such as those who are comatose. This article serves as a proof of concept for improving VAP prevention strategies. It is consistent with the practice of antimicrobial prophylaxis in high-risk surgical procedures. I believe that a prospective randomized clinical trial would confirm these findings and increase the degree of evidence. Meanwhile, it is an important contribution to reduce antibiotic exposure in the ICU. This strategy is rational because bacterial burden is high within the first hours of pneumonia onset, whereas persistent inflammatory response is independent of the eradication of organisms. We propose to adjust therapy in a patient-based approach because some episodes, such as the presence of ARDS or methicillin-resistant *Staphylococcus aureus* pneumonia have a delayed pattern of hypoxemia resolution.⁸

An important challenge is how to design strategies to overcome barriers to stewardship.¹³ The three most important issues are strategic, operational, and support measures based on education. Efforts on these three issues are required.

In summary, the data reported by Vallés et al¹² support a new paradigm of prophylaxis, which significantly contributes to reduced exposure to antibiotics in patients who are critically ill. This is important because shortened periods of antibiotic exposure are crucial in stewardship programs of antibiotic prescription.

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When Should Specific Occupational Challenge Tests Be Performed?

Occupational asthma (OA) resulting from sensitization at work has implications for the patient that include not only medical management but also changes at work to completely avoid further exposure to the causal agent and optimize asthma outcome.¹⁻⁴ Occasionally, the workplace can remove the causative sensitizing agent, but often, this is not considered feasible. In a large company, the affected worker may be moved to a different location, to a job with no further exposure. However, in many cases, especially within smaller companies, OA results in the worker leaving the workplace. Despite support from workers' compensation systems, OA has been associated with a significant negative psychosocioeconomic impact.^{5,6}

Therefore, correctly diagnosing OA is important. An incorrect diagnosis of OA can lead to unnecessary job changes and restrictions, loss of job satisfaction, and economic loss. Although some symptomatic improvement in asthma severity may be seen if work exposure had been aggravating or exacerbating the worker's

condition, only true OA may clear after removal from further exposure to the sensitizer.

For these reasons, guidelines and consensus statements in North America (including the American College of Chest Physicians [ACCP] statement on the diagnosis and management of work-related asthma¹) and in Europe have emphasized the importance of detailed evaluation for workers with suspected OA. This usually is suspected from a history of asthma starting during a work period, with asthma symptoms worse during work and improved on weekends or holidays away from work.^{1,4} Diagnostic steps include objectively confirming asthma; immunologic testing, when feasible, to assess specific sensitization; serial recording of peak expiratory flow rates, symptoms and medication needs during work and off-work periods; and recording of changes in the severity of nonspecific airway responsiveness (and percentages of induced sputum inflammatory cells, when feasible) during work vs nonwork periods. Individually, none of these tests is diagnostic, and although a combination of these tests is commonly used in the diagnosis or exclusion of OA, the reference standard remains the specific occupational challenge test.

Should all patients with suspected OA undergo a specific occupational challenge when this option is available? In some regions, occupational challenge is the usual practice for diagnosis, such as in Quebec, Canada; Leuven, Belgium; Barcelona, Spain; and several other centers in Europe. Conversely, outside Quebec, most North American centers do not use specific challenges for confirmation of OA, and the ACCP consensus statement advises a relatively limited use of the test.¹

Specific occupational challenges require specialized facilities to generate exposures to the suspected sensitizing agent that can be monitored either in a separately ventilated chamber or by using equipment that delivers a known concentration of the agent to the patient without risking exposure to others in the laboratory. Measurement of exposures can require specialized equipment and personnel. Asthma should be stable before the tests, and usually patients are asked to withhold use of bronchodilators prior to testing to prevent masking of the response. A placebo exposure day is advised with a similar-appearing exposure as is used on the active exposure days. Because responses can occur as isolated late responses starting 4 to 8 h after the onset of exposure, especially with low-molecular-weight (LMW) sensitizers, monitoring of spirometry compared with preexposure results is advised for several hours after each increase in exposure dose; therefore, the test may take several days to complete.⁷ In some patients, the test may result only in increased airway hyperresponsiveness or number of airway inflammatory cells as assessed

by induced sputum, and these tests have been recommended at least at baseline and after the highest challenge day to exclude OA or occupational eosinophilic bronchitis.^{8,9} Therefore, the tests can be technically difficult, time consuming, and expensive. In addition, there can be false-positive and false-negative results.¹⁰

