Is sputum evaluation useful for patients with community-acquired pneumonia?

**EVIDENCE-BASED ANSWER**
No high-quality studies specifically address the utility of sputum Gram stain or culture in the assessment or treatment of community-acquired pneumonia (CAP) or nursing home–acquired pneumonia (NHAP). The available evidence suggests that analysis of the sputum adds little to the care or outcomes of patients with CAP (strength of recommendation [SOR]: B, inconsistent results from non-randomized case control, case series, and a systematic review of disease-oriented evidence).

**EVIDENCE SUMMARY**
Studies investigating the role of sputum Gram stain and culture are both difficult to interpret and compare. The difficulty in obtaining an adequate sputum sample, variation in preparation, levels of skill in interpretation, and the lack of a gold standard for the microbiologic diagnosis of pneumonia all contribute to these difficulties.¹

The sole meta-analysis identified 12 studies that met 17 specified study criteria regarding the use of sputum Gram stain for patients with community-acquired pneumococcal pneumonia.¹ Sample sizes ranged from 16 to 404; reference standards were most frequently sputum culture but also included culture of transtracheal and bronchial aspirates. Results revealed that patients with community-acquired pneumococcal pneumonia were able to produce a valid sputum sample (≥20 neutrophils, <10 squamous epithelial cells per low-power field) 70% of the time; the sensitivity of sputum Gram stain ranged from 15% to 69% (when reviewed by a lab technician); and specificity ranged from 11% to 100%.

Because of the heterogeneity of test characteristics, interpreter skill levels, study populations, and reference standards among the studies in this meta-analysis, no single estimate of Gram stain sensitivity or specificity could be reached. Similarly, information regarding the sensitivity and specificity of sputum culture is lacking. Small studies (n=13–85) using blood culture, transthoracic aspirate, or transtracheal aspirate as reference standards in untreated cases of definite pneumococcal pneumonia demonstrate sensitivities ranging from 36% to 100%.² There are no reliable data regarding the specificity of sputum culture.

Recent nonrandomized studies and case series have called into question the role of sputum analysis in CAP. In a case-control study of 605 patients hospitalized with CAP diagnosed by chest x-ray and either cough, chest pain, auscultatory findings, or leukocytosis, establishing an etiologic diagnosis did not influence the choice of antibiotic therapy, length of hospital stay, or mortality.³ Of the 482 patients who had microbiological diagnostics performed (Mycoplasma pneumoniae serology, respiratory virus serology, blood culture, or sputum culture), only 132 (27%) had a presumptive etiologic diagnosis made. Therapy was narrowed or focused in 49 of the 132 (37%) patients who had a presumptive etiologic diagnosis, while 84 of the 350 (24%) without a presumptive diagnosis had their therapy narrowed (P>.05). There was no difference in in-hospital changes of therapy, the proportion of new regimens having a narrower antimicrobial spectrum than the initial one, length of hospital stay, death in hospital, or death within 3 months after admission.

A prospective study of 74 patients suggested sputum studies had little use in a highly selected population aged <65 years with nonsevere, uncomplicated CAP and no comorbidities. In the 74 patients who produced a valid sputum sample, Gram stain failed to identify the causative agent in any patient (sensitivity 0%), and sputum cultures identified a pathogen in only 4 patients (sensitivity 5%). All patients responded similarly and, even with the identification of a pathogen in 4 patients, there were no changes in initial empiric antibiotics.⁴ In a retrospective case series, 19 of 54 (35%) patients with SCAP did not respond to initial empiric antibiotics and had a change in their
antibiotic regimen. There was no difference in mortality between the group that had empiric antibiotic change (11 patients) and the group that had a change based on sputum culture results (3 patients) (relative risk reduction = -0.14; 95% confidence interval, -0.47 to 0.12). While these studies suggest the need for re-evaluation of routine sputum analysis, the strength of their conclusions are weakened by lack of randomization, small sample size, inadequate blinding, and lack of control group comparison.

