

ONLINE DATA SUPPLEMENT

Moraxella catarrhalis in Chronic Obstructive Pulmonary Disease: Burden of Disease and
Immune Response

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Study Design

The Human Studies Subcommittee of the Veterans Affairs Western New York Healthcare System approved the study protocol. All participants gave written informed consent. A total of 104 patients were enrolled between March 1994 and December 2000. Inclusion criteria were the presence of chronic bronchitis (E1), absence of other lung disease on the basis of a clinical assessment, absence of immunosuppressive or life-threatening disorders and willingness to make monthly clinic visits. Patients were seen at the Buffalo Veterans Affairs Medical Center monthly and whenever they had symptoms suggestive of an exacerbation.

At each clinic visit, clinical information and sputum and serum samples were obtained. The patients were questioned about the status of their chronic respiratory symptoms (dyspnea, cough, sputum production, viscosity and purulence) and responses were graded at 1 (at the usual level), 2 (somewhat worse than usual), or 3 (much worse than usual). A minor worsening of two or more symptoms or a major worsening of one or more symptoms prompted a clinical assessment of the cause. If the patient had fever (a temperature that exceeded 38.3°C), appeared ill, or had signs of consolidation on examination of the lungs, a chest film was obtained to rule out pneumonia. If other causes of the worsening of symptoms, such as pneumonia, upper respiratory infection, and congestive heart failure were ruled out, the patient was considered to be having an exacerbation of COPD (E2). The determination of whether the patient had stable

disease or an exacerbation was made by one of 2 examiners (SS, TFM) before the results of sputum cultures were available.

Sputum Samples

Study personnel who processed sputum samples were unaware of the clinical status of patients. Sputum samples that were spontaneously expectorated the morning of the clinic visit were homogenized, diluted and plated in a quantitative manner as previously described (E2). Bacterial pathogens were identified with the use of standard techniques. The identity of an isolate as *M. catarrhalis* was confirmed by colony morphology and the presence of butyrate esterase.

All isolates were subjected to molecular typing by pulsed field gel electrophoresis (E2). Each isolate was categorized as pre existing or new on the basis of molecular typing. A new strain was one that had not been isolated from sputum samples obtained previously from an individual patient.

After aliquots of the homogenized sputum sample were removed for culture, the remainder of the sample was centrifuged at 27,000 g for 30 minutes at 4°C. The supernatant was stored at -80°C.

Table E1. Characteristics of study clinic visits

Characteristic	Value
No. of visits during stable disease (%)	2449 (81.4%)
No. of visits during exacerbations (%)	560 (18.6%)
Total no. of visits per patient	
Mean	28.9
Range	1-98
No. of visits per patient with <i>M. catarrhalis</i>	
Mean	2.0
Range	0-26
Proportion of total visits per patient with <i>M. catarrhalis</i>	
Mean	7.0%
Range	0-58.3%

References

- E1. American Thoracic Society. 1995. Standards for the diagnosis and care of patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 152(5 Pt 2):S77-S121.
- E2. Sethi, S., N. Evans, B. J. B. Grant, and T. F. Murphy. 2002. New strains of bacteria and exacerbations of chronic obstructive pulmonary disease. *N Engl J Med* 347:465-471.