However, an additional reason for physicians not using occupational challenge tests is safety. A physician must be present for the tests, and the patient must be monitored for several hours after each exposure. Even with careful attention to detail, there is the potential for a severe asthmatic response, with a fall in FEV₁ of $\geq 50\%$ having been reported.¹¹ The report by Vandenplas and colleagues¹² in this issue of *CHEST* (see page 1261) is an important analysis of the frequency and characteristics of adverse responses during specific occupational challenge tests. The authors have extensive experience with specific challenge tests, and the findings are likely to represent those from centers using similar methods. Twenty percent of the 335 consecutive subjects with positive challenge results required treatment with a short-acting β_2 -agonist (SABA) during the test (median maximum FEV₁ fall from baseline, 40%). Moderate responses (requiring repeat SABA use over 24 h posttest) and severe responses (requiring repeat SABA use and oral or IV corticosteroids) occurred in 12% and 3% of subjects, respectively. SABA and corticosteroid treatment was needed more often among those being challenged with an LMW sensitizing agent perhaps because of the abbreviated protocol of increased exposures within the same day. Limiting the daily number of LMW exposure doses (ideally to one per day), therefore, may reduce risk. The only other predictive factor was pretest daily doses of inhaled steroids in the medium to high range, suggesting more severe baseline asthma (although there was no association with prechallenge need for ED visits or for systemic corticosteroids).

The findings of Vandenplas et al¹² emphasize the caution needed in occupational challenge testing, especially when using LMW (chemical) sensitizers. Particularly concerning in this series was that one subject had a life-threatening response after exposure to only 30 s of methylene diphenyl diisocyanate at a low concentration of 5 parts per billion. Therefore, although the authors considered the rate of severe responses to be small (3%), such responses require careful consideration when discussing risks with patients. This report should allow for more-informed discussions with patients on the risks and benefits of occupational challenge testing when deciding whether a specific diagnostic challenge should be performed. It also supports the approach advised in the ACCP consensus statement¹ of performing specific challenges in specialized centers only when the diagnosis remains

in doubt despite other investigations and when indications for the test outweigh the risks.

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A New Application for CPAP in Preventing Atrial Fibrillation

In this issue of *CHEST* (see page 1277), Bazan and colleagues¹ examine the link between obstructive sleep apnea (OSA) and recurrent atrial arrhythmias

in patients undergoing catheter ablation for the treatment of typical right atrial flutter (AF). All subjects underwent a sleep-study evaluation after a cavotricuspid isthmus ablation; 82% had OSA. CPAP was initiated in those with the highest apnea-hypopnea index (AHI), involving about one-half of the patients. Atrial fibrillation (AFib) was noted in 38% of patients during follow-up in the first year postablation, with less than one-half being “new” diagnoses of AFib. The authors demonstrated that CPAP treatment of OSA did not reduce the overall AFib rate but was associated with lower rates of new-onset AFib in these patients postablation.

This study raises as many questions as it answers. The principal finding is intriguing; namely, a significantly reduced incidence of new AFib following catheter ablation in patients without antecedent AFib who are placed on CPAP. This suggests that the mechanism by which OSA promotes AFib can be inhibited or prevented by CPAP. However, if the anatomic/electrical substrate for AFib exists already in the setting of OSA, CPAP may not be sufficient to prevent recurrent AF.

There are a variety of potential mechanisms for this beneficial effect of CPAP, including a reduction in pulmonary arterial and right atrial pressures, and different effects of pharmacologic treatment or conducting system anatomy, as suggested in the article. OSA is also associated with systemic inflammation with elevations in tumor necrosis factor- α and IL-6 levels.^{2,3} The ability of CPAP to reduce local inflammation³ or other factors related to repeated hypoxemia and hypercarbia might also play a role.⁴ OSA is associated with sleep disruption and nocturnal arousals, which contribute to elevated sympathetic activation.^{5,6} This autonomic stimulation promotes atrial arrhythmias, including AFib, and CPAP reduces the sleep deprivation, thereby lowering the degree of sympathetic activation and incidence of subsequent arrhythmias.^{7,8} Any of these, or combinations, may be responsible for the prophylactic benefit of CPAP in patients without pre-existing AFib.

It is interesting to consider how these findings should be used in the prevention of AFib. The major observation, that CPAP prevents occurrence, but not recurrence, of AFib following AF ablation in OSA, suggests greater vigilance is warranted in screening subjects being considered for AF ablation. Effective use of CPAP in those with moderate to severe OSA would not only protect against daytime somnolence and lead to improvements in BP, stroke risk, and functional capacity in heart failure but would appear from these data to also reduce the risk of developing AFib.

However, there are also several limitations. This was not a randomized evaluation of CPAP as a treatment strategy; initiation of CPAP was at the discretion of the treating physicians and occurred selectively in the