Clinical features fail to distinguish respiratory infections caused by *Branhamella catarrhalis* from those caused by *Haemophilus influenzae*

KEVIN ROY FORWARD, MD, FRCPC

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Branhamella catarrhalis is being isolated with increasing frequency from patients with symptoms and signs of respiratory tract infection. Records of 77 patients were reviewed to define the spectrum of respiratory illness and to compare clinical and laboratory features with those of respiratory infection due to *Haemophilus influenzae*. Both *B catarrhalis* and *H influenzae* caused respiratory infection predominantly in elderly males with underlying heart or lung disease. There were no clinical or laboratory features aside from sputum Gram stain and culture which differentiated the two groups. Although fewer than one-half of each group received antibiotics, no patient developed progressive respiratory disease.

Key Words: *Branhamella catarrhalis*, Bronchitis, *Haemophilus influenzae*, Infection, Pneumonia, Respiratory infection

Les particularités cliniques ne permettent pas de distinguer les infections respiratoires causées par *Branhamella catarrhalis* de celles causées par *Haemophilus influenzae*

RESUME: *Branhamella catarrhalis* est de plus en plus fréquemment isolé chez les patients qui présentent des signes et symptômes d'infection des voies respiratoires. On a passé en revue les dossiers de 77 patients dans le but de définir la gamme des affections respiratoires et de comparer leur tableau clinique et leurs résultats de laboratoire avec ceux des patients qui souffraient d'une infection à *Haemophilus influenzae*. *B catarrhalis* et *H influenzae* causaient tous deux des infections respiratoires chez une clientèle masculine âgée souffrant de cardiopathie ou de maladie pulmonaire sous-jacente, surtout. Aucune donnée clinique ou de laboratoire autre qu'une coloration de Gram et culture de l'expectoration ne distinguait les deux groupes. Bien que moins de la moitié des sujets de chaque groupe ait reçu une antibiothérapie, aucun patient n'a développé une affection respiratoire évolutive.

Departments of Medicine and Laboratory Medicine, St Boniface General Hospital, Winnipeg, Manitoba

Correspondence and reprints: Dr KR Forward, Head, Department of Microbiology, Victoria General Hospital, 5788 University Avenue, Halifax, Nova Scotia B3H 1V8. Telephone (902) 428-3624

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BRANHAMELLA CATARRHALIS IS AN AEROBIC GRAM-NEGATIVE diplococcus generally regarded as a normal respiratory tract commensal. In the past decade, *B catarrhalis* has been recognized as causing both upper and lower respiratory tract infections. Infectious syndromes in which *B catarrhalis* have been implicated include sinusitis, laryngitis, otitis media, pneumonia, acute bronchitis and exacerbations of chronic bronchitis (1-7). Such infections may be either community or hospital acquired (8). *B catarrhalis* may be one of the more frequently isolated respiratory pathogens (4,5). Many strains of this microorganism produce beta-lactamase, and since empiric ampicillin or amoxicillin is frequently used for respiratory infections, it may be important that the presence of this organism be recognized promptly (4,6,9,10). Although a sputum Gram stain should be helpful in recognizing the presence of *B catarrhalis*, the results of the Gram stain may not be immediately available. In order to determine other clinical or laboratory clues which might identify patients likely to have respiratory tract infections due to *B catarrhalis*, the author compared features of patients infected with *B catarrhalis* with those of patients infected with *Haemophilus influenzae*. *H influenzae* was chosen because it is a well recognized respiratory pathogen and produces a range of clinical syndromes similar to those seen with *B catarrhalis*.

PATIENTS AND METHODS

Patients were identified through the clinical microbiology laboratory at St Boniface General Hospital, an 830-bed teaching hospital offering a broad spectrum of hospital services. Patients were considered for entry if lower respiratory tract secretions submitted to the laboratory were purulent (moderate to heavy pus on Gram stain); if *H influenzae* or *B catarrhalis* were present in a moderate to heavy amount; and if no other respiratory pathogen was isolated. Patients were randomly selected from those with positive *B catarrhalis* or *H influenzae* cultures at St Boniface General Hospital in 1987. Each patient's chart was reviewed and information compiled using a standardized data collection form designed for the study.

Clinical case definitions: Chronic obstructive pulmonary disease (COPD) was deemed to exist if so indicated in the medical record. An acute exacerbation of COPD was present if there was a history of COPD and if there was an increasing volume or change in the character of the sputum produced. Acute bronchitis was diagnosed if the patient had cough and sputum or a change in the volume or character of sputum and no history of previous COPD. Pneumonia was deemed present if there was radiological evidence of an infiltrate consistent with pneumonia, with fever and/or purulent sputum production.

