**Symptoms of Rhinosinusitis in Patients With Unexplained Chronic Fatigue or Bodily Pain**

**A Pilot Study**

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**Background:** Recent otolaryngologic studies document significant fatigue and bodily pain (BP) in patients with chronic rhinosinusitis. Studies of general medical patients are lacking.

**Methods:** A case-control study of 297 consecutive general medical outpatients.

**Results:** Sixty-five patients noted unexplained chronic fatigue (UCF), 33 reported BP, and 26 had both. Compared with 232 patients without UCF, patients with UCF more frequently had the following rhinosinusitis symptoms: facial pressure (odds ratio [OR], 9.7; 95% confidence interval [CI], 5.2-18.2), heavy-headedness (OR, 21.9; 95% CI, 10.9-44.0), nasal obstruction (OR, 4.3; 95% CI, 2.3-7.9), frontal headache (OR, 13.6; 95% CI, 6.5-28.5), postnasal drip (OR, 2.8; 95% CI, 1.6-5.0), sore throat (OR, 3.1; 95% CI, 1.3-6.6), and tender cervical lymph nodes (OR, 9.2; 95% CI, 4.3-19.7). A similar predominance of rhinosinusitis symptoms was noted in patients with BP and in 15 patients with UCF who had chronic fatigue syndrome. No increased prevalence of pollen allergy was noted in association with UCF, BP, or chronic fatigue syndrome. Gastrointestinal, sleep, and psychiatric problems were similar between patients with UCF and 38 patients with explained fatigue. Rhinosinusitis symptoms, however, were more common in UCF.

**Conclusions:** There is an increased prevalence of rhinosinusitis symptoms but not pollen allergy among general medical outpatients with UCF, BP, or both. Rhinosinusitis symptoms are at least as common as gastrointestinal complaints, sleep disturbance, and psychiatric problems (previously well documented complaints associated with UCF and BP). Rhinosinusitis symptoms, furthermore, are more common in UCF than in fatigue explained by a physical or mental illness.

Arch Intern Med. 2003;163:1832-1836

*C. HRONIC FATIGUE and bodily pain (BP) are familiar and frustrating symptoms seen by the internist. The differential diagnosis of chronic fatigue is long; an answer, if not apparent after a focused evaluation, is usually lacking. Similarly, widespread BP often eludes an adequate explanation. Inexplicable fatigue and pain, however, characterize numerous unexplained clinical conditions, including chronic fatigue syndrome (CFS), fibromyalgia, and multiple chemical sensitivity syndrome.6

Otolaryngology textbooks mention fatigue as a symptom of rhinosinusitis. Indeed, the Task Force on Rhinosinusitis of the American Academy of Otolaryngology—Head and Neck Surgery established fatigue as a minor diagnostic criterion of chronic rhinosinusitis. In contrast, chronic rhinosinusitis is not listed in the differential diagnosis of fatigue or BP in any general medical textbook, to my knowledge, and studies in the general medical literature of any association are scattered and few.8,9

Recently, otolaryngologists, armed with an interest in health-related quality-of-life issues and improved survey instruments, have demonstrated diminished vitality and increased BP in patients with chronic rhinosinusitis. Scores for both were significantly lower (indicating worse symptoms of disease) than in older populations with serious medical problems.11 Functional endoscopic sinus surgery improved vitality and reduced BP, often to levels comparable to those of the general population.13-17

Fatigue and BP are treated by internists; yet, the intriguing reports of the results of endoscopic sinus surgery are limited to otolaryngology journals. Studies examining general medical outpatient populations with fatigue or BP for rhino-
sinusitis symptoms are lacking. The objective of this pilot study was to explore the prevalence and significance of rhinosinusitis symptoms among these populations: Do the relationships noted in the otolaryngologist’s office hold true in the internist’s office?

