Clinical Judgment Predicts Culture Results in Upper Respiratory Tract Infections

Henry R. Bloom, MD, Stephen J. Zyzanski, PhD, Lynn Kelley, CLPN, Amy Tapolyai, MBA, and Kurt C. Stange, MD, PhD

Background: **We wanted to describe the natural history, familial transmission, microbiology, and accuracy of clinical judgment of potential pathogens of respiratory tract infections in a community family practice.**

Methods: **The study was a prospective case series in which consecutive patients requesting treatment for respiratory tract infections were evaluated after nurse triage during 3 fall-spring months in a solo family practice in suburban Cleveland, Ohio. According to the physician's usual practice, patients were classified into high-, medium-, and low-risk groups for bacterial illness based on their clinical signs and symptoms. Cultures were performed and sensitivities were determined for pathogens from the infected throat, nasopharynx, conjunctiva, or other sites. Patient symptoms and well-being were scored at the initial visit and at 3, 7 and 14 days later.**

Results: **There were 111 illness episodes in 86 patients; 94% had cultures taken, of which 38% grew a potentially pathogenic bacteria, most commonly group A streptococci, *Branhamella catarrhalis* or *Staphylococcus aureus*. The physician's judgment of bacterial infection was associated ($P < .001$) with having a positive culture (sensitivity 53%, specificity 78%, positive and negative predictive values 60% and 73%, respectively). A positive culture was associated with 2 of 16 signs or symptoms: purulent discharge from any site or a red swollen eye. There was no association of treatment status with clinical outcomes during 2 weeks of follow-up observation.**

Conclusion: **Infection with a potentially pathogenic bacteria is difficult to determine solely by clinical signs and symptoms, but clinical judgment is associated with positive culture results. The effect of selective treatment of upper respiratory tract infection based on clinical signs and symptoms and patient and family culture results remains to be determined, but using clinical judgment could result in more selective antibiotic use than found in current practice patterns.(J Am Board Fam Pract 2002;15:93–100.)**

There is great concern that the widespread increase in drug-resistant bacteria results from the overuse of antibiotics to treat common infections,[1–5] particularly purulent nasopharyngitis[3] or upper respiratory tract infection. Although many studies have failed to find an association between patient outcomes and the use of antibiotics for upper respiratory tract infection,[5–7] a number of findings show a beneficial effect of antibiotics for subgroups of patients with respiratory tract infections, purulent discharge, or positive bacterial cultures.[8–16] Even so, the limited association of culture findings with clinical signs and symptoms of upper respiratory tract infection and a lack of data to determine which patients should have cultures for potentially pathogenic bacteria[6–15,17–19] have restricted clinicians' ability to use antibiotics selectively. As a result, data on current practice patterns suggest a wide variation in rates of prescription of antibiotics for upper respiratory tract infection, with prescriptions based on patient desires as much as clinical findings.[5,20,21]

In addition, the existing literature on the diagnosis and treatment of upper respiratory tract infection deals mostly with specific syndromes in one anatomic location, (eg, pharyngitis, otitis media, bronchitis), and then only within the individual patient.[22–24] Only in the case of classic pharyngitis

Submitted, revised, 31 May 2001.

From the Department of Family Medicine (HRB, SJZ, AT, KCS), Case Western Reserve University School of Medicine, Cleveland; and a private practice (LK), Cleveland. Address reprint requests to Henry R. Bloom, MD, Heights Medical Building, Suite 302, 2460 Fairmount Blvd at Cedar Rd, Cleveland Heights, OH 44106.

This project was supported by a grant awarded to Henry R. Bloom, MD, from the Ohio Academy of Family Physicians Foundation, and by a Family Practice Research Center grant from the American Academy of Family Physicians.

is culture or rapid streptococcal antigen detection recommended.[22–24] A lack of fit of the current evidence with the diverse patient populations in family practice might explain a recent study that found that only 13% of 3,163 cases of upper respiratory tract infection could be evaluated using an evidence-based protocol.[25] In addition, current evidence fails to take into account the clinical findings of diverse and often nonspecific symptoms among multiple family members who are often cared for in the same family practice. Since the studies by Dingle et al[26] many years ago, the familial transmission of infection has seldom been examined.