Laboratory methods: Both *H influenzae* and *B catarrhalis* were identified using conventional laboratory

TABLE 1

Characteristics of patients from whom *Branhamella catarrhalis* and *Haemophilus influenzae* were isolated from respiratory tract secretions

	<i>Branhamella catarrhalis</i> (n=37)	<i>Haemophilus influenzae</i> (n=40)	P
Age (years)	64.3±19.0	61.1±17.7	NS
Male/female	22/15	27/13	NS
Smoker/nonsmoker	14/23	19/21	NS
Prior antibiotics	12	8	NS
Comorbidity			NS
Chronic lung disease	18	18	
Ischemic heart disease	13	13	
Malignancy	7	7	
Diabetes	4	2	
Alcohol abuse	2	4	
None	2	4	

NS, Not significant ($P > 0.05$ by Student's *t* test or Fisher's exact test)

methods (11,12). *H influenzae* was biotyped using the method of Kilian (12). *H influenzae* serotyping was performed using a commercially available particle agglutination test (Phadebact, New Jersey) (13). Susceptibilities were performed using the agar dilution method. *B catarrhalis* susceptibilities were performed using Mueller-Hinton agar (Scott Laboratories, Rhode Island). *H influenzae* susceptibilities were performed using Mueller-Hinton agar with 1% IsoVitalX (BBL Microbiology Systems, Maryland). Beta-lactamase production was determined using the nitrocefin disk method (Cefinase; BBL Microbiology Systems, Maryland).

Statistical methods: Data analysis was performed using GraphPad InStat software (Intuitive Software for Science, California). Categorical variables were analyzed using Fisher's exact test or χ^2 as appropriate. Student's *t* test was used for continuous variables. All *P* values were calculated for two tails. Ninety-five per cent confidence intervals were used.

RESULTS

The characteristics of patients from whom *B catarrhalis* or *H influenzae* were isolated are shown in Table 1. Age, smoking history and previous antibiotics were not statistically different. Similar numbers of patients had pre-existing COPD, ischemic heart disease or congestive cardiac failure, or malignancy. Only two patients with *B catarrhalis* infections and four with *H influenzae* infections had no identifiable predisposing illness.

Table 2 shows the clinical presentation of patients in each group. Similar numbers of patients had acute bronchitis, pneumonia and acute exacerbations of underlying COPD. Only five patients with *B catarrhalis* infections and three with *H influenzae* infections had temperatures greater than 38°C in the 24 h period before or after the specimen culture was submitted.

TABLE 2

Respiratory infections produced by *Branhamella catarrhalis* and *Haemophilus influenzae*

	<i>Branhamella catarrhalis</i> (n=37)	<i>Haemophilus influenzae</i> (n=40)
Acute bronchitis	11	8
Pneumonia	8	10
Chronic obstructive lung disease		
Stable	4	5
Acute	10	13
Other	4	4

 $\chi^2=1.083$; $P=0.90$ two-tailed

Table 3 shows the laboratory features of infections caused by these organisms. Of the parameters examined no statistically significant differences were observed between the two groups.

Only one of the 40 *H influenzae* strains was serotypeable. Nineteen were biotype II; 14 were biotype III; and five were other biotypes. Seven of the 40 *H influenzae* strains produced beta-lactamase, whereas 26 of 37 (70%) *B catarrhalis* strains were beta-lactamase positive ($P<0.001$ by Fisher's exact test).

Only 16 patients in the *B catarrhalis* group and 18 in the *H influenzae* group received antibiotics either empirically or upon receipt of the microbiology report. Two patients in the *B catarrhalis* group and three in the *H influenzae* group died. One patient with severe COPD had *B catarrhalis* pneumonia due to a beta-lactamase-producing strain, and died. Death was possibly attributable to *B catarrhalis* pneumonia; however, no autopsy was performed to confirm this impression. The patient had received ampicillin for treatment of his pneumonia. None of the others that died had pneumonia.

DISCUSSION

B catarrhalis and *H influenzae* share many important characteristics. Both frequently colonize the mouth and pharynx and cause a variety of infectious syndromes in both the upper and lower respiratory tracts. In a predominantly adult population, both caused acute bronchitis, exacerbation of chronic bronchitis and pneumonia (2-6,14-17). Despite clinical evidence to implicate *B catarrhalis* as a lower respiratory pathogen, it is seldom recovered either from blood or pleural fluid. It is perhaps for this reason that investigators have been slow to acknowledge its role as a cause of lower respiratory tract infection. More recently, the recovery of *B catarrhalis* from transtracheal aspirates in patients with clinically apparent infections has contributed to the acceptance of this organism as a lower respiratory pathogen (7). The present patients had neither transtracheal aspirates nor serological studies to confirm that they were infected rather than colonized with *B catarrhalis*. How-