### METHODS

Three hundred eight consecutive outpatients younger than 41 years presenting for a general physical examination were questioned. This group included patients free of specific medical complaints and patients consulting for a particular problem. Eleven were excluded (8 refused to participate and 3 provided insufficient data). After obtaining consent, the 297 remaining patients were interviewed and examined by a single general medical practitioner (A.C.C.). Each was asked the standard medical history questions and specific questions related to fatigue, BP, and rhinosinusitis. The following laboratory data were obtained: complete blood count, erythrocyte sedimentation rate, thyroxine, standard 24-channel chemistry screen, rapid plasma reagin test, urinalysis, and, for those older than 30, a chest roentgenogram.

After review of the history, physical examination, and laboratory test results, patients with fatigue were separated into 3 groups: those with unexplained chronic fatigue (UCF), explained fatigue (EF), and acute fatigue. Unexplained chronic fatigue was defined as chronic fatigue, a continuing troublesome tiredness or lack of energy for longer than 1 month that was not a normal response to excessive physical or mental demands and not due to a physical or mental illness. By definition and study design, patients with UCF were young and free of fatiguing diseases. Illnesses, when present, were generally minor and brief or were conditions unassociated with fatigue, such as mitral valve prolapse. Six patients with UCF required chronic medication other than oral contraceptives: antidepresants (3 patients), a tranquilizer (1 patient), and low-dose prednisone (1 patient with congenital adrenal hyperplasia and 1 patient with ulcerative colitis). In these 6 patients, symptoms were well controlled, and a contemporaneous relationship of fatigue to disease or medication was lacking.

The EF group included patients with chronic fatigue that was apparently caused by a physical or mental illness. The acute fatigue category was limited to those with explained or unexplained fatigue of less than 1 month’s duration. Those with mild fatigue, defined as fatigue causing no significant effect on well-being, were not considered fatigued for the purposes of this study. Some patients with UCF met previously published criteria for CFS, a severe and often disabling illness characterized predominantly by unexplained fatigue.19 Unexplained chronic BP was defined as widespread musculoskeletal pain for longer than 1 month from no apparent cause. Symptoms were considered as positive for this study if they were constant or recurrent, present for longer than 1 month, and problematic (eg, those with “sore throat” had sore throats frequently and severely enough to be troublesome). Nasal obstruction was the perception of insufficient airflow in either nostril. Sleep disturbance was defined as a troublesome difficulty in initiating or maintaining sleep. Symptoms of depression were obtained from the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV).20 Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters.

Selected symptoms of chronic rhinosinusitis were adapted from the Task Force on Rhinosinusitis of the American Academy of Otolaryngology–Head and Neck Surgery1 (Tables 1, 2, and 3). In addition, as recommended by the task force, the term chronic sinusitis was abandoned in this article, substituting chronic rhinosinusitis for terms of clarity and accuracy.

Statistical analysis was performed using the unpaired t test to compare means, and Fisher exact test to compare differences between groups, using Yates continuity correction and the approximation of Woolf, when applicable. Analyses were performed using GraphPad InStat software, version 3.0 for Windows (GraphPad Software, Inc, San Diego, Calif). The significance level, the probability of a type I error, was set at P < .05 (2-sided).

### RESULTS

The study sample comprised 297 patients (46% women and 54% men) with a mean ± SD age of 30.3 ± 6.9 years (range, 14–40 years). The population was well edu-
cated, averaging 17 years of schooling, overwhelmingly white, and middle class. Sixty-five (22%) were found to have UCF. Fifteen (23%) of these patients had CFS. Explained fatigue was noted in 38% of the 297 and acute fatigue in 13% of UCF experience. Thirty-three (11%) of the 297 patients complained of BP, and 26 (79%) of the 33 with UCF complained of BP. Sixty-five (22%) were found to have UCF. Fifteen (22%) of the 65 patients and occurred in 14 (58%) of the 24 after an upper respiratory tract illness.