This study critically examines the clinical signs and symptoms, familial transmission, microbiologic characteristics, and clinical outcome of upper respiratory tract infections, based on a unique clinical protocol in use since 1985 in a solo family practice. The protocol involves initial clinical judgment,[27] frequent culture results and sensitivity testing, and a strong focus on familial transmission of illness. The study described in this article asks (1) whether a clinician's judgment is predictive of culture results and (2) what signs and symptoms predict a culture that is positive for potentially pathogenic bacteria. The study also describes (3) the clinical signs and symptoms, (4) course, and (5) microbiologic characteristics of respiratory tract infection in families being cared for at a single family practice.

Methods

This prospective case series study was conducted in a solo family practice according to its usual procedure for caring for families with respiratory tract illnesses. This clinical approach was developed by a board-certified family physician during his 25 years of practice. Consecutive nonpregnant patients older than 3 months with respiratory tract illnesses and seeking care after usual nurse telephone triage were enrolled during 3 alternating months (20 families each month) within a 6-month period (fall 1997 to spring 1998). Only patients' families, all of whose family household members were cared for in the practice, were eligible.

The physician's (HRB) clinical protocol began with a focused history and physical examination. A pharyngeal culture for group A streptococci was taken on all patients aged 1 year and older. Any patient with purulent nasal discharge (as judged by the physician or nurse) or focal infection of the ear, eye, or sinus also had a nasopharyngeal culture or culture of the purulent discharge, eg, sputum, eye discharge, wound, etc. Throat cultures were performed in the office in a standard manner.[28] All other cultures were sent to local branches of two national laboratories for organism identification and sensitivity testing.

A clinical judgment was made about the likelihood of the respiratory tract illness being viral, bacterial, or indeterminate based on the patient's clinical signs and symptoms, the prevalence of diseases in the practice patient population, and any illnesses recently experienced by members of the patient's household.

Next, the physician made a decision regarding the use of antibiotics. Patients whose condition was judged initially to be viral were observed and prescribed antibiotics only if cultures grew a respiratory tract pathogen and the patient was still ill based on telephone follow-up conversation. Patients whose cultures grew *Staphylococcus aureus*, group A streptococci, or drug-resistant *Streptococcus pneumoniae* were given treatment even if they were asymptotic. The physician's best clinical judgment was used to guide treatment for the indeterminate group.

The antibiotic prescribed initially was typically amoxicillin or another older antibiotic to which the patient was not allergic. The antibiotic was subsequently changed if the culture result showed resistance to the initially prescribed drug. Findings of group A streptococci, *Staph aureus*, or drug-resistant *Strep pneumoniae* initiated attempts to take cultures from the rest of the family or household.

Any person in the family who subsequently became ill within 2 weeks was enrolled in the study and treated according to the clinician's usual medical practice. Symptomatic family members were cared for according to the positive culture of the index patient. If 2 persons were positive for *Staph aureus* or group A streptococci, the entire household was treated, if possible.

A patient questionnaire, administered by the office nurse (LK) at the initial visit and by telephone at 3, 7 and 14 days later, assessed demographics, 16 specific respiratory tract symptoms, and global well-being rated on a five-point scale.

