The Role of Sinus Imaging in the Treatment of Chronic Cough in Adults*

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**Primary study objective:** To determine the appropriate role and timing of sinus imaging studies in the evaluation and treatment of chronic cough.

**Design:** Prospective study of chronic cough. All patients underwent sinus imaging, the results of which identified prospectively the following: (1) fluid in sinuses, with or without opacification, and (2) mucosal thickening. Patients then were treated using an algorithm that sequentially addresses the etiologies of chronic cough. Patients whose sinus imaging studies had demonstrated fluid were treated initially for sinusitis, but mucosal abnormalities alone were not considered an indication to change the algorithm. After workup, relationships between abnormalities on sinus imaging studies and diagnoses were determined.

**Setting:** University hospital pulmonary outpatient clinic.

**Patients:** Thirty-six patients (31 women, 5 men; mean age, 58.4 years). Cough duration averaged 5.2 years (range, 4 weeks to 30 years).

**Results:** Diagnoses were made in 100% of patients, and cough resolved in 86%. Mucosal thickening correlated with sinusitis as a cause of cough in only 29% of cases.

**Conclusions:** Mucosal thickening is not diagnostic of sinusitis as a cause of chronic cough; in most patients, cough will resolve without treatment for sinusitis. Given this lack of specificity, it is reasonable to delay sinus imaging until after efforts at treating rhinitis have failed and, in the absence of complaint or findings of postnasal drip, until after completion of evaluation for asthma. The principles of diagnosis and treatment of chronic cough remain simple: go sequentially from the most common to the least common cause; use tools that begin with the most available and least expensive and invasive modality; then move as needed to tools that are more expensive and invasive.

Key words: chronic cough; postnasal drip; sinusitis

Abbreviations: PND = postnasal drip; PND-Rh = PND due to rhinitis; PND-Si = PND due to sinusitis

Over the past 20 years, the clinical approach to chronic cough has been defined and refined.1–11 The importance and prevalence of postnasal drip (PND) syndrome, asthma, and gastroesophageal reflux disease have all been established. While this knowledge has enhanced the accuracy and speed with which clinicians can diagnose and relieve chronic cough, there is still no test for any of the three conditions that can establish a causal relationship between that factor and cough other than an empiric therapeutic trial with retrospective diagnosis based on the efficacy of the intervention in decreasing cough.

Our primary goal was to determine the optimal role and timing of sinus imaging in workup and treatment. This was achieved through the prospective evaluation of sinus imaging in chronic cough. We wanted to determine which findings separated PND due to rhinitis (PND-Rh) from PND due to sinusitis (PND-Si).

**Materials and Methods**

Patients enrolled prospectively into the study were consecutive patients referred to a university-based pulmonary service for chronic cough. In this case, chronic cough was defined as cough present for ≥ 3 weeks. Exclusion criteria were the following: (1) immunocompromise; (2) use of an angiotensin-converting enzyme inhibitor within the prior 4 weeks; and (3) contraindication to the use of an antihistamine/decongestant or to bronchodilator challenge. The exclusion criteria were thus similar to those...
used in a prior study\textsuperscript{6} with one exception: long-term smokers with a "new-onset" chronic cough were included in the study.

Patients were studied according to an algorithm.\textsuperscript{9} The algorithm is a sequential workup that addresses diagnosis in stages, first determining whether PND is the cause of cough beginning with an empiric diagnostic/therapeutic trial of therapy for PND-Rh, after which nonresponders with persistent symptoms of PND are evaluated for PND-Si. After addressing PND, the diagnosis of asthma is considered, followed by gastroesophageal reflux, and, last, uncommon causes of chronic cough.\textsuperscript{7} If a patient's cough resolved only partly with treatment for a particular condition, that condition was considered to be a cause of cough. The algorithm was continued, however, with the goal of defining additional causes of cough and effecting cough resolution; patients could thus have more than one etiology of cough. Patients whose cough resolved dropped out of the protocol, and, as a result, the majority of patients whose conditions were diagnosed using the algorithm never reached the last stages.

The algorithm used in this study was similar to the algorithm already published,\textsuperscript{9} with two exceptions. The two exceptions were the timing of the radiographs, and the treatment of patients with symptoms of gastroesophageal reflux. All patients enrolled in the study had sinus imaging studies and chest radiographs obtained at the outset of evaluation and treatment. Two abnormalities seen on sinus imaging were considered to be significant.\textsuperscript{10,12} The first abnormality was mucosal thickening of \(>\) 6 mm, and the second was the presence of air/fluid levels. These are findings traditionally considered to represent sinusitis. If sinus imaging demonstrated fluid in the sinuses (opacification or air/fluid levels), then treatment for sinusitis was begun along with the initial antihistamine/decongestant for PND. If the imaging studies were normal or demonstrated mucosal thickening without fluid, the algorithm was not altered;\textsuperscript{9} rather, the films were acted upon at the time that the algorithm had stated that imaging studies should be obtained. Patients with symptoms of gastroesophageal reflux were treated with omeprazole rather than with ranitidine because of the increased efficacy of the proton pump inhibitors and their now proven safety profile. In addition to these changes, there was also documentation at the initial visit of whether or not the patient complained that the chronic cough was productive. As with cough itself, the complaint of productivity of cough was addressed as a symptom and was not quantified.\textsuperscript{10}