Demographic evidence and nonrandomized trials suggest that patients with CAP who have increased risk of infection from multiple-resistant bacteria, such as patients from long-term care facilities, are a unique population that might need to be evaluated differently. However, the only evidence available regarding the utility of either sputum Gram stain or culture for patients with NHAP derives from expert opinion. These authors suggest that determining a causative diagnosis of pneumonia in this population is desirable and postulate that sputum examination would permit recognition of multiply resistant organisms that are being isolated with increasing frequency in long-term care facilities. However, the same authors acknowledge that the elderly are often too weak or too confused to provide adequate sputum specimens, resulting in a low diagnostic yield, and no data demonstrate that sputum evaluation favorably influences the outcome of pneumonia in these patient populations.

**RECOMMENDATIONS FROM OTHERS**

The Infectious Disease Society of America (IDSA) and the Canadian Infectious Disease Society/Canadian Thoracic Society (CIDS/CTS) recommend routine sputum analysis for all patients with CAP or NHAP, while the American Thoracic Society (ATS) recommends performing sputum analysis only if a drug-resistant pathogen or an organism not covered by usual empiric therapy is suspected. For those with CAP or NHAP treated as outpatients, the ATS, the IDSA, and the CIDS/CTS recommend microbiological testing only if drug-resistant bacteria or an organism not covered by usual empiric therapy is suspected.

**REFERENCES**

What is the best regimen for newly diagnosed hypertension?

- **EVIDENCE-BASED ANSWER**
  Low-dose thiazide diuretics (eg, hydrochlorothiazide 12.5 to 25 mg/d) are the best first-line pharmacotherapy for treating uncomplicated hypertension (strength of recommendation [SOR]: A, based on randomized trials [RCTs] and 1 meta-analysis). Alternate first-line agents include angiotensin-converting enzyme (ACE) inhibitors, beta blockers, and calcium channel blockers (SOR: A, based on RCTs).

- **EVIDENCE SUMMARY**
  Three landmark placebo-controlled studies have established that thiazide diuretic–based treatment reduces morbidity and mortality among patients with hypertension.1-3 Based on these data, thiazide diuretic therapy is considered the gold-standard treatment for uncomplicated hypertension.

  Several other clinical trials have subsequently compared the effect of thiazide diuretics with that of other antihypertensive agents (beta-blockers, calcium channel blockers, and alpha-blockers) on patient-oriented outcomes. These were analyzed in a recent meta-analysis of 42 clinical trials that included 192,478 patients randomized to 7 treatment strategies including placebo.4 Results from the largest antihypertensive clinical trial, the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALL-HAT), were included in this meta-analysis.5 Comparative results are depicted in the Table. Although these data showed no differences between drug therapies in total and cardiovascular disease mortality, low-dose diuretics reduced certain cardio-vascular endpoints (ie, heart failure, stroke, cardiovascular disease events) more than other drug therapies.

  Angiotensin receptor blockers (ARBs) have not been compared with thiazide diuretics in a trial. Two long-term trials have compared an ARB to other types of drug therapy: losartan vs atenolol in the Losartan Intervention for Endpoint Reduction (LIFE) trial,6 and valsartan vs amlodipine in the Valsartan Antihypertensive Long-Term Use Evaluation (VALUE) trial.7 In the LIFE trial, the primary composite endpoint of cardiovascular death, myocardial infarction, and stroke was less with losartan than atenolol (23.8 vs 27.9 events per 1000 patient-years, losartan and atenolol, respectively; number needed to treat=243 people-years, P=.021).6 However, in the VALUE trial, the primary endpoint of time to cardiac event was not different between valsartan and amlodipine (25.5 vs 24.7 events per 1000 patient-years, valsartan and amlodipine, respectively; P=.49).7

- **RECOMMENDATIONS FROM OTHERS**
  The Seventh Report of the Joint National Committee (JNC7) recommended thiazide diuretics as preferred initial agents in uncomplicated hypertension.8 The European Society of Hypertension/European Society Cardiology recommended either a diuretic, beta-blocker, calcium channel blocker, ACE inhibitor, or ARB for initial therapy stating that blood pressure control to recommended values via any agent is more important than the type of agent used.9 Both guidelines identified other antihypertensives that may be used in addition to or in place of thiazide diuretics for compelling indications, such as heart failure, diabetes, high-risk cardiovascular disease, chronic kidney disease, post-myocardial infarction, and secondary stroke prevention.