Descriptive statistics were calculated. The associations of specific symptoms with the clinician's clinical classification and culture results were analyzed with the chi-square statistic. Sensitivity, spec-

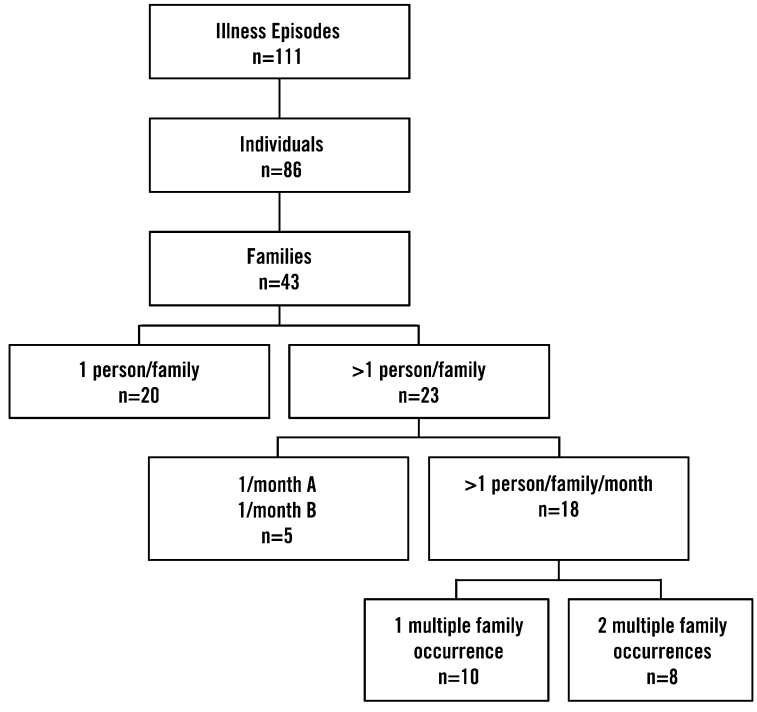

Figure 1. Respiratory illness in a solo family practice (study sample).

ificity, and positive and negative predictive values were calculated. The mean number of symptoms for the three follow-up periods was analyzed using analysis of covariance adjusted for symptoms at the first visit.

Results

The complexity of the familial manifestation of respiratory tract illness in family practice is illustrated in Figure 1. There were 111 illness episodes, representing 86 patients from 43 families.

Patient and visit characteristics are shown in Table 1. Of the 111 illness visits, 56% were index cases; the rest of the visits were for respiratory tract illnesses in family members who were seeking care within 2 weeks of the index case or who had cultures done as part of the clinical protocol. Cultures were taken in 94% of all patient visits, 38% of which were found to be positive. Of the 27 episodes in which more than 1 patient was seen from one family, 30% (8) had more than 1 culture-positive family member infected with the same organism; 15% (4) had 3 culture-positive family members infected with the same organism in one episode.

The physician's clinical classification was highly associated with a positive culture in the expected direction ($\chi^2 = 11.4$, $P = .001$). The sensitivity, specificity, and predictive values of the physician's classification of bacterial infection compared with indeterminate or viral infection are shown in Table 2.

Associations among initial clinical classification, symptoms at first visit, and culture results are dis-

Table 1. Respiratory Tract Infection and Treatment in a Family Practice (mean patient age 20.3 years).

Variable	Percent
Sex (female)	55
Index cases	56
Clinical classification	
Viral	24
Bacterial	37
Indeterminate	39
Culture	
Patient episodes cultured	94
Patient episodes with positive culture	38
Sites cultured	
Throat	91
Nasopharyngeal	43
Other	15
Treatment	
Given antibiotics initially	41
Given antibiotics only after positive culture	23
Patients on antibiotics requiring a change based on culture or sensitivity results	20

Table 2. Sensitivity, Specificity and Predictive Values of Physician Judgment of Bacterial Infection Compared with a Positive Culture.

	Culture		
Physician's Judgment	Positive	Negative	Total
Bacterial	21	14	35
Indeterminate or viral	18	51	69
Total	39	65	104

Chi square = 11.4, $P < .001$, sensitivity = 53%, specificity = 78%, positive predictive value = 60%, negative predictive value = 73%, percent correctly classified = 69%.

played in Table 3. The clinical assessment of the patient's respiratory tract illness as bacterial was significantly associated with two symptoms—purulent discharge and red or swollen eye—which also were associated with a positive culture. Although there were too few cases to be tested statistically, each time a sore or impetiginous lesion was associated with an upper respiratory tract infection, *Staph aureus* or group A streptococci were grown in a culture.