No significant differences in mean age (30.9 vs 30.1 years; P = .45), BMI (22.2 vs 23.5; P = .05), or laboratory findings were noted in patients with UCF vs control. Education and marital status were similar. Women were overrepresented in the UCF group (60% vs 42%; P = .01), as were smokers (26% vs 13%; P = .02).

Physical examination results were similar. A lower recumbent but not semirecumbent systolic and diastolic blood pressure, however, was noted in patients with UCF compared with control (SBP: 120.8 vs 125.3 mm Hg, P = .02). In addition, more rapid recumbent and semirecumbent heart rates were noted in the UCF group (70.2 and 66.7/min, P = .04; and 74.3 and 70.3/min, P = .02, respectively). No difference in pollen allergy history was noted between the 2 groups (51% of patients with UCF vs 38% of control, P = .09). Gastrointestinal symptoms were more prevalent among the UCF group than control (odds ratio [OR], 1.8; 95% confidence interval [CI], 1.0-3.1; P = .04). The presence of any DSM-IV symptom of depression was more common in the UCF group than in control (58% vs 38%; OR, 2.3; 95% CI, 1.3-4.0; P < .005), as was a history of sleep disturbance (26% vs 8%; OR, 4.0; 95% CI, 1.9-8.2; P < .001) and a lifetime history of psychiatric care (62% vs 42%; OR, 2.2; 95% CI, 1.3-3.9; P = .007).

The prevalence of rhinosinusitis symptoms among the UCF group compared with control is noted in Table 1.

The UCF group included 15 patients with CFS. The mean age of the patients with CFS was similar to that of control (30.8 and 30.1 years, respectively). The fatigue started suddenly in 6 patients (40%), 4 of whom developed fatigue after an upper respiratory tract infection.

No significant differences in BMI, physical examination, or laboratory findings were noted in the CFS group compared with control. Education, marital status, and smoking history were similar. Women were not overrepresented (53% of the CFS group vs 42% of control, P = .43).

Compared with control, all rhinosinusitis symptoms (except postnasal drip) were significantly more common in patients with CFS: facial pressure (80% vs 13%; OR, 26.0; 95% CI, 7.0-97.2; P < .001), heavy-headedness (80% vs 8%; OR, 44.8; 95% CI, 11.6-172.9; P < .001), nasal obstruction (87% vs 42%; OR, 9.1; 95% CI, 2.0-41.0; P < .001), frontal headache (53% vs 6%; OR, 19.2; 95% CI, 6.0-61.4; P < .001), postnasal drip (40% vs 20%; OR, 2.6; 95% CI, 0.9-7.7; P = .10), sore throat (33% vs 8%; OR, 5.6; 95% CI, 1.7-18.1; P = .01), and cervical node tenderness (60% vs 6%; OR, 25.3; 95% CI, 7.8-81.8; P < .001).

The following psychiatric symptoms were more common in patients with CFS than in control: any DSM-IV symptom of depression (73% vs 38%; OR, 4.4; 95% CI, 1.4-14.3; P = .01), sleep disturbance (47% vs 8%; OR, 9.8; 95% CI, 3.2-30.0; P < .001), and a lifetime history of psychiatric care (73% vs 42%; OR, 3.8; 95% CI, 1.2-12.4; P = .03). A history of pollen allergy was not more common in patients with CFS than in control (47% in the CFS group vs 38% in control, P = .06).

Explained fatigue was noted in 38 patients. Compared with those of patients with UCF, physical examination, BMI, and laboratory findings were similar. No differences in age (32.2 vs 30.9 years), sex (58% vs 60% women), marital status (58% vs 68% married, P = .31), current smoking history (11% vs 26% smokers, P = .08), or education (17 vs 17 years) were apparent between patients with EF vs UCF. The prevalence of gastrointestinal complaints (47% and 48%), sleep disturbance (18% and 27%, P = .47), or any symptom of depression (66% and 58%, P = .53) among patients with EF and UCF, respectively, was no different. All rhinosinusitis symptoms except postnasal drip (24% vs 42%, P = .09) and sore throat (21% vs 22%, P = .99), however, were less common in EF (Table 3).