In this study, sinusitis was considered to be a cause of chronic cough if a patient's cough did not respond to treatment for PND-Rh alone, (ie, an antihistamine/decongestant with or without nasal steroids) and did respond to treatment for PND-Si, which involved the addition of an antibiotic and a 5-day course of local vasoconstrictor therapy (oxymetazoline hydrochloride).\textsuperscript{9} The presence on sinus imaging studies of mucosal thickening alone was not considered sufficient to make a diagnosis of sinusitis. Thus, we had the opportunity to see how often patients with mucosal thickening responded to treatment for PND-Rh.

The cases were reviewed to determine the utility of the imaging studies and their relationship to symptoms. Specific questions asked in this determination were the following: How often do abnormal sinus imaging studies predict sinusitis to be a cause of chronic cough? How often do abnormal sinus imaging studies predict PND to be a cause of chronic cough? Is the presence or absence of a productive cough of any diagnostic value, especially with respect to sinus disease? The protocol used also allowed the assessment of the role of chest radiographs in the evaluation of chronic cough.

Results

Forty patients were enrolled into the study. Four patients did not complete the protocol after enrollment and were therefore eliminated, leaving 36 for evaluation. There were 31 women and 5 men in the study, with a mean (\(\pm\) SD) age of 58.4 \(\pm\) 12.8 years (range, 33 to 77 years). Duration of cough ranged from 4 weeks to 29 years, with a mean of 5.2 years.

Cough was effectively treated in 31 patients and did not resolve in 5 patients. The etiology seemed to have been established in all five of the patients who did not respond. Of those five patients, three had PND refractory to all interventions. All three had obvious PND, and each had normal sinus imaging studies and negative results to methacholine challenges and 24-h pH-probe studies. One patient had severe gastroesophageal reflux with Barrett's esophagus. The reflux was refractory to medical therapy, there was no response to antihistamine/decongestant, sinus imaging studies were unremarkable, and the result of a methacholine challenge was negative. The last nonresponder was believed to have psychogenic cough, a diagnosis of exclusion. She had a positive result for a methacholine challenge but had not responded to treatment including oral steroids. The results of all other studies had been negative. Most important, on review of extensive contact with the patient, no physician or staff member had ever heard her cough. The ultimate diagnoses in the 36 cases are depicted in Figure 1. In Figure 1, PND-Rh and PND-Si are grouped under PND, and are not separated.

Sinus imaging studies were available for all 36 patients; 35 studies were plain radiographs, and 1 was a CT scan of the sinuses. The relationships between abnormalities on sinus imaging studies and diagnoses are documented on Table 1. Twenty-six imaging studies were normal, and 10 were abnormal, with 7 showing only mucosal thickening and 3 showing air/fluid levels, complete sinus opacification, or both. On examination of the relationship between sinus film findings and etiology of cough, it is first noted that no patient with a normal sinus imaging study had a final diagnosis of sinusitis. In addition, all patients with abnormal imaging studies had either PND-Rh or PND-Si as a final diagnosis. Finally, of the 10 patients with abnormal sinus imaging studies, 5 patients (50\%) eventually had sinusitis diagnosed as a cause of cough. When the cases of patients with mucosal thickening alone were reviewed, only two of seven patients (29\%) had an ultimate diagnosis of sinusitis.

A complaint of productive cough correlated only weakly with abnormal sinus imaging studies (Table 1); 41\% of patients with a productive cough had abnormalities on sinus imaging, while 16\% of pa-
tients with a nonproductive cough had abnormalities. When all 17 cases of patients with complaints of productive cough were reviewed with ultimate diagnosis in mind, 13 patients had PND (either PND-Rh or PND-Si) as an etiology of cough, while 4 patients did not have PND. Of these four patients, three had asthma and one had psychogenic cough.

Chest radiographs were not the primary focus of the study but were performed in 34 of the patients (94%). Three radiographs were abnormal: one showed interstitial fibrosis, while two demonstrated focal scarring. Cough resolved in all three cases, and in none did the radiographic abnormality bear any causal relationship to the cough.

