COMPUTED TOMOGRAPHIC STUDY OF THE COMMON COLD

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Abstract *Background.* Colds are common, but the abnormalities they produce in the nasal passages and sinus cavities have not been well defined.

Methods. We studied healthy adult volunteers with self-diagnosed colds of 48 to 96 hours' duration and obtained the following data: information on symptoms, computed tomographic (CT) studies of the nasal passages and sinuses, mucosal-transport times, measures of nasal-airway resistance, and viral-culture studies. Thirty-one subjects (mean age, 24 years) had complete evaluations, including CT scans, which were read without knowledge of the clinical data. An additional 79 subjects underwent the same evaluations, except the CT scans.

Results. Of the 31 subjects with CT scans, 24 (77 percent) had occlusion of the ethmoid infundibulum; 27 (87 percent) had abnormalities of one or both maxillary-sinus cavities; 20 (65 percent) had abnormalities of the ethmoid sinuses; 10 (32 percent) had abnormalities of the frontal sinuses; and 12 (39 percent) had abnormalities of the sphenoid sinuses. Infraorbital air cells were present in 14 subjects (45 percent), and pneumatization of the middle turbinate (concha bullosa) was noted in 11 subjects (35 percent). Also common were engorged turbinates (in 7 subjects) and thickening of the walls of the nasal passages (in 13). After two weeks, the CT studies were repeated in 14 subjects, none of whom received antibiotics. In 11 of these subjects (79 percent) the abnormalities of the infundibula and sinuses had cleared or markedly improved. Nasal-airway resistance was abnormal in 29 (94 percent) and mucosal transport in 19 (61 percent) of the 31 subjects who had CT scans. Rhinovirus was detected in nasal secretions from 24 (27 percent) of 90 subjects.

Conclusions. The common cold is associated with frequent and variable anatomical involvement of the upper airways, including occlusion and abnormalities in the sinus cavities. (N Engl J Med 1994;330:25-30.)

STUDIES of the common cold have relied on diagnosis by the patients themselves[1-3] or diagnosis by an investigator using individual symptoms reported by the patients.[4-6] These methods have limited usefulness for determining which anatomical areas of the upper airway are involved in the illness. There is a general assumption that in the upper airway the cold is mainly confined to the nasal passages and pharynx. Extension of the illness to the paranasal sinuses is thought to represent a complication.

Computed tomographic (CT) scanning allows detailed imaging of the nasal passages, ostiomeatal complex, and paranasal sinuses. We obtained CT scans of the nasal passages and sinuses of subjects with early, naturally acquired colds and correlated the findings with symptom scores, data on nasal-airway resistance, and mucosal-transport times to determine how the common cold involves the upper airway.

METHODS

Subjects

Subjects 18 years of age or older were recruited by solicitations for volunteers with a "fresh common cold." Volunteers were screened by telephone for eligibility in a way designed to mask the criteria for enrollment in the study. These criteria included good health other than having the common cold; duration of symptoms of at least 48 hours but less than 96 hours; no active allergic rhinitis or other respiratory illness; no history of recurrent or chronic sinusitis or nasal polyps; no use of cough, cold, or analgesic drugs within 8 hours before enrollment; and reported nasal or head congestion at the time of the initial visit. After 28 subjects had been enrolled, the last criterion was eliminated to allow investigation of CT findings in subjects without congestion.

Of the 356 people who volunteered to participate in the study, 129 were excluded because they could not or did not keep the initial appointment or could not be accommodated in the study at a given time; 65 because they had been ill too long; 13 because their cold symptoms had subsided; 15 because of a history of allergy, asthma, or chronic sinus disease; 8 because they did not report congestion; 5 because they were being treated for another illness; 2 because they could not tolerate dye in the nose; and 2 because they were under 18 years of age. A total of 117 volunteers were enrolled in the study, and 110 completed it (8 of the 110 missed an appointment on one day of the study but were included for the purpose of data analysis). After enrollment, patients were observed for six days, during which time they did not use acetaminophen as an analgesic. The study was approved by the Human Investigation Committee of the University of Virginia.

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Subjective Measurement of Illness

The subjects reported symptoms by entering information in a computer program with a rating scale from 0 (not present) to 10 (very severe). They used the scale to respond to questions about sneezing, runny nose, nasal stuffiness, sore throat, cough, fatigue or lethargy, muscle aches and pains, chills, feverishness, and headache. The subjects were also asked whether they had nasal or head congestion. Symptoms were assessed at the time of enrollment and daily between the hours of 8 a.m. and 11 a.m. for six days.

Nasal-Airway Resistance

Nasal-airway resistance was measured by single-nostril active anterior rhinomanometry.[7] Beginning with the left nostril, nasal airflow and transnasal pressure at the contralateral nostril were measured over the course of four consecutive breaths with the use of a commercial rhinomanometer (John Connell, Englewood, N.J.). During the measurement, pressure and flow signals were digitized at a sampling rate of 100 Hz and displayed on the computer monitor. The primary measure of nasal patency was the rate of flow (in liters per second) at a reference transnasal pressure of −1.5 cm of water during inspiration. A value under 0.6 liter per second for white subjects or under 0.7 liter per second for black subjects was considered abnormal.[8]

Virologic Studies

Viral-culture studies were performed with nasal secretions from the last 90 subjects enrolled in the study. The subjects expelled the contents of their nasal passages onto a plastic film. Secretions were then transferred by cotton swab to a vial containing 5 ml of beef-heart infusion broth with 1 percent bovine serum albumin and antibiotics. This method was used to avoid irritation of the nose

by nasal swabbing or washing. Specimens were inoculated into three human embryonic lