE NECESSARY FOR THE HOSPITALIZED PATIENT

Many of us draw blood cultures for admitted patients with pneumonia, as recommended by both the American Thoracic Society and the Infectious Disease Society of America (10,11). The cost is less than 1% of the hospital bill, and culture results will help to direct specific therapy and track resistance patterns. However, only 10% of blood cultures in pneumonia are positive, and less than 10% of the positive results mandate a change in therapy. Considering that some patients die within 24 hours and that cultures do not reveal the number of mixed infections, less than 1% of blood cultures will actually have an impact on treatment. A study of 517 patients with community-acquired pneumonia (CAP) at Emory showed that only 7/517 had management changed by culture result (12). A study of 93 cases of severe CAP in a German hospital could not demonstrate any impact at all of blood cultures (13). Of 939 pediatric patients with pneumonia at the University of Pittsburgh, not one had a treatment change from blood cultures (14). At a minimum charge of $100 for a set of blood cultures, it might cost in the range of $10,000 to get one treatment-altering result. The PORT study found lower in-patient mortality in patients who had blood cultures drawn, but this did not change when the blood cultures were drawn post-treatment, suggesting that blood cultures may have been a surrogate marker for an overall more aggressive approach to management.

5. SPECIFIC THERAPY YIELDS BETTER RESULTS THAN EMPIRIC THERAPY

Possibly, but there is no evidence for this. Retrospective studies actually show lower mortality with empiric therapy than when a specific organism is identified (15). This is an on-going controversy between the American Thoracic Society and the Infectious Disease Society of America. It is more of a philosophical argument, the practical issue being whether or not to routinely obtain sputum gram stains in the ED. While gram stains are inexpensive, they are of low yield, have poor sensitivity and specificity and may delay treatment. There is no evidence that obtaining them improves outcomes.

6. QUINOLONES ARE THE AGENTS OF CHOICE FOR OUT-PATIENT CAP

Quinolones are attractive choices for out-patient pneumonia, as they are effective against both atypical agents and penicillin-resistant *Streptococcus pneumoniae*. In point of fact, we may be overly concerned about drug-resistant strep pneumo. The CDC Drug-Resistant *Streptococcus Pneumoniae* Therapeutic Working Group reports, "We estimate that 0.14% to 1.9% of out-patients with pneumonia have pneumococcal infections resistant enough to warrant alternative therapy." Drug resistance in strep pneumonia is not based upon beta-lactamase resistance, but rather the lack of a protein-receptor on the cell wall so that these organisms can still be overwhelmed by high enough concentrations of penicillin. The CDC specifically recommends doxycycline or macrolide for out-patient pneumonia, not quinolones (20). For the patient unable to take doxycycline or macrolides, the recommendation is for cefuroxime or amoxicillin-clavulanate. The ATS guidelines, while somewhat dated, also recommend macrolide or doxycycline. IDSA guidelines recommend doxycycline, macrolide or quinolone, but specifically state that some authorities prefer macrolides or doxycycline for patients aged <50 years who have no comorbidities.

Of course, the mortality rate in out-patient pneumonia is less than 1%, so it is difficult to obtain outcomes research to tell us if there is really a difference in results. There are not enough studies to evaluate admission rates after out-patient treatment failures, or other parameters such as return to work or length of convalescence. That these recommendations are not really evidence-based can be seen by the recommendations of the British Thoracic Society, which had access to the same evidence and came up with quite different recommendations for out-patient pneumonia (amoxicillin or amoxicillin-clavulanate) (21). The BTS felt that out-patient therapy should be focus on strep pneumonia.

The antibiotic armamentarium for out-patients is, for the moment, relatively straightforward. Drugs such as trimethoprim-sulfa, first-generation cephalosporins and penicillin are no longer recommended because of high resistance or poor coverage of atypical organisms. Doxycycline (alone among the tetracyclines) and macrolides are agents of choice. Because of their high tissue penetration and intracellular activity, they are effective against the atypical agents.