As shown in Table 4, 5 pathogens represented most of the positive cultures. Among positive cultures, 20% had more than 1 organism, including 5 cultures with *Staph aureus* and group A streptococci; 4 with *Branhamella catarrhalis* and *Strep pneumoniae*, *Staph aureus*, or group A streptococci; and 1 with *Staph aureus* and two other organisms. Of the 29 positive cultures from patients initially classified as having a bacterial infection, 8 involved mixed pathogens, as did 2 of the 15 clinically indeterminate cultures, and 0 of the 5 clinically viral cultures. During the January influenza season, only 25% of the nasopharyngeal swabs grew bacteria, whereas in November and May, 55% and 69% of nasopharyngeal swabs, respectively, grew bacterial pathogens. During the 3 study months, the number of episodes classified as indeterminate rose from 16% to 49% to 68%, respectively.

A total of 89 prescriptions were written in the 71 episodes in which patients received treatment. Of these prescriptions, 82% were written at the initial visit or after culture or sensitivity results were reported, and 18% were changed after the culture and sensitivity results were available. Adverse effects of antibiotic use occurred in 3 patients who had new rashes, 2 of which were thought to be allergic. One patient reported diarrhea.

All persons who had a positive culture were given antibiotics, whereas 38% of patients subsequently found to have a negative culture were also given antibiotics. Of the 38% who had negative

Table 3. Percentage of Association of Initial Clinical Classification and Culture Results with Symptoms at First Visit.

Symptoms	Viral (n = 27)	Bacterial (n = 41)	Indeterminate (n = 43)	Positive (n = 39)	Negative (n = 65)
Runny, stuffy nose	63	78	61	69	65
Cough	59	61	54	54	60
Sore throat	44	44	51	41	52
Other (eg, headache)	44	27	19	26	31
Purulent discharge	0	59	12†	41	17*
Fever, chills	15	29	21	28	17
Hoarseness	7	32	23	23	26
Sputum	19	22	16	15	22
Fatigue	11	12	19	10	15
Nausea, vomiting	22	12	5	15	9
Ear pain	7	12	12	10	9
Diarrhea	15	7	9	13	9
Rash	4	15	9	18	6
Swollen lymph nodes	15	7	7	8	9
Sinus pain	4	10	7	5	8
Red, swollen eye	0	20	0†	13	3‡

*$P < .01$.
†$P < .001$.
‡$P < .05$.

Table 4. Pathogen Distribution by Clinician's Classification of Infection Status.

Clinical Classification	Pathogen	Number of Positive Cultures		
		Index Case	Family Contact	Total
Bacterial (41 patient episodes)	*Staphylococcus aureus*	9*	3	12
	Group A streptococci	8	3	11
	Branhamella catarrhalis	4	7	11
	Streptococcus pneumoniae	4	1†	5
	Haemophilus influenzae	2	2	4
	Other bacteria	2	0	2
	Total	29	16	45
Indeterminate (43 patient episodes)	*Staph aureus*	0	5	5
	Group A streptococci	5	5	10
	B catarrhalis	7	5	12
	Strep pneumoniae	2	3	5
	H influenzae	1	0	1
	Total	15	18	33
Viral (27 patient episodes)	*Staph aureus*	1	0	1
	Group A streptococci	1	0	1
	B catarrhalis	1	0	1
	Strep pneumoniae	2†	1	3
	H influenzae	0	1	1
	Total	5	2	7

*One case was methicillin resistant but sensitive to clindamycin and others.
†Penicillin-resistant *Strep pneumonia*, sensitive to cefuroxime and clindamycin. Both cases were from the same family.

