Principles of Appropriate Antibiotic Use: Acute Pharyngitis

TO THE EDITOR: To reduce unwarranted antibiotic therapy, the American College of Physicians–American Society of Internal Medicine proposed new guidelines for the diagnosis and treatment of group A streptococcal pharyngitis in adults (1). These guidelines depart from recommendations of other expert committees (2) by endorsing antibiotic treatment of group A streptococcal pharyngitis on the basis of typical clinical criteria alone. For clinical manifestations that are not fully expressed, laboratory confirmation is restricted to rapid antigen diagnostic tests. Throat cultures are relegated to special studies.

As the authors acknowledge, prospective studies will be necessary to prove that these guidelines will reduce the overuse of antibiotics for pharyngitis. Such studies would be most appropriate before dispensing with throat cultures, the most reliable negative predictors of group A streptococcal throat infection by which antibiotic therapy can safely be eschewed. Recently improved rapid antigen diagnostic tests may also be adequate negative predictors, but we badly need positive tests that differentiate strains of group A streptococcus that cause asymptomatic throat colonization or relatively mild pharyngitis from encapsulated virulent strains that cause more serious infections and rheumatic fever (3).

Understanding of the genetic expression of virulence factors of group A streptococcus, particularly that of the hyaluronate capsule (4), is rapidly evolving. Although large mucoid colonies of group A streptococcus usually reveal such dangerous encapsulated clones on blood agar cultures, fewer clinical laboratories are now likely to offer throat cultures at all, especially to note colonial morphology of group A streptococcus. Moreover, these guidelines may encourage practitioners to believe what most authorities do not, namely that group A streptococcal pharyngitis can be dependably diagnosed by clinical criteria alone. During recent outbreaks of rheumatic fever in the United States, the “mucoid” culprits were recognized only retrospectively by intense efforts of special investigative teams, after the dangerous bugs had been widely disseminated (5). These dangerous strains still lurk, and others may be transported by airplane from developing countries.

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Principles of Judicious Antibiotic Use: Acute Rhinosinusitis

TO THE EDITOR: According to the background paper by Hickner and colleagues on antibiotic use in acute rhinosinusitis (1), “The greatest barrier to efficient antibiotic treatment of acute bacterial rhinosinusitis is lack of a simple and accurate diagnostic test.” This and the accompanying guideline (2) do not mention the possible utility of the Gram stain. Dr. Bartlett, a coauthor of the Hickner paper, has advocated use of the sputum Gram stain in patients with community-acquired pneumonia (3). Since the gold standard for bacterial rhinosinusitis is more than 10^5 colony-forming units per mL of bacteria in purulent sinus fluid (1), a Gram stain of nasal secretions showing many neutrophils and bacteria should be predictive. The authors’ opinions regarding the available data or the need for further study of Gram stains in rhinosinusitis would be welcome.

Of the diagnostic studies listed in Hickner and colleagues’ Table, only one used a microbiological criterion to define bacterial sinusitis, and only as a secondary end point. The other studies relied on imaging studies that imperfectly predict purulent sinusitis, let alone bacterial infection. However, the text describes these studies as “...reports attempting to identify signs and symptoms specific to acute bacterial rhinosinusitis.” No evidence is provided to show that radiographic findings predict culture-positive bacterial sinusitis rather than simply purulent sinusitis. Furthermore, Hickner and colleagues do not address the predictive value for a bacterial cause of purulent sinus fluid, other than mentioning that three fourths of purulent sinus aspirates yielded positive bacterial cultures in one study. Two other accompanying guidelines (4, 5) emphasize that purulent rhinorrhea has a low predictive value for a bacterial cause. These observations further underscore the need for a simple and accurate test to specifically identify bacterial infection among patients with clinically or radiographically suspected rhinosinusitis. The humble Gram stain deserves consideration.