Thirty-three patients with BP were compared with 264 patients without BP (control). No significant differences in mean age (31.7 years in the BP group vs 30.1 years in control; P = .43), BMI (22.2 vs 23.5 in control; P = .13), or laboratory findings were noted. Marital status and educational level were similar. Women were not overrepresented in the BP group compared with control (61% vs 44%, P = .09), nor were smokers (24% vs 15%, P = .21). No difference in pollen allergy prevalence was noted between those with BP and control (48% vs 39%, P = .45).

Except for a more rapid semirecumbent heart rate in patients with BP (75.3 vs 70.7/min, P = .04), no differences in blood pressure or other physical examination findings were noted.

The prevalence of rhinosinusitis symptoms among patients with BP is noted in Table 2.

Psychiatric symptoms were more common in patients with BP than in control: any DSM-IV symptom of depression (73% vs 39%; OR, 4.2; 95% CI, 1.9-9.3; P < .001), history of psychiatric care (70% vs 43%; OR, 3.0; 95% CI, 1.4-6.6; P = .005), and sleep disturbance (30% vs 10%; OR, 4.0; 95% CI, 1.7-9.3; P = .002).

Among the 65 patients with UCF, the 26 patients with concurrent UCF and BP did not differ from those without BP in population characteristics, physical examination results, or laboratory findings. Gastrointestinal complaints, sleep disturbance, and psychiatric symptoms were all comparable. Likewise, except for facial pressure, which was more common in those with concurrent UCF and BP (OR, 3.5; 95% CI, 1.2-10.6; P = .04),
the prevalence of all other rhinosinusitis symptoms was similar.

**COMMENT**

This pilot study found a preponderance of rhinosinusitis symptoms in patients with UCF, BP, or both. Headache, frontal headache, and facial pressure are most commonly associated. Sore throat and postnasal drip are the least commonly associated symptoms. Although rarely mentioned in the general medical literature, these nasal associations are at least as prevalent as the previously well-described associations of UCF and BP with gastrointestinal, sleep, and psychiatric illnesses.

Otolaryngologists note similar findings. Bhat-tacharya describes severe or very severe fatigue in 32% of patients with chronic rhinosinusitis. Furthermore, he notes that patients often relate their fatigue to the severity of their sinonasal symptoms. Gliklich and Metson, measuring health-related quality of life using the Medical Outcomes Study 36-Item Short Form Health Survey, found scores for vitality and BP in patients with chronic rhinosinusitis that were significantly lower (indicating worse symptoms of disease) than those in a population 20 years older with congestive heart failure, chronic obstructive pulmonary disease, angina, or back pain. Sinus surgery restored these quality-of-life measurements to near normative levels. In a similar study, children with chronic rhinosinusitis had significant BP and were more limited in their activities than children with asthma, rheumatoid arthritis, and other chronic diseases. Other studies note comparable burdens of fatigue and BP in patients with chronic rhinosinusitis and improvement after sinus surgery.

Postoperative improvement was not related to preoperative sinus disease severity as judged by computed tomographic findings. To my knowledge, no surveys have addressed the prevalence of rhinosinusitis among general medical outpatients with UCF or BP. Unlike studies from the otolaryngologist’s practice, which reflect more serious sinus disease, this study mirrors the internist’s practice: the 22% prevalence of UCF and 11% prevalence of unexplained generalized BP are representative of general medical outpatient populations. The female predominance in UCF (60% of the UCF group vs 42% of controls, P = .01) is consistent with other studies, as is the abundance of rhinosinusitis symptoms in outpatients. This study suggests that the association of rhinosinusitis with UCF and BP noted by otolaryngologists is not the product of a skewed sample of severe sinus disease but is typical also of a general medical outpatient population.