TABLE 3

Laboratory features of patients from whom *Branhamella catarrhalis* and *Haemophilus influenzae* were isolated from respiratory tract secretions

	<i>Branhamella catarrhalis</i> (n=37)	<i>Haemophilus influenzae</i> (n=40)	P
WBC ($\times 10^9$ /L)	12.3 $\pm$ 6.3	11.2 $\pm$ 4.9	0.34 ¹ NS
WBC $\geq 10.8 \times 10^9$ /L	18 (32)	16 (38)	0.40 ² NS
Neutrophils (%)	73 $\pm$ 14.6	78 $\pm$ 10.6	0.29 ¹ NS
Arterial blood gases			
pO ₂ (mmHg)	61.1 $\pm$ 15.5	55.7 $\pm$ 18.4	0.35 ¹ NS
pO ₂ <60 mmHg	8	9	0.74 ² NS
pCO ₂ (mmHg)	39.8 $\pm$ 9.1	40 $\pm$ 7.0	0.94 ¹ NS
pO ₂ >40 mmHg	9	7	0.75 ² NS

WBC White blood cell count; NS Not significant ($P>0.05$ by ¹Student's *t* test or ²Fisher's exact test). P values are for two-tailed tests

ever, patients with a heavy growth of *B catarrhalis* in sputum usually have positive cultures of transtracheal aspirates (7). In addition, patients with symptoms and signs of pneumonia or acute exacerbations of chronic bronchitis usually develop bactericidal antibodies during the course of their illness, suggesting a causative role for *B catarrhalis* (18). It was therefore assumed that most of the symptomatic patients included in this analysis were infected. Adults are frequently colonized with *B catarrhalis*, therefore, it is not possible to say with certainty that some were not simply colonized. Since *B catarrhalis* frequently produces beta-lactamase, and since treatment of such infections with ampicillin may result in failure, it may be important that infection with *B catarrhalis* be recognized (6,19). To this end, it would be useful to identify on clinical grounds a subset of patients more likely infected with *B catarrhalis*.

It was not possible to identify any clinical or laboratory parameters outside of those provided by a microbiological examination of the sputum that might identify patients more likely infected with *B catarrhalis*. In the present population, infection occurred most frequently in older males with chronic lung disease or other comorbidities that might impair normal host defences. As with *H influenzae*, few patients had no significant underlying disease. Eight patients with *B catarrhalis* infections had pneumonia. Since the diagnosis of pneumonia was based upon radiological features and not all patients had chest radiographs, it is possible that the proportion with pneumonia might have been higher had x-rays been available for all patients.

Patients were seldom seriously ill with either *B catarrhalis* or *H influenzae*. Few patients in either group had fever greater than 38°C. A number of patients had significant hypoxemia, but this was likely due to the presence of underlying lung disease. More than half of the patients in either group received no antibiotics, and

infections were usually self-limited. Although five patients died, in only one did infection possibly play a role.

Most of the *H influenzae* strains were not serotypeable and were usually biotype II or III. These characteristics were typical of *H influenzae* strains encountered in respiratory secretions from adults (20,21). The proportion with beta-lactamase production is less frequent in nonserotypeable nonbiotype I isolates.

The proportion of *B catarrhalis* producing beta-lactamase was considerably higher than for *H influenzae* and similar to the proportion observed by others (2,4,5,9). All *B catarrhalis* isolates were susceptible to erythromycin, tetracycline, trimethoprim-sulphamethoxazole, cefaclor, cephalexin and ampicillin-clavulanic acid. The author noted, as have others, that beta-lactamase-producing strains of *B catarrhalis* frequently have ampicillin minimal inhibitory concentra-

tions (MICs) less than 2 mg/L (22,23). For this reason it may be wise not to test beta-lactamase positive strains for susceptibility to ampicillin using either disk diffusion or agar dilution methodology. On the other hand, it has been argued that in the case of *B catarrhalis*, MICs may be a better predictor of clinical outcome, since infection due to beta-lactamase-producing strains may respond to ampicillin-like antibiotics.

In this predominantly adult population, *B catarrhalis* caused a spectrum of infections of the respiratory tract identical to that produced by *H influenzae*. Infections were usually mild and often self-limited. *B catarrhalis* isolates remain highly susceptible to a number of oral agents other than ampicillin or amoxicillin. Very ill patients with community-acquired respiratory tract infections superimposed on COPD should probably receive an agent effective in vitro against both *H influenzae* and beta-lactamase-producing *B catarrhalis*.