cultures, 23% were family contacts of those who had a positive culture. Of the 46 patients receiving treatment initially, 40 had swabs cultured, and 6 received treatment presumptively as family contacts of a culture-positive patient. Of the 40 who had culture taken, 55% were positive. Of the 71 total persons who were given antibiotics, 55% also had positive cultures. Thirty-one percent of the 46 patients who initially received treatment and 31% of the total who received treatment were family contacts of those whose cultures were positive. Sixteen of the 22 family contacts who received treatment had negative cultures. Of the 71 total patients who received treatment, 14% were not themselves culture positive, nor were their contacts. According to the clinician's protocol, therefore, 86% of those receiving treatment either had positive cultures or were family contacts of someone who had a positive culture.

The association of treatment status, symptom resolution, and global well-being is shown in Table 5. The number of symptoms reported at the initial illness visit was significantly different among treatment groups. Patients initially started on antibiotics and those for whom antibiotics eventually were changed reported significantly more symptoms than patients receiving antibiotics after a positive culture or patients never given an antibiotic. Adjusting for day 1 differences in the number of reported symptoms, symptom resolution after 3, 7 and 14 days was similar for all comparison groups.

There was a moderate correlation between the number of symptoms a patient reported and the patient's perception of global well-being initially and at each of the three follow-up periods. The average Spearman correlation across 2 weeks of observation was 0.49, $P < .001$. Symptom resolution within a 2-week follow-up period was not associated with the month, global well-being score, or treatment status. Similarly, a positive culture was not associated with symptom resolution or global well-being.

The practice sees approximately 100 patients per week and has excellent follow-up as a result of strong relationships with families. A preponderance of managed care patients also made available knowledge of the patients' health system use. No patient in the practice required tonsillectomy-adenoidectomy or tympanostomy tubes for recurrent streptococcal infection or recurrent otitis or serous otitis during the study year or for many years previously. No study patients were known to have

Table 5. Association of Treatment Status, Symptom Resolution, and Global Well-Being.

Outcomes	Antibiotic Initially (n = 34)	Antibiotic Initially Then Changed (n = 12)	Antibiotic After Positive Culture (n = 25)	No Antibiotic (n = 40)	*P* Value
Symptoms (No.)					
Day 1	4.4	5.3	2.4	3.5	.001
Day 3*	2.5	3.8	2.3	2.6	.081
Day 7*	1.6	2.5	1.4	1.3	.076
Day 14*	1.1	1.7	1.3	1.1	.600
Global well-being score†					
Day 1	3.5	3.3	3.1	3.5	.378
Day 3	2.9	3.2	2.5	2.8	.186
Day 7	2.5	2.2	2.1	2.4	.390
Day 14	2.3	2.2	1.9	2.0	.362

*Means adjusted for initial (day 1) differences.
†Based on a 5-point Likert scale, where 1 = excellent, and 5 = poor.

invasive sequelae, and none was hospitalized or seen in the emergency department for respiratory tract illness. After the study, however, two families with *Staph aureus* infection who refused outreach support and case finding follow-up have had repeated episodes of various manifestations of infection (eg, purulent nasopharyngitis, paronychia, impetigo) in multiple family members.

Discussion

This study shows the natural history of respiratory tract illnesses in a solo family practice during the late fall to early spring. In addition, the study documents the microbiologic characteristics of different clinical and family illnesses and shows the process and outcome of one solo family physician's unique family-centered approach to treatment of respiratory tract illness based on a clinical protocol and culture findings.

