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The overdiagnosis of pneumonia

PNEUMONIA WAS ONCE CONSIDERED the "old man's friend," but in the modern world, has it become the physician's?

See related editorial, page 619

The definition of pneumonia has increasingly been stretched, and physicians occasionally make the diagnosis without canonical signs or symptoms, or even with negative chest radiography. The hallmark of overdiagnosis is identifying illness for which treatment is not needed or is not helpful, and some cases of pneumonia likely fit this description. Empirical evidence over the last 3 decades shows a sustained increase in the diagnosis of pneumonia, but little evidence of a decrease in the rates of pneumonia morbidity and mortality. The central problem with pneumonia is one common to many diagnoses, such as pulmonary embolism, coronary artery disease, and infectious conditions—diagnostic criteria remain divorced from outcomes data. Linking the two has the potential to improve the evidence base of medicine.

We are hospitalizing more patients with 'pneumonia,' but this hasn't improved outcomes beyond global trends in mortality rates

Like many long-recognized diagnoses, pneumonia lacks a standardized definition. Most physicians believe that although fever, cough, sputum production, dyspnea, and pleurisy are hallmark symptoms, confirmatory chest radiography is needed to cement the diagnosis.[1] But what if a patient has only a fever, cough, and infiltrate? What if the infiltrate is not visible on radiography, but only on computed tomography (CT)? And what if the patient has a cough but is afebrile and has nonspecific findings on CT?

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THE RATE OF HOSPITAL ADMISSIONS FOR PNEUMONIA IS RISING

In current clinical practice, any or all of the above cases are called pneumonia. The pneumonia label, once applied, justifies the use of antibiotics, which patients or physicians may overtly desire. One prospective observational study of six hospitals found that 21% of patients admitted with pneumonia and 43% of those treated as outpatients had negative chest radiographs.[2] Empirical evidence suggests that the incidence of these "soft" diagnoses may be growing in number.

In the United States, hospitalizations with discharge codes listing pneumonia increased 20% from the late 1980s to the early 2000s.[3] The rates of hospitalization for the 10 other most frequent causes of admission did not change significantly over this same period, suggesting a selective increase in hospital admissions for pneumonia.

This focus on pneumonia would be justified if it led to a proportionate benefit for pneumonia outcomes. However, in the same data set, the risk of death from pneumonia did not improve more than that from the other 10 common conditions—all improved similarly—and the rate of discharge from the hospital to a long-term care facility was unchanged. We are hospitalizing more patients with pneumonia, but this has not improved outcomes beyond global trends in mortality.

Data from England suggest that overdiagnosis may be a worldwide phenomenon. Between 1997 and 2005, hospitalization rates in England for pneumonia, adjusted for age, increased 34% from 1.48 to 1.98 per 1,000 persons.[4] The 30-day in-hospital death rate for pneumonia remained about the same over this period. In the absence of a paradigm-shifting

technology, one that would alter hospitalization practices, or an environmental cause of increased incidence—and with pneumonia there has been neither—the most likely explanation for these documented trends is that hospitals are admitting patients with pneumonia that is less severe.

Finally, data from the 2000s that at first seemed to reverse the trend of increasing hospitalizations for pneumonia have been reanalyzed to account for alternative coding.[5] For instance, a pneumonia admission may be coded with respiratory failure as the primary diagnosis and pneumonia as the secondary diagnosis. Examining data from large populations from 2002 to 2009, and correcting as such, shows that the incidence of pneumonia has reached a plateau or has declined only slightly from the elevated rates of the early 2000s. The death rate remains unchanged.

PNEUMONIA: A DIAGNOSIS IN THE EYE OF THE BEHOLDER

Apparently, when it comes to pneumonia, the diagnosis is in the eye of the beholder. Different physicians have different thresholds for applying the label. In the wake of quality efforts to ensure that emergency physicians deliver antibiotics within 4 hours, emergency doctors have been shown to have worse accuracy in diagnosing pneumonia.[1] But worse accuracy compared with what standard?

In an investigation by Welker et al,[1] the standard definition of pneumonia was based on the one favored by the US Food and Drug Administration for clinical trials. Patients had to have all of the following:

- A new or increasing infiltrate on radiography or CT
- A fever, an elevated white blood cell count, or a shift to immature polymorphonuclear leukocytes
- At least two signs or symptoms of the condition (eg, cough, dyspnea, egophany).

