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Bacteriology of the Upper Respiratory Tract: What Is Important?

SUMMARY

Oropharyngeal and nasopharyngeal swabs are commonly collected from patients with a variety of respiratory infections. Unfortunately, the significance of potential pathogens in such specimens is clouded by the prevalence of these organisms in asymptomatic patients and in patients with non-bacterial upper respiratory tract illnesses. Specimens from the oro-and nasopharynx seldom predict the flora in other parts of the respiratory tract, and empiric antibiotic therapy for infections such as acute otitis media, sinusitis, and pneumonia is usually inevitable. The author of this article reviews the bacteriology of the upper respiratory tract and makes recommendations for diagnosis and treatment. (*Can Fam Physician* 1988; 34:2155–2159.)

RÉSUMÉ

Quelle que soit l'infection respiratoire que présente le patient, on lui impose routinièrement des prélèvements oropharyngés et nasapharyngés. Malheureusement, la valeur significative des agents pathogènes retrouvés dans ces spécimens est altérée par la prévalence de ces organismes chez des patients asymptomatiques et chez des patients souffrant de maladies non bactériennes des voies respiratoires supérieures. Les spécimens provenant de l'oropharynx et du nasopharynx permettent difficilement de prédire la flore présente dans les autres parties des voies respiratoires et, habituellement, l'empirisme de l'antibiothérapie devient presque inévitable dans des infections comme l'otite moyenne, la sinusite et la pneumonie. L'auteur révise la flore bactérienne des voies aériennes supérieures et propose des recommandations diagnostiques et thérapeutiques.

Key words: bacteriology, upper respiratory tract, antibiotic therapy

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UPPER RESPIRATORY infections (URIS) are a common problem in the practice of community practitioners.[1] Although many of the pathogens are viral, a bacterial etiology is commonly sought because of the potential for successful treatment by means of antibiotics. Throat and nasopharyngeal specimens are therefore frequently taken for diagnostic purposes. Although beta-hemolytic Group A streptococci (Streptococcus pyogenes) are routinely sought in these specimens, less common bacterial pathogens including Mycoplasma pneumoniae, Neisseria gonorrheae, Corynebacterium diphtheriae, and Corynebacterium hemolyticum (Arcanobacterium hemolyticum) may require special transport, culture media, and provision of relevant information or specific requests to the laboratory. Nasopharyngeal specimens are useful for detecting Bordetella pertussis in association with acute lower respiratory tract disease and are also employed occasionally to determine carrier states.

Nose and throat cultures are, however, also commonly employed by community practitioners, with the understanding that they may give information about infection elsewhere in the respiratory tract. Bacteria with the potential for causing systemic disease, such as Streptococcus pneumoniae, Hemophilus influenzae, Staphylococcus aureus, and Branhamella catarrhalis, are commonly cultured from both throat and nasopharyngeal specimens and yet are often part of the normal flora. Are they however, primary agents of pharyngitis? And does their presence predict disease secondary to the same organism elsewhere? Do these organisms deserve laboratory work-up in these sites? And should their presence bias treatment?

Berger and colleagues[2] have recently examined the attitudes of a group of Canadian physicians towards the importance of certain bacteria as primary etiologic agents of pharyngitis. Although their poll included only a small subset of south-

ern Alberta physicians, it indicated that over-treating of pharyngitis was probably common. Specifically, there was a significant bias towards treating patients with pharyngitis when throat culture reports demonstrated the presence of Hemophilus sp., S. aureus, S. pneumoniae, and N. meningitidis.

Despite the large amount of resources expended Canada-wide to study antibiotic use and resistance mechanisms, these findings point to a need for study and education in the area where many antibiotic prescriptions are made: community-acquired infectious diseases, particularly pharyngitis. The laboratory work-up of these specimens and appreciation of laboratory reports are equally important. The significance of bacterial cultures from the nose and throat in respiratory disease is reviewed here, and recommendations are made for their proper use and interpretation.

Asymptomatic Carriage

Numerous studies have documented the presence of potentially systemic pathogens as normal flora of the respiratory tract. In asymptomatic adults and children, organisms including S. aureus, H. influenzae and S. pneumoniae may be cultured from throat and nasopharyngeal specimens[3-9] and high isolation rates are especially obtainable with use of selective culture media in the laboratory.[10] The incidence of isolation from these sites appears to be higher in children, especially for H. influenzae and S. pneumoniae, and prospective family studies have not demonstrated a significant seasonal variation. Carrier rates, which varied among different geographical areas, have ranged from 5%–60% for H. influenzae and S. pneumoniae. S. aureus and N. meningitidis carriage in the nasopharynx is also commonly encountered.

Pneumonia

Two studies have examined the value of upper respiratory tract cultures for predicting pathogens in acute bacterial pneumonia by simultaneously culturing upper respiratory tract and transthoracic lung-puncture specimens.[11,12] Using the lung puncture specimen as the "gold standard", both studies demonstrate the insensitivity of upper respiratory cultures for demonstrating a pathogen.

Poor specificity is also evident, as a significant number of upper respiratory specimens that were positive for a putative pathogen had either an alternate pathogen or no pathogen demonstrated in lung aspirate.