**DISCUSSION**

Although PND-Rh and PND-Si are known to be important in the differential diagnosis of chronic cough, the timing and use of sinus imaging have not been fully defined. Some studies have obtained sinus imaging studies in every case in which PND was suspected, which can be close to 100% of patients,\(^8\) and treated all cases with abnormal sinus imaging studies for sinusitis as soon as the studies were available for review.\(^8,10\) Other studies have obtained sinus imaging only if signs of sinusitis (facial pain with colored nasal discharge) were present\(^4\) or if PND persisted despite treatment for PND-Rh.\(^6,9\) The only way to determine the relevance of mucosal thickening to diagnosis and treatment is to obtain imaging studies but not to treat patients immediately for sinusitis based on thickening, as was done in this study.

With our prospective sinus imaging studies, we were able to determine the sensitivity and specificity of sinus imaging in the diagnosis of PND-Si as an etiology of chronic cough. The sensitivity was 100%, but the specificity was only 50%. If mucosal thickening alone is examined, then the sensitivity remains 100% but the specificity drops to 29%, as 71% experienced resolution without treatment for sinusitis. In these cases, either the radiographic findings did not show bacterial infection or that infection, or the rhinitis it produced, was effectively treated with an antihistamine/decongestant, with or without nasal steroids and without antibiotics. The tradition with cough has been to define the etiology based on

**Table 1—Relationship Between Sinus Imaging Studies, Diagnoses, and Productive Cough**

<table>
<thead>
<tr>
<th>Data</th>
<th>No. of Patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal sinus imaging studies (n = 36)</td>
<td>10</td>
<td>28</td>
</tr>
<tr>
<td>Normal sinus imaging studies and eventual diagnosis of sinusitis (n = 26)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Abnormal sinus imaging studies from which either PND-Rh or PND-Si were ultimately diagnosed as an etiology of cough (n = 10)</td>
<td>10</td>
<td>100</td>
</tr>
<tr>
<td>Abnormal imaging studies from which sinusitis was ultimately diagnosed as a cause of cough (n = 10)</td>
<td>5</td>
<td>50</td>
</tr>
<tr>
<td>Ratio of breakdown and fluid/opacification mucosal thickening (n = 10)</td>
<td>3:7</td>
<td>30.70</td>
</tr>
<tr>
<td>Mucosal thickening alone ultimately diagnosed with sinusitis as a cause of cough (n = 7)</td>
<td>2</td>
<td>29</td>
</tr>
<tr>
<td>Complaint of productive cough (n = 36)</td>
<td>17</td>
<td>47</td>
</tr>
<tr>
<td>Complaint of productive cough in patients who had abnormal sinus imaging studies (n = 17)</td>
<td>7</td>
<td>41</td>
</tr>
<tr>
<td>Normal sinus imaging studies from patients with complaint of productive cough (n = 26)</td>
<td>10</td>
<td>38</td>
</tr>
</tbody>
</table>
response to treatment for that etiology. Using the previous definition, the patients with mucosal thick-ening who responded to treatment for PND-Rh alone had PND-Rh and false-positive imaging studies.

There were some positive correlations for sinus imaging studies, as all patients with abnormal sinus imaging studies had either PND-Rh or PND-Si as an etiology of cough. All three patients with air/fluid levels, opacification, or both were treated for sinusitis from the outset, because it would have involved deviation from normal practice not to do so. We cannot, therefore, assess whether any of these patients would have responded to treatment for PND-Rh alone. All three patients responded to their treatment for sinusitis.

We also examined the implications of a complaint of productive cough. The complaint was too nonspecific to have an impact on the diagnostic workup of any specific individual (Table 1). This finding is in keeping with others\textsuperscript{11} and with the conclusion that “a carefully taken history with detailed questioning of the character, timing, and complications of cough is not likely to be useful in diagnosing the cause of cough.”\textsuperscript{11}

The concept that an abnormality is not necessarily an etiology has been documented for asthma and chronic cough. We have demonstrated in a previous study that bronchial hyperresponsiveness as documented by methacholine challenge has a positive predictive value of only 68% for asthma as an etiology of cough.\textsuperscript{9} To our knowledge, no study has

\textbf{Figure 2. Algorithm for treatment of chronic cough, updated.}\textsuperscript{9}

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**Step 1: Post-Nasal Drip (PND)**

**Antihistamine-Decongestant (A/D)** at first visit regardless of findings. Use classic first-generation antihistamine. Assess at one week:

- If no response, go to step 2.
- If improvement, continue to point of maximum benefit. Then:
  - If cough still present and there are no symptoms of PND, go to step 2.
  - If cough still present and there are persistent symptoms of PND,
    - Add nasal steroids (NS). If ineffective,
      - Obtain sinus films and treat if sinus abnormalities consistent with sinusitis by adding oxymetazoline nasal spray and appropriate antibiotics. (For economy, get a chest x-ray if sinus films done.)

Alternatives to standard A/D include NS + antihistamine for patients intolerant of the decongestant component or NS + decongestant for those intolerant of the antihistamine. If cough persists after maximal benefit from step 1, go to step 2.