Although this definition is reasonable and ensures homogeneity in clinical trials, it is not steadfastly adhered to in clinical practice and has never been shown to cleanly delineate a population that benefits from antibiotics.

Another challenge to devising a perfect definition of pneumonia is the lack of a pathologic gold standard. Based on a review of 17,340 Medicare patients hospitalized for community-acquired pneumonia, microbial confirmation is often of little assistance, and a probable pathogen is identified in only 7.6% of cases.[6]

RATES OF OUTPATIENT DIAGNOSIS ARE LIKELY SIMILAR

Thus far, we have examined trends in inpatient diagnosis but not those of outpatient diagnosis. There is no well-done observational study that documents outpatient trends, but there is little reason to suppose the trends are different. Risk-scoring systems in pneumonia, such as the PORT[7] and the CURB-65,[8] have been designed to decrease unnecessary inpatient admissions, but they do not lend clarity to the diagnosis itself.

The central problem with pneumonia, as with many long-recognized clinical conditions, is that the diagnosis is separated from the treatment. In other words, although physicians are confident that antibiotics benefit patients who have what Sir William Osler would have called pneumonia (elevated white blood cell count, fever, cough, dyspnea, pleurisy, egophany, lobular infiltrate), we don't know whether the treatment benefits patients whose pneumonia would have been unrecognizable decades ago (with cough, low-grade fever, and infiltrate on CT alone). Improvements in imaging may exacerbate the problem. In this sense, pneumonia exists on a spectrum, as do many medical diagnoses. Not all cases are equally severe, and some may not deserve to be labeled as pneumonia.

A rational clinical trials agenda may end most of the uncertainty regarding pneumonia

No randomized trial has compared antibiotics against supportive care in pneumonia, and, likely, no such trial is needed for clear cases. However, with the growing number of soft diagnoses, randomized trials are desperately needed to delineate where harms outweigh benefits, and where the fuzzy edge of the pneumonia diagnosis must end. And as is always the case with studies that challenge a standard of care, null results should prompt further trials.

WELL-DESIGNED TRIALS COULD END THE UNCERTAINTY

In the next few years, clinical trials, rationally planned, may end most of the uncertainty regarding pneumonia.

Existing observational data may be used to identify groups of patients who, in today's world, are diagnosed with pneumonia but who do exceptionally well (eg, younger patients with fewer comorbidities, who present with low-grade fever but no signs of consolidation on physical examination, and with dubious results on chest radiography). These are patients for whom equipoise exists, and randomized trials should compare a strategy of antibiotics with a strategy of best supportive care. Trials should be powered for patient-centered outcomes, such as the duration and the complications of illness. The death rate should be scrupulously recorded.

Patients whose pneumonia would have been unrecognizable decades ago should be another target population for the trials I propose.

In a short time, pneumonia may become synonymous with a set of factors for lung infection that predict who will benefit from antibiotics, and who can be safely followed. Already, we are moving toward this standard in other diseases.[9] For pulmonary embolism, ongoing trials are testing if anticoagulation can be safely omitted in patients with subsegmental clots (clinicaltrials.gov identifier NCT01455818). Such trials are, at last, translating old diagnoses into the language of evidence-based medicine.

For patients with pneumonia who are not hospitalized, the current outpatient therapy is based on data from studies that show a low rate of failure with empiric treatment based on consideration of the common pathogens for this condition, with few patients subsequently requiring hospitalization. Today, this reasoning is inadequate. The basis for any therapy must be proven benefit for patients with a defined condition compared with a lesser strategy. Data already demonstrate that a short course of antibiotics is no worse than a long course for many hospitalized and outpatients with pneumonia,[10,11] but many other patients may require no treatment at all. The time has come to find out. ■

The views and opinions of the author do not necessarily reflect those of the organizations with which he is affiliated.

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CME ANSWERS

Answers to the credit tests on page 668 of this issue

Antidepressants 1D 2B
Hepatocellular carcinoma 1D 2C
Jugular venous pressure 1A 2C
Antisynthetase syndrome 1D 2B