

### Treatment of postviral nonasthmatic cough with corticosteroids

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#### Clinical Implication

- Patients with a history of prolonged cough after upper respiratory infections with no evidence of asthma may improve dramatically with the use of oral corticosteroids.

#### TO THE EDITOR:

Postviral cough is a common problem, affecting approximately 5% of the population annually.<sup>1</sup> Cough is the most common symptom leading patients to offices of primary care physicians.<sup>2</sup> Antibiotics, antitussives, mucolytics,  $\beta$ -agonists, and inhaled corticosteroids have only limited efficacy in the treatment of postviral cough. The modest cough suppression of the latter two agents might be indicative of occasionally undiagnosed reactive airway disease.<sup>3</sup>

The usual therapies for managing acute postviral cough have been shown to be ineffective.<sup>3</sup> The symptoms typically persist for approximately 3 weeks.<sup>4</sup> However, a cough may be prolonged for 8 weeks (subacute) or longer (chronic cough).<sup>5</sup> The lack of effective treatments may prompt some frustrated physicians to the empiric use of antibiotics, which may lead to the possibility of developing resistant organisms and allergies. However, not treating these patients with antibiotics often results in an equally frustrated patient who will then seek help elsewhere to obtain a frequently expensive and ineffective treatment for a viral infection. Although viruses are responsible for 90% of post-infectious coughs, approximately two-thirds of patients in the United States diagnosed with this entity are treated with antibiotics.<sup>6</sup> A recent article reports that the greatest risk to human health comes in the form of antibiotic-resistant bacteria.<sup>7</sup> Although other factors are involved, their inappropriate use can result in antibiotic resistant infections. While the use of oral corticosteroids seems reasonable for a troublesome cough, no previous clinical data have been presented to support the use of oral corticosteroids in patients with postviral cough who do not have asthma.<sup>3,8</sup>

In this case series of eight patients with histories of recurrent postviral nonasthmatic coughs, the cough was markedly improved by treatment with oral corticosteroids, supporting this modality of treatment for this troublesome condition. All patients with histories of recurrent coughs after upper respiratory infections and no evidence of asthma seen over the past 8 years are included in this series. Eight patients presented with a postviral nonproductive cough that lasted from 4 days to 3 months (Table I). Except for patient JF, all were nonsmokers, and none were taking angiotensin-converting enzyme inhibitors. Previously, they had been treated with one or more of the following: antibiotics (frequently more than once), antitussives, mucolytics,  $\beta$ -agonists, and inhaled corticosteroids, with no significant decrease in the cough. Physical examinations, except for swelling of the nasal turbinates, were entirely within normal limits in all of the patients. Specifically, on

auscultation of the chest no wheezing, rhonchi, or rales was heard. Cough was induced on forced expiration. Vital signs were within normal limits. The pulse oximetry was 99% or 100% in all patients.

Pulmonary function tests were performed with a Puritan Bennett Spirometer 900 (Wilmington, Mass). All test results were within normal limits (Table II). Because many patients with recurrent bronchitis may have unrecognized asthma<sup>9</sup>, cough variant asthma was considered,<sup>10</sup> and a methacholine challenge test was performed on all patients by means of a modification of the protocol described by Catham et al<sup>11</sup> with the use of a nebulizer for the inhalation of methacholine. This modified screening methacholine challenge method correlated with results obtained from the traditional lengthy protocol and correctly identified levels of airway reactivity in all subjects. The screening challenge consisted of one breath followed by four breaths of a 5 mg/mL methacholine solution. Subsequently, the protocol included one breath and then four breaths of a 25 mg/mL methacholine solution. Spirometric tests were performed after each inhalation. The solutions were delivered via a DeVilbiss Pulmo-Aide nebulizer (Somerset, Pa). The methacholine challenges would be terminated if the FEV<sub>1</sub> decreased by more than 20% from the baseline, the determining factor for a positive methacholine challenge (indicative of asthma).

In these eight patients, the FEV<sub>1</sub> decreased an average of -9% with a range from -7% to -11%, and the FVC decreased an average of -2.68% with a range from 2% to -8% (Table II). The negative methacholine challenges supported the conclusion that these patients did not have asthma. The patients were treated with 25 to 50 mg of prednisone per day for 5 to 7 days with resolution of the cough within 1 week in all patients (Table II).

No clinical data support the use of inhaled or oral corticosteroids for the treatment of postviral induced cough in patients without asthma.<sup>3,8</sup> Although the positive predictive value for methacholine challenge ranges from 60% to 88%, the negative predictive value is considered to be 100%.<sup>12</sup> The sensitivity of the methacholine challenge in ruling out asthma, coupled with the fact that the patients did not report a history of wheezing, chronic cough, or exercise-induced dyspnea strongly suggests that none of the patients in the current series had asthma. They only reported a cough after upper respiratory infections, which are invariably viral.<sup>5</sup>

The only other clinical entity characterized by a cough and a negative methacholine challenge and responsive to corticosteroids is an entity known as eosinophilic bronchitis. The distinguishing feature in patients with this condition from those in this report is that patients with eosinophilic bronchitis must remain on long-term corticosteroids for symptom control, whereas the patients presented here are entirely symptom free between episodes of postviral cough without the need for chronic corticosteroids.<sup>13</sup>

In recent years, the concept has been evolving that postviral coughs reflect an inflammatory response to infection.<sup>3</sup> Specifically, the inflammatory response affects the epithelium of the bronchi with epithelial cell desquamation and denuding of the airway to the level of the basement membrane. These findings