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Letters

Principles of Judicious Antibiotic Use: Nonspecific Upper Respiratory Tract Infections

TO THE EDITOR: In their position papers regarding acute upper respiratory tract infections, Gonzales and colleagues (1) and Snow and coworkers (2) state that physicians commonly interpret purulent sputum and purulent nasal secretions as evidence of bacterial infection and therefore as an indication for antibiotic therapy. The authors juxtapose this observation with the statement that purulent secretions do not actually predict a bacterial cause or a response to antibiotic therapy (1, 2). It is unfortunate, in view of the importance of persuading physicians to modify their entrenched erroneous ideas, that this assertion, which was repeated three times in each paper, was of persuading physicians to modify their entrenched erroneous ideas, that this assertion, which was repeated three times in each paper, was not better supported with specific data.

Physicians are unlikely to be swayed by expert opinion in the absence of convincing evidence. However, Gonzales and colleagues provided no data on the microbiological correlates of purulent rhinorrhea or sputum and minimal data regarding the efficacy of antibiotic therapy in patients with these symptoms. Their Table provided an excellent opportunity to lay out the evidence but shows response data for patients with purulent sputum from only one trial, even though the text shows that another of the trials in the Table addressed this issue. Moreover, two additional trials whose titles seem highly relevant (3, 4) are mentioned only in the text of the article and not in the paragraph that corresponds with the Table (1). Specific data in support of Gonzales and colleagues’ Principle 3 would increase the “persuasion power” of these two position papers and would greatly assist those of us who advocate for restraint in the use of antibiotics to treat upper respiratory infections.

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IN RESPONSE: Dr. Johnson believes that evidence relating to the cause of purulent secretions associated with acute respiratory tract infections and evidence of response to antibiotic therapy should have been more prominently displayed in our paper. We agree that purulent secretions are a poor predictor of microbial cause and response to antibiotic therapy and that better communication of this fact will aid in improving physician prescribing practices. Our Table was intended to display randomized, controlled trials of nonspecific upper respiratory tract infections and was not intended to reflect the evidence for Principle 3. The other studies Dr. Johnson mentions (1, 2) were not displayed in the Table because they enrolled patients with the diagnosis of “acute bronchitis.” Nonetheless, we referred to these studies in our paper because they also address the question of purulence as an indication for antibiotic therapy. We believe the text accompanying Principle 3 reflects the best evidence from studies in adults. We would be interested in additional studies to help bolster this recommendation.

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Physicians and Joint Negotiations

TO THE EDITOR: The American College of Physicians–American Society of Internal Medicine (ACP–ASIM) position paper on physicians and joint negotiations (1) is thoughtful and intriguing but fails to deal explicitly with some of the most critical aspects of this issue. For example, in discussing the possibility of strikes by physicians, the position paper states “. . . withholding needed medical services from an individual patient for the greater good of future patients is never justified.” This statement reflects an ideal that many of us have clung to, but perhaps it needs to be modified in a world of limited resources for medical treatment in which tradeoffs are essential. I wonder if the position paper should state explicitly whether it is ever justified for managed care organizations to withhold needed services from individual patients. The weak link in the position statement is the word needed. Physicians, patients, and health maintenance orga-
nizations have been battling over this definition for years, and the lack of detail in the College’s position paper reduces its utility.

In discussing the issues suitable for joint negotiation, the position paper states that physicians should have the right to negotiate jointly over payment policies only when such policies “are unrealistic or unfair” and are therefore “likely to adversely affect access and quality.” The problem lies in who gets to define unrealistic or unfair or adversely. The position paper states explicitly that performance targets should be negotiable, but such targets are tied so closely to pay that it seems virtually meaningless to negotiate over one and not the other; a more relaxed performance target could simply be offset by lower pay.

I applaud the College for bringing these issues into the forefront of discussion, but it seems clear to me that we have a long way to go before we come to a satisfactory rationalization that joins modern business ethics with traditional medical ethics.