Pharyngitis

Although references to pharyngitis secondary to H. influenzae exist, the data are insufficient to implicate this organism or S. pneumoniae, S. aureus, or N. meningiditis as a primary etiologic agent of pharyngitis. Antibiotic treatment may well be motivated, in part, by the physician's and patient's desire to take active steps and by lack of unequivocal proof that these pathogens never cause illness in any patient. However, the strong balance of probability that treatment may be harmful or ineffective should be weighed against the remote possibility of doing good.

Concern on the presence of H. influenzae in throats is probably based on the high incidence of this organism in throats of patients with systemic disease.[13,14] This concern is compounded by the clinical finding of pharyngitis in a majority of patients with invasive H. influenzae illnesses.[14] It is unlikely, however, that one could prospectively confer significance to such bacteria in view of isolation rates from throat swabs in asymptomatic patients and patients with non-specific upper respiratory tract illnesses. Pharyngitis accompanying invasive H. influenzae disease might be secondary to an antecedent viral infection that could subsequently facilitate the entry of H. influenzae.

One study that examined cultures from asymptomatic patients and patients with pharyngitis did not demonstrate a significant difference in isolation rates for S. pneumoniae, staphylococci, enteric bacilli, and Neisseria sp.[15] A minor association was observed between Hemophilus sp. and sore throats, but most positive cultures for H. influenzae yielded this organism as a total of only 10%–30% of all bacteria cultured. Therefore, a predominance of H. influenzae would not have signaled significance.

In another study of predominantly upper respiratory infections that included pharyngitis patients, no differences could be demonstrated between symptomatic patients and controls for H. influenzae, H. parainfluenzae, H. parahemolyticus, S. aureus, S. pneumoniae, Neisseria sp., and enteric bacilli.[16]

In a study lacking adequate case controls, it was suggested that H. influenzae could be important in upper respiratory tract infection.[17] However, a "significant number" of Hemophilus isolates were recovered from both asymptomatic and symptomatic patients. Furthermore, the symptomatic patients in this study had "upper respiratory tract infection" that was not further defined.

A high incidence of H. influenzae in throat swabs from adults with "upper respiratory infection" and "common cold" was also recognized by Dick and colleagues.[18] Again, however, the cause and effect were poorly established.

Nasopharyngitis

Nasopharyngitis is frequently a consequence of viral infection, although bacterial nasopharyngitis is occasionally suspect when heavy growths of potential pathogens such as H. influenzae, S. pneumoniae and B. catarrhalis are isolated from nasopharyngeal swabs. The incidence of these organisms is higher in those patients with upper respiratory infection who have nasal discharge. Although less commonly isolated, the presence of S. pyogenes is considered important. Todd and colleagues have addressed the issue of bacterial nasopharyngitis with a placebo-controlled trial[19] and have demonstrated a lack of benefit in the use of an antibiotic (cephalexin). Despite the isolation of S. pneumoniae and H. influenzae from a majority of nasopharyngeal specimens, antibiotic use did not appear to reduce symptoms when compared to placebo treatment. Although some patients with nasopharyngitis may have an underlying sinusitis, it would appear at this time that nasopharyngitis alone should not prompt the physician to obtain nasopharyngeal cultures, nor should treatment be initiated if H. influenzae, S. pneumoniae, or B. catarrhalis is isolated.

Sinusitis

Poor predictive values of nasopharyngeal isolates for predicting bacterial causes of acute sinusitis have been documented.[20] In their study, Axelsson and Brorson found that only 64% of nasopharyngeal and sinus specimens yielded the same bacteria. The specificity of nasopharyngeal culture would also be a concern, in view of the incidence of potential systemic pathogens in non-specific upper respiratory infections. These findings were reaffirmed by Evans and colleagues.[21]

Otitis Media

Otitis media ranks as one of the most common clinical pediatric diagnoses for which antibiotics are prescribed. Because of the inherent difficulty in acquiring cultures from the middle ear, the nasopharyngeal specimen is occasionally obtained to provide information for predicting middle-ear pathogens. This practice has led to much study and several insights.[22-31]

The results of throat swabs correlate poorly with middle-ear isolates in patients with both acute otitis media and effusions. Colonization studies in which investigators have examined the incidence of H. influenzae type b (the type commonly associated with invasive disease) in the throat did not demonstrate a difference between well patients and those with acute otitis media. This result might be anticipated, however, since most H. influenzae isolates from the middle ear are non-typable (i.e., unencapsulated).

When routine culture methods are used, nasopharyngeal specimens also correlate poorly with middle-ear isolates. Quantitative nasopharyngeal cultures have been proposed, but they would be cumbersome for routine use. In the study carried out by Long and colleagues,[31] predominant growth of H. influenzae correlated positively with tympanocentesis isolates. However, predominant growth of S. pneumoniae was not significantly correlated with the middle-ear isolate, and the predominant growth of B. catarrhalis correlated negatively with the presence of bacterial otitis media. The value of semi-quantitative cultures has been suggested by Schwartz and colleagues,[32] who have found that predominating numbers of a single organism in nasopharyngeal specimens have a high positive predictability for determining a middle-ear pathogen. Unfortunately, the predictive value of a negative result was not high.