Prior studies of patients with UCF or BP also suggest a nasal association. In 1988, initial consensus diagnostic criteria were established to define CFS, a particularly severe form of UCF usually accompanied by BP. Despite vigorous research, no cause has been identified, and no specific diagnostic test is available. Chronic fatigue syndrome criteria were also noted in other forms of UCF. Of the 8 criteria, 3 are possibly of sinus origin: sore throat, tender cervical lymph nodes, and new headaches. Four other criteria have been described in rhinosinusitis as well: impaired memory or concentration, muscle pain, multijoint pain, and unrefreshing sleep. Furthermore, CFS is frequently sudden in onset, often after an upper respiratory tract infection (as is rhinosinusitis). In this study, 37% of patients with UCF and 40% of patients with CFS experienced fatigue of sudden onset, with 58% and 67%, respectively, occurring after an upper respiratory tract infection. A preponderance of rhinosinusitis symptoms noted in patients with UCF was also found in those with CFS.

The prevalence of rhinosinusitis among patients with BP has not, to my knowledge, been examined. Cleveland et al, in a study of outpatients with rhinitis, noted a history of diffuse, aching pain, or tiredness for at least 3 months in 49%. In addition, a 38% prevalence of fibromyalgia vs an expected 4% to 5% prevalence was noted. Included among the necessary fibromyalgia diagnostic criteria are widespread BP for at least 3 months and tenderness of at least 11 of 18 tender points on palpation.

Despite the abundance of rhinosinusitis symptoms and the established relationship between rhinosinusitis and pollen allergy, no significant relationship was noted in this study between UCF, CFS, or BP and pollen allergy. In addition, Cleveland et al found no correlation of atopy with fibromyalgia in patients with rhinitis. These results also corroborated those of Baraniuk et al and Repka-Ramirez et al, who described a preponderance of rhinosinusitis and irritant rhinitis in patients with CFS but not a disproportionate prevalence of positive allergic skin test results or elevation of IgE. Irritant rhinitis, they noted, was also common in control subjects with fatigue not meeting CFS criteria (P < .001). Increased mucin production and mucosal friability characterized the secretions of those with CFS.

Rhinosinusitis symptoms in this study were more common in patients with UCF than in those with fatigue explained by a physical or mental cause (Table 3). No difference, however, was noted in the prevalence of symptoms often termed functional: gastrointestinal, sleep, and psychiatric complaints. If, as suggested by prior studies, UCF may be related to rhinosinusitis, an increased prevalence of rhinosinusitis symptoms would be expected in UCF compared with other forms of fatigue.

It appears that the internist’s office mirrors the otolaryngologist’s office. The results of this study, like prior ones, suggest a relationship between the nose and the syndromes of UCF and BP. Limitations of this study include the small size, cohort study design, and possible observer bias with the use of an orally administered survey. In addition, the results are based on patient-derived (ie, subjective) reporting. Computed tomographic findings, however, correlate poorly with symptoms. Strengths of this study include reduced bias because of minimal patient exclusion and a study population characteristic of other typical outpatient survey groups.

Although the findings of this pilot study require confirmation, the results suggest that rhinosinusitis symptoms are at least as common as other well described associations in UCF and BP (ie, gastrointestinal, sleep, and psychiatric complaints) and that rhinosinusitis symptoms in part differentiate UCF from EF. Other stud-
ies noting nasal symptoms and mucus abnormalities in UCF lend support to the findings noted herein. Whether functional endoscopic sinus surgery can help the internist's tired achy patient as it appears to do with such success for the otolaryngologist's cohort awaits further investigation.

Accepted for publication October 21, 2002.

This study was presented in part at the Cambridge Symposium on Myalgic Encephalomyelitis/Chronic Fatigue Syndrome, Cambridge University; April 12, 1990; Cambridge, England; and at the Fourth International American Association of Chronic Fatigue Syndrome Conference; October 11, 1998; Boston, Mass.

I thank Corinna M. Vance for help with data analysis.

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