Quinolones have overly broad coverage with increasing gram-negative resistance but are still preferred for patients with high risk of drug-resistant strep pneumoniae. These patients include the very old, the immune-compromised patients, possibly the alcoholic patients, and, in particular, anyone who has had beta-lactam therapy in the previous three months. Of course, the landscape of antibiotic choices is about to change significantly. There will soon be whole new classes of agents from which to choose, including streptogramins, ketolids, oxazolidinones and glycopeptides. Before long, physicians will look back on 2001 as a time of beguilingly simple choices in terms of antibiotic therapy.

For in-patients, ceftriaxone and cefotaxime along with levofloxacin provide excellent coverage of strep pneumonia. Levofloxacin is considered acceptable monotherapy for non-ICU patients, while the beta-lactams might need additional coverage of a macrolide. Azithromycin is listed as an acceptable monotherapy by IDSA, but there are concerns that low serum levels might not prevent sepsis. Levofloxacin is not good monotherapy for ICU patients because of its lack of activity against anaerobes. ICU patients, particularly those with structural lung disease, on ventilators, or steroid-dependent nursing home patients, need aminoglycoside coverage for pseudomonas.

7. STREP PNEUMONIAE IS THE MOST COMMON ORGANISM IN PATIENTS HOSPITALIZED WITH CAP

Maybe. Almost all studies show that the most common organism is "unknown." In those patients in whom the etiology can be identified, strep pneumoniae is found 15-60% of the time (8). Both chlamydia and mycoplasma have been found in up to 30% each. The bacterial mass surges and fluctuates, so it should not be surprising that studies done in a particular year in a particular location will yield differing prevalences of pathogens. Mixed infections are said to be less than 5% of hospitalized cases, but that may reflect the limits of our technology. One meticulous study, in Finland, showed that 41% of patients with confirmed strep pneumonia also had chlamydia, and these patients with mixed infection had a length of stay that was twice as long (22). Additional pathogens not previously recognized as causing pneumonia continue to be identified, including group A streptococcus, hantavirus, enterococcus, acenitobacter, rhodococcus, aeromonas, bacilllus cereus and eikenella (23). The fact is, we usually do not know what we are treating. Microbiologists tell us that we have identified only 1/2 of 1 per cent of extant bacteria. It is not reasonable to think that we have identified all the causative organisms of pneumonia.

8. ANAEROBES ARE NOT SIGNIFICANT IN CAP

They are not significant because we do not test for them. When specifically looked for in transtracheal aspirates, anaerobes are found in as many as 30% of patients (24). Alcoholics, I.V. drug users, patients with poor dental hygiene and, of course, nursing home patients, should be covered for anaerobes. For out-patients who are at risk of anaerobic infection, amoxicillin-clavulanate is recommended. Hospitalized patients may need coverage with clindamycin or metronidazole.

9. PATIENTS WITH PNEUMONIA NEED OXYGEN

All right, maybe it's a reach to call this a myth. A medical myth "plays to our hearts, to get us to do things for which logic or evidence is lacking" (16). The logic for administering oxygen to patients with pneumonia is certainly there. Hypoxia correlates with poor outcome, and the need for oxygen is an important determining factor in the need for hospitalization (17). Administering oxygen to patients with pneumonia is a universally standard practice. In spite of the logic, there is a lack of evidence for this practice. In fact, there is indirect evidence that it does harm. The PORT study showed increased mortality in patients in whom oxygen level was assessed. This finding (based on a study of over 15,000 patients) could possibly relate to spectrum bias. That is, we can postulate that the sicker patients were the ones who had their oxygen levels measured, and therefore they had poorer outcomes. The authors themselves dismissed their own finding, saying, "It is not clinically plausible that oxygenation assessments are causally related to an increased 30-day mortality" (6).