In summary, it would appear at this time that semi-quantitative culture of nasopharyngeal swabs for H. influenzae have limited clinical value.

Other Respiratory Infections

Several studies have examined the utility of upper respiratory tract cultures in a variety of "upper respiratory infections". In a Scandinavian study of children with chronic cough,[33] nasopharyngeal cultures of symptomatic and control children did not reveal differences for S. pneumoniae and H. influenzae, although a trend to increased colonization with B. catarrhalis was noted in the symptomatic group. In other populations with a variety of respiratory illnesses, specimens from the anterior nares, nasopharynx, and oropharynx have not been of value in discriminating symptomatic and asymptomatic patients, nor have they been of value in indicating etiology.[16,34-38] These findings have applied to organisms including S. pneumoniae, H. influenzae, and S. aureus. It is suggested, however, that many of these illnesses have a viral etiology and that there is a positive correlation between the presence of virus and the higher isolation rates for some of these bacteria.[36,37]

Viral cultures are expensive, and although the information gained is of epidemiological significance, it is seldom of value in managing individual out-patients with respiratory infections. Even in patients whose pharyngeal inflammation was a component of upper respiratory infection, oropharyngeal cultures were not of demonstrable value.

Implications for Therapy

The lack of benefit of antibiotic treatment in non-specific upper respiratory infections has long been noted[39-44] and is commonly a point of instruction in undergraduate medical education. However, the report of isolation of a potential systemic pathogen from oropharyngeal and nasopharyngeal sites can bias physicians towards prescribing treatment even when they cannot localize infection.

This review provides evidence supportive of the belief that oropharyngeal and nasopharyngeal cultures are generally of poor predictive value for determining the bacterial cause of pneumonia, sinusitis, and otitis media. Furthermore, there is insufficient evidence to implicate organisms, including H. influenzae, S. pneumoniae, S. aureus, H. parainfluenzae, and N. meningiditis, as primary agents of pharyngitis.

Table 1
Bacterial Etiology of Out-Patient Upper Respiratory Infections

	Etiology	
Disease	**Common**	**Less Common**
Pharyngitis	Streptococcus pyogenes	Corynebacterium diphtheriae[a] Neisseria gonorrheae[a] Mycoplasma pneumoniae[a] Corynebacterium (Arcanobacterium) hemolyticum[a] (? other beta-hemolytic Streptococci)
Nasopharyngitis	–	Streptococcus pyogenes
Sinusitis	Hemophilus influenzae Streptococcus pneumoniae	Branhamella catarrhalis Staphylococcus aureus anaerobes
Otitis media	Streptococcus pneumoniae Hemophilus influenzae	Branhamella catarrhalis Streptococcus pyogenes Staphylococcus aureus

a. Require special consideration for culture.

Given, as well, the high colonization rate of potentially systemic pathogens in the upper respiratory tract, I would propose the following protocol:

- culture and identify bonafide pathogens of the respiratory tract when possible;
- treat empirically those infections where specimen collection is difficult, but where the knowledge of the bacteriology in infection is established (Table 1).

These recommendations would, of course, apply to out-patients with uncomplicated illness. The perception of significant bacteria in oropharyngeal and nasopharyngeal sites might be biased in patients with underlying chronic diseases such as oncology or cystic fibrosis patients, or hospitalized patients with other diseases. Knowledge of carrier states for some organisms such as N. meningiditis in epidemics and S. aureus in recurrent staphylococcal skin infections may be useful. In addition, in a patient with recurrent or non-responding infection, diagnostic aspiration of a sinus or middle ear might be preferred to determine the specific etiologic agent.

The choice of empiric chemotherapy for sinusitis and otitis media should be directed to the more common isolates (i.e., H. influenzae and S. pneumoniae), and ampicillin or amoxicillin is often chosen. Such therapy commonly results in clinical cure. Regimens that make use of cefaclor, co-trimoxazole, sulphonamide-erythromicin, and amoxicillin-clavulanic acid have a broader or different spectrum of antimicrobial coverage that may be beneficial in some cases (e.g., beta-lactamase positive strains which are ampicillin and amoxicillin resistant) of H. influenzae and B. catarrhalis. The incidence of beta-lactamase positive H. influenzae in both hospitalized and community patients is approximately 15%–25%.[45,46] The value of screening nasopharyngeal isolates for beta-lactamase positivity to predict strains in the sinuses or middle ear that are beta-lactamase positive has not been well studied. Such screening might be of value in therapeutic failures of otitis media, where nasopharyngeal specimens have yielded predominant growths of H. influenzae, but, again, this possibility warrants further study.

Upper respiratory infections in the community are common, and therefore overuse of antibiotics could raise significantly the costs of treatment, the incidence of side-effects, and the development of antibiotic-resistant micro-organisms. A balanced approach to the interpretation of upper respiratory tract cultures and to the choice of antimicrobial chemotherapy is imperative. ■

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