This study documents the ability of an experienced family physician who provides continuity of care for whole families to predict whether culture results will be positive for potentially pathogenic organisms. The predictive value of clinical judgment in this and other studies[6–15,17–19,29–31] is insufficient to discern all patients who might benefit from antibiotics or to exclude all patients for whom antibiotics are unlikely to be helpful. The ability to use clinical judgment to identify potentially pathogenic bacteria from multiple sites in patients with diverse clinical signs and symptoms could open future inquiry into using selective samples for culture to guide antibiotic use in upper respiratory tract infection and is supported by recent findings.[16]

Whether these organisms are causally associated with the diverse clinical signs and symptoms of respiratory tract illness will require further study with explicit comparison groups. Even so, these findings are consistent with a body of literature that suggests there might be subgroups of patients with respiratory tract infections that benefit from antibiotics.[7–15,29–31] The suggestion of familial transmission of these organisms warrants additional study. Not since the Dingle et al studies of the 1950s,[26] and certainly not in our era of drug-resistant bacteria, has family spread of upper respiratory tract pathogens been critically examined. The incidence of colonization, spread, and disease associated with these bacteria, as well as the possible prevention of disease and sequelae within families, deserves revisiting.

The clinical strategy yielded specific knowledge about bacterial pathogens in patients and families, and this knowledge allowed treatment with antibiotics that were usually narrow spectrum, cheaper, and specific to the organisms. It is possible that for many episodes the patients were simply carriers and treatment was unnecessary; however, all the patients had cultures for other illnesses before and after the study, and none was positive for the same bacteria. Although this physician's protocol might unnecessarily result in treatment in those with mixed pathogens or with *Staph aureus*, these organ-

isms have been documented as causes of invasive upper respiratory tract disease when they are found in middle ear aspirate[19,32] and deep tonsillar tissue.[33] Furthermore, recent case studies have shown familial transmission of disease by drug-resistant *Staph aureus*[29] as well as familial clusters of invasive group A streptococci.[30] Military and civilian studies of streptococcus and acute rheumatic fever in the 1950s through the 1990s[9–13] showed epidemic spread within living facilities, the lack of association of upper respiratory tract infection symptoms with invasive disease, and the need to treat all those living together. Those studies implied, and now there is decisive evidence, that invasive group A streptococci can be spread by asymptomatic carriers.[8]

It is also possible that treatment in some of these cases might have engendered drug-resistant bacteria.[1–5] This concern is mitigated by the observation that the practice has had an unchanging rate of only one case of methicillin-resistant *Staph aureus* per year and encountered its first case of drug-resistant *Strep pneumoniae* in 1997, when the Cleveland area resistance rate was 40% to 50% (personal discussion by HRB with Michael Jacobs, MD, PhD, Director of Microbiology, University Hospitals of Cleveland, July, 1998). Despite the cost of cultures and office visits, it is even conceivable this approach might be more cost-effective than the frequent and often indiscriminate use of antibiotics based on clinical signs and symptoms alone.

Results for familial transmission apply to those family members cared for by the study practice, and additional familial transmission of illness to family members not seeking care at the practice undoubtedly occurred. The study findings are limited to a single solo family practice, and interpolation to other settings and approaches to care should be done with caution. Additional study involving comparison groups with other approaches to care would help assess the effect of this culture-driven, family-centered, and continuity-of-care approach on patient and family outcomes.

The study also shows the potential of systematic study of clinical approaches developed by self-reflective clinicians. We believe that many practicing family physicians have developed innovative approaches to aspects of patient care that would benefit from systematic study. Some innovations, when studied, could justify additional research and eventually change practice standards. Others might be proved ineffective. The wisdom of the practicing clinician remains a relatively untapped resource for innovation.[31] In addition to its larger potential benefit, practice-based research also has great potential to change the clinician investigator. For example, the systematic study of this solo family physician's longtime clinical practice for treatment of upper respiratory tract infection caused him to become less certain of his clinical classification of this condition, with the indeterminate group rising from 16% to 49% to 68% during the 3 months of the study (although the onset and waning of the influenza season and other seasonal factors might have contributed).

What other ideas lurk in the minds and daily practices of reflective clinicians? We challenge our discipline to bring these ideas to the light of systematic study.

The authors are grateful to the patients who participated in this study.

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