REFERENCES

1. Wald ER, Milmo GJ, Bowen AD, Ledesma-Medina J, Salamon N, Bluestone CD. Acute maxillary sinusitis in children. *N Engl J Med* 1981;304:749-54.
2. DiGiovanni C, Riley TV, Hoyne GF, Yeo R, Cooksey P. Respiratory tract infections due to *Branhamella catarrhalis*: Epidemiological data from western Australia. *Epidemiol Infect* 1987;99:445-53.
3. Srinivasan G, Raff MJ, Templeton WC, Givens SJ, Graves RC, Melo JC. *Branhamella catarrhalis* pneumonia. Report of two cases and review of the literature. *Am Rev Respir Dis* 1981;123:553-5.
4. Davies BI, Maesen FPV. *Branhamella catarrhalis* chest infections. *Lancet* 1986;ii:278.
5. Pollard JA, Wallace RJ, Nash DR, Luman JI, Wilson RW. Incidence of *Branhamella catarrhalis* in the sputa of patients with chronic lung disease. *Drugs* 1986;31(Suppl 3):103-8.
6. Slevin NJ, Aitken J, Thornley PE. Clinical and microbiologic features of *Branhamella catarrhalis* bronchopulmonary infections. *Lancet* 1984;i:782-4.
7. Aitken JM, Thornley PE. Isolation of *Branhamella catarrhalis* from sputum and tracheal aspirate. *J Clin Microbiol* 1983;18:1262-3.
8. Patterson TF, Patterson JE, Masecar BL, Barden GE, Hierholzer WJ, Zervos MJ. A nosocomial outbreak of *Branhamella catarrhalis* confirmed by restriction endonuclease analysis. *J Infect Dis* 1988;157:996-1001.
9. Calder MA, Croughan MJ, McLeod DT, Ahmad F. The incidence and antibiotic susceptibility of *Branhamella catarrhalis* in respiratory infections. *Drugs* 1986;31(Suppl 3):11-6.
10. Forward KR, Degagne PA, Bartlett KR. The comparative activity of lomefloxacin (SC-4711, NY-198) and other orally absorbable agents against *Haemophilus influenzae* and *Branhamella catarrhalis*. *Diagn Microbiol Infect Dis* 1989;12:437-40.
11. Morello JA, Janda WM, Bohnhoff M. Neisseria and branhamella. In: Lenette EH, Balows A, Hauslet WJ Jr, Shadomy HJ, eds. *Manual of Clinical Microbiology*, 4th edn. Washington: American Society for Microbiology, 1985:275-92.
12. Kilian M. *Haemophilus*. In: Lenette EH, Balows A, Hauslet WJ Jr, Shadomy HJ, eds. *Manual of Clinical Microbiology*, 4th edn. Washington: American Society for Microbiology, 1985:387-93.
13. Himmelreich CA, Barenkamp SJ, Storch GA. Comparison of methods for serotyping isolates of *Haemophilus influenzae*. *J Clin Microbiol* 1985;21:158-60.
14. Stratton CW, Hawley HB, Horsman TA, et al. *Hemophilus influenzae* pneumonia in adults. *Am Rev Respir Dis* 1980;121:595-8.
15. Smith CB, Golden CA, Kanner RE, Renzetti AD. *Haemophilus influenzae* and *Haemophilus parainfluenzae* in chronic obstructive pulmonary disease. *Lancet* 1976;i:1253-5.
16. Tillotson JR, Lerner AM. *Hemophilus influenzae* bronchopneumonia in adults. *Arch Intern Med* 1968;121:428-34.
17. Berk SL, Holtsclaw SA, Wiener SL, Smith JK. Nontypeable *Haemophilus influenzae* in the elderly. *Arch Intern Med* 1982;142:537-9.
18. Darling WM. *Branhamella catarrhalis*. *Lancet* 1982;i:1244.
19. Chapman JE, Musher DM, Jonsson S, Clarridge JE, Wallace RJ. Development of bactericidal antibody during *Branhamella catarrhalis* infection. *J Infect Dis* 1985;151:878-82.
20. Oberhofer TR, Back AE. Biotypes of haemophilus encountered in clinical laboratories. *J Clin Microbiol* 1979;10:168-74.
21. Holdaway MD, Turk DC. Capsulated *Haemophilus influenzae* and respiratory tract disease. *Lancet* 1967;i:358-60.
22. Doern GV, Tubert T. Disk diffusion susceptibility testing of *Branhamella catarrhalis* with ampicillin and seven other antimicrobial agents. *Antimicrob Agents Chemother* 1987;31:1519-23.
23. Sweeney KG, Verghese A, Needham CA. In vitro susceptibilities of isolates from patients with *Branhamella catarrhalis* pneumonia compared with those of colonizing strains. *Antimicrob Agents Chemother* 1985;27:499-502.

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