**Step 2: Bronchial Hyperresponsiveness**

Methacholine challenge (or histamine challenge).

- If negative, go directly to step 3.
- If bronchial hyperresponsiveness demonstrated,
  - Inhaled bronchodilator for one week. If ineffective (often the case),
  - Prednisone, 1 mg/kg/day with max 60 mg/d for one week.

If cough persists after maximal benefit from step 2, go to step 3.

**Step 3: Radiologic Evaluation**

At this point, it becomes cost-effective to get sinus and chest films if not already done. Treat as appropriate based upon findings. If cough persists after maximal benefit from step 3, go to step 4.

**Step 4: Gastroesophageal Reflux (GER)**

- If symptoms of GER clearly present, 2-week trial of proton pump inhibitor
- No clear response to above or no clear symptoms of GER: 24-hour pH probe study:
  - If within normal limits, go to step 5.
  - If abnormal, prolonged proton-pump inhibitor therapy + anti-reflux measures until maximum benefit achieved.

If cough persists after maximal benefit from step 4, go to step 5.

**Step 5: Bronchoscopy et al.**

Bronchoscope patient looking for undiagnosed endobronchial disease. If bronchoscopy negative, consider uncommon causes of chronic cough.\textsuperscript{9}
performed prospective 24-h pH-probe evaluations on all subjects in a study to determine similar statistics for gastroesophageal reflux disease.

Our data agree with data from other studies that suggest that plain radiographs of the sinuses are adequate for evaluation of sinusitis as an etiology of cough.\textsuperscript{6,8,9,10} Thirty-five of the sinus imaging studies were plain radiographs, and no case of sinusitis was missed. Thus, although CT scans of the sinuses with sagittal views are considered the “gold standard” in sinus imaging,\textsuperscript{12} they appear to add little to plain radiographs in the search for an etiology of chronic cough.

Cough resolved in only 86% of patients in this prospective study. This percentage is lower than that of several major studies,\textsuperscript{3,8,9,10} including one performed at this institution.\textsuperscript{9} We surmise that this is due to more effective treatment of cough by referring physicians, resulting in more difficult cases being sent to this practice. One hundred percent of patients seen for this study were patients who were referred after an initial failure to treat their cough by at least one other physician.

Note also that a diagnosis was believed to have been made in 100% of cases, but that despite the solid rationales presented above, the diagnoses in the five patients whose cough did not resolve are less secure than those for whom specific therapy eliminated cough. Using resolution criteria, the diagnostic accuracy in this series would be the same as the resolution rate, or 86%. This percentage is similar to the 88% reported by Poe et al\textsuperscript{6}. We did not in our series use the diagnostic category “postinfectious,”\textsuperscript{6,8} as we feel that in the vast majority of cases the mechanism of cough following a respiratory tract infection is PND or bronchial hyperresponsiveness.

In order to avoid a repeat radiology appointment for patients who reached the point in the algorithm at which a chest radiograph was indicated,\textsuperscript{9} chest radiographs were obtained at the time of the sinus imaging studies. This allowed a prospective look at chest radiographs. The utility in this series was 0%. The data in this study reinforce the concepts that chest radiographs are rarely useful in the workup of isolated chronic cough in nonsmokers,\textsuperscript{3,6,8,9} and that they need not be part of the initial approach to chronic cough.\textsuperscript{9}

This study, unlike most of those that have established the workup and treatment of chronic cough,\textsuperscript{3,8,9,10} did not eliminate active smokers, although smoking was not a focus of this study. The inclusion of smokers was based on two clinical observations. First, smokers with smoker’s cough rarely complain of the cough as a problem. Second, over the years we have noted that smokers with a chronic cough that does not appear to bear any relationship to smoking respond to our algorithm,\textsuperscript{9} which was established for nonsmokers. The number of patients in the study was too small to make any formal conclusions; therefore, this area deserves further scrutiny.

In conclusion, mucosal thickening shown on sinus imaging studies is not diagnostic of sinusitis as a cause of chronic cough and does not mandate antibiotic treatment for sinusitis; most patients will respond to treatment for rhinitis alone. The sensitivity of sinus radiographs is high, but specificity is low. The most efficient and effective way to treat chronic cough is to approach each diagnosis one at a time in the order of frequency of occurrence. The updated algorithm is presented in Figure 2. Studies for a specific diagnosis should be delayed until that diagnosis is under active investigation. In each instance, a negative study result, whether it is from sinus imaging, methacholine challenge, or pH-probe study, makes the diagnosis in question extremely unlikely,\textsuperscript{8,9,10} while an abnormal study does not establish the relationship between that finding and chronic cough. When studies are performed sequentially after elimination of more common etiologies of chronic cough, fewer studies will be performed, and those that are will have higher diagnostic yields and lower false-positive rates.

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