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TO THE EDITOR: The ACP–ASIM position paper on joint negotiations (1) fails to address a key question: Who should be the negotiator for our patients? The critical relationship is between patients and physicians. Physicians should negotiate with patients, not with insurers. Of course, we cannot negotiate our fees one patient at a time. Health care has changed. The community must share the costs of medical care to make new, beneficial technologies affordable; hence the need for an insurance mechanism. For-profit insurance corporations have taken on part of this community role, but their legal and fiduciary duty is not to patients but to stockholders. Should insurers take the place of our patients at the negotiating table? Is this done with the consent of our patients? Our professional, ethical, and moral obligations are to our patients, and this will temper the tone and quality of any negotiations. To protect patients’ interests, any negotiations between insurers and physicians should be open and publicly accountable. It would probably be wise to include impartial patient representatives in any negotiations as well.

As good physicians, we should note the natural history of the disease that has created our painful condition. Although joint negotiations may be a balm for the festering wound of marketplace medicine, they are not the cure. The more radical but effective remedy is a national health insurance program. In Germany, a single public negotiation exists among hundreds of “sickness funds” and all physicians, resulting in one set of benefits and fees that applies to nearly everyone. However, the involvement of multiple insurers will never have the efficiency of a single public payer with tax-based financing. In light of the increasing number of uninsured persons and the sharp rise in health care costs, it appears that marketplace medicine has become the disease it was supposed to cure. A national health insurance program is the most effective and efficient remedy, not joint negotiations with for-profit insurers.

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1. Physicians and joint negotiations. American College of Physicians–American Society of Internal Medicine. Ann Intern Med. 2001;134(9 Pt 1):787-92. [PMID: 11329239]

IN RESPONSE: Dr. Glass highlights some of the thorny issues that ACP–ASIM struggled with in developing its position paper. The College recognized that it will be a major challenge for physicians to fulfill their individual and collective responsibilities for professionalism in the face of organized activity to negotiate collectively with managed care organizations and other third-party payers. The College felt strongly that as members of the medical profession, physicians have ethical responsibilities and obligations to patients that must limit the scope of negotiations and restrict physicians from engaging in activities, such as strikes or other organized actions, that
Thalidomide and Venous Thrombosis

TO THE EDITOR: Thalidomide is an antiangiogenic drug used in cancer therapy. On the basis of encouraging preliminary results, we performed a phase II trial of thalidomide (Laphal, Allauch, France) in 40 patients with metastatic renal-cell carcinoma. The starting dosage of thalidomide was 400 mg/d, with titration to 800 mg/d after 6 or 12 weeks if progressive disease occurred and to 1200 mg/d if disease still progressed with 800 mg/d.

Nine of the 40 patients developed venous thrombosis 4 to 12 weeks after starting thalidomide treatment. Thromboses occurred in the legs in 5 patients and in the vena cava in 4 patients. Pulmonary embolism occurred in 4 patients. No patients stopped taking thalidomide because of thrombosis, and anticoagulants alleviated that condition in most cases.

Metastatic cancer is associated with an increased incidence of venous thrombosis. However, our observed incidence is much higher than that reported in phase II trials in renal cancer. For instance, in a recent phase II study with similar patients, Stadler and colleagues (1) reported four cases of venous thrombosis in 35 patients.

The link between venous thrombosis and thalidomide needs to be reassessed. For example, Flageul and colleagues (2) recently reported three cases of venous thrombosis in patients with lupus erythematosus who were given thalidomide. We hypothesize that this high incidence of thrombosis is due to thalidomide. We have explored hemostasis in 15 consecutive patients treated with thalidomide and have found no obvious explanation (3). Although the relation between thalidomide and venous thrombosis is not certain, we believe it is necessary to draw more attention to this possible adverse event and to conduct additional studies.

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Correction: Mixed Hepatocellular–Cholestatic Liver Injury after Pioglitazone Therapy

In a recent summary for patients (1) that accompanied the paper by May and colleagues (2), the section “What are the implications of the study?” should read “Liver damage may occur in patients who take pioglitazone. Patients who are taking this drug should have periodic blood tests to check liver function. If patients develop new symptoms while taking pioglitazone, they should contact their doctors.”

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