If we are to practice evidence-based medicine, we can't pick and choose the evidence with which we agree. We cannot assume that those patients who had oxygen levels assessed were sicker, but that those who received antibiotics sooner were not sicker. It is actually possible that oxygen therapy does some harm. After all, oxygen toxicity is not a new concept. Textbooks tell us that high levels of alveolar oxygen "cause severe alveolar epithelial and vascular endothelial damage, leading to perivascular and alveolar edema" (18). Animal models of aspiration pneumonia exhibit distinct pathological changes (increased pulmonary edema, decreased lung compliance, decreased type II alveolar cell surfactant synthesis) with 50% oxygen, with increased mortality (19). There is likely little toxicity with low flow oxygen by nasal canula, so it is not recommended at this time to withhold oxygen. There may be a tradeoff, as with cardiac patients, who might need oxygen to prevent non-pulmonary complications. If, in fact, there is worsened outcome for patients who receive oxygen therapy, it could be due to factors other than the oxygen itself. The patient on the nasal canula is tethered to the wall, leading to decreased ambulation, increased incidence of DVT, poorer mobilization of secretions and other deconditioning factors. It is intuitive that hypoxic patients need oxygen, but further study of the effect of oxygen on infected and non-infected lung tissue is needed.

10. PHYSICIANS CAN ACCURATELY ESTIMATE THE PROBABILITY OF MORTALITY IN PNEUMONIA

No, we can't. Hospital-based physicians, at least, consistently over-estimate the likelihood of death. The Pneumonia Severity Index, derived from a cohort of over 50,000 patients hospitalized with pneumonia, divides patients into five classes, according to age, co-morbidities, physical findings and diagnostic studies. Classes I and II have very low mortalities and can be treated as out-patients. Patients with Pneumonia Severity Index of 3 includes males over the age of 70, females over the age of 80, and younger patients with co-morbidities (25). This category of patients, usually hospitalized, has a mortality rate of 2.6%. Of course, these figures are derived from in-patients, so we do not know if the mortality rate would have been higher (or lower) if these patients had been sent home. We are hospitalizing some patients with low risk of death for whom little, if anything, is accomplished by their hospitalization. There is a lack of evidence for some of our admission decisions. Third-party payors are starting to poke into this gap in our knowledge.

The role of rapid-treatment/observation beds to identify those patients at risk of sepsis from pneumonia is not yet defined. Milliman-Robertson, the national utilization-review organization whose guidelines have been adopted by a number of managed care organizations, recommends a period of out-patient observation for pneumonia patients who do not need ICU level of care and who do not have significant co-morbidities. Twelve hours of observation, it is thought, will determine the need for admission. Since patients who are hospitalized with pneumonia have a length of stay on average of 6 days, it is not clear that such an observation period will reliably identify those who may become septic. There may even be a risk that PSI Class III patients can be placed at bed rest and given fluids and anti-pyretics and see an improvement in vital signs. It is conceivable that they might then be re-classified as Class II patients, without actually altering the underlying progression of disease. There is a need for outcome-based studies of such patients, as has been done for chest-pain patients.

11. ED PHYSICIANS NEED THE DIRECTION OF OTHER SPECIALTY SOCIETIES TO TELL US HOW TO TREAT PNEUMONIA

Not hardly. While the ATS, IDSA and CDC guidelines are important and helpful, they are not evidence-based. ED physicians actually see most of the sick patients with pneumonia. We initiate antibiotics and make the hospitalization decisions. 3% of office patients with lower respiratory symptoms have pneumonia, as opposed to 28% of ED patients (26). 45% of patients with pneumonia are seen in the ED (27). While at tertiary care hospitals, infectious disease specialists are often involved in the management of pneumonia patients, a study in Utah found that ID specialists saw less than 1% of the pneumonia patients in that state (27). The diagnosis and treatment of pneumonia is about to go through huge changes, as new diagnostic studies (serologies, antigen-specific tests, DNA probes) and new treatments (new classes of antibiotics and new treatments for sepsis) become available. Hospitalization decisions and the use of rapid treatment units need foundations of evidence that do not now exist. Unfortunately, for this ubiquitous and lethal disease, there is very, very little work published in the emergency literature. ED physicians need to take the initiative in defining the management of pneumonia in the coming era.

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