TABLE I. Clinical summaries

Patient	Age (y)/sex	Length of current cough	History of length of cough	Past medical history	Past treatment	Allergy skin tests
DH	56/female	2 wk	1–1.5 mo	Chronic rhinitis	Antibiotics, fluticasone propionate/salmeterol inhaler	Positive reaction to cat
RC	38/female	1 mo	1–1.5 mo	Negative	Antibiotics, guaifenesin/dextromethorphan	Multiple positive skin tests
JF	38/female	4 d	1 mo	*	Antibiotics	All negative
SV	45/female	1 mo	1–3 mo	Negative	Montelukast, albuterol inhaler, antibiotics, guaifenesin/dextromethorphan	Multiple positive skin tests
JR	33/female	2.5 mo	2 wk	Negative	Multiple cough suppressants	Multiple positive skin tests
PJ	38/female	1 mo	1–1.5 mo	Negative	Antibiotics, prednisone for 3 d	Multiple positive skin tests
VP	40/male	3 wk	1–2 mo	Chronic rhinitis	Antibiotics, fluticasone propionate/salmeterol inhaler	Multiple positive skin tests
SA	54/female	3 mo	1–2 mo	Chronic rhinitis, Graves disease	Antibiotics, fluticasone propionate/salmeterol inhaler	Not performed

\*Smoked 1.5 packs of cigarettes per day for 10 years, previous upper respiratory infection resulted in severe hemoptysis; extensive workup, including chest x-ray, computed tomographic scan of chest, bronchoscopy, and bronchoalveolar lavage were all within normal limits.

TABLE II. Pulmonary function tests, treatment, and results

Patient	Percentage of FVC predicted before MC challenge	Percentage of FVC predicted after MC challenge (% change)	Percentage of FEV <sub>1</sub> predicted before MC challenge	Percentage of FEV <sub>1</sub> predicted after MC challenge (% change)	Treatment	Results
DH	100	93 (–7)	108	98 (–9)	Prednisone 15 mg b.i.d. × 5 d fexofenadine 180 mg mometasone nasal spray	Cough resolved in 4 d
RC	83	81.5 (–1.8)	94	88 (–7.2)	Prednisone 25 mg b.i.d. × 5 d	Cough resolved in 5 d
JF	95.7	94.3 (–1)	98.5	87.9 (–11)	Prednisone 15 mg b.i.d. × 7 d Fexofenadine/pseudoephedrine hydrocodone at h.s.	Cough resolved in 1 wk
SV	84	80 (–5)	98	91 (–7)	Prednisone 25 mg × 7 d/c albuterol	Cough resolved in 1 wk
JR	100	102 (2)	107	103 (–4)	Prednisone 15 mg b.i.d. × 7 d triamcinolone nasal spray aq fexofenadine/pseudoephedrine	Cough resolved in 3 d
PJ	92	91 (–1)	100	90 (–10)	Prednisone 15 mg b.i.d. × 7 d	Cough resolved in 1 wk
VP	85	85 (0)	97	83 (–14)	Prednisone 15 mg b.i.d. × 7 d hydrocodone at h.s.	Cough resolved in 3 d
SA	94	86 (–8)	109	98 (–10)	Prednisone 15 mg b.i.d. × 7 d montelukast 10 mg budesonide nasal spray aq continue fluticasone 220, guaifenesin/dextromethorphan as needed fexofenadine 180 mg	Cough improved in 3 d and resolved in 6 d

Aq, Aqueous; b.i.d., twice daily; d/c, discontinue; FVC, forced vital capacity; FEV<sub>1</sub>, forced expiratory volume in 1 second; h.s., bedtime; MC, methacholine. Pulmonary function tests were performed with Puritan Bennett Spirometer 900.

were detected in a study of adults without asthma with a chronic cough.<sup>14</sup> Biopsies showed that the chronic cough was associated with airway inflammation, manifested by epithelial desquamation and an increased number of inflammatory cells, mostly mononuclear.

Epithelial cell function plays an important role in airway inflammation.<sup>15</sup> The cause of cough in postviral infections is likely multifactorial but presumably begins with mucosal injury, epithelial cell damage, and the release of proinflammatory mediators. Epidemiologic evidence and clinical observation of natural infections in humans suggest that different viruses may be associated with different magnitudes of airway inflammation.<sup>16</sup> During viral infections the epithelium can be injured with the consequent loss of integrity. Corticosteroids are well-established

suppressors of viral inflammation and may modulate epithelial damage, injury, and repair. Studies have shown that corticosteroids assist in healing damaged epithelial cells by suppressing the infiltration of inflammatory cells.<sup>17</sup> The dramatic response of these eight patients to prednisone is consistent with the concept that the patient's cough, although precipitated by viral infections, is predominantly an inflammatory response of the bronchial epithelium, which may be responsible for the history of prolonged coughs.

A recent practice guideline for the diagnosis and management of cough<sup>18</sup> mentions the use of 30 to 40 mg of prednisone per day for a short period of time for postinfectious cough, although the evidence presented in the practice guidelines justifying the use of corticosteroids is weak. The present case series supports

this recommendation. A double-blind study would be needed to confirm the efficacy of prednisone in the type of patient presented in this study. Pending such a study, a 7-day course of 30 to 40 mg of prednisone a day could be offered to patients who had a cough for longer than 2 weeks after an upper respiratory infection without evidence of pertussis. This diagnosis could be reasonably excluded if the patient had no known contacts with persons who had pertussis and did not present with an inspiratory whoop and/or post-tussive emesis. One might use oral corticosteroids sooner in patients with past histories of severe prolonged cough after an upper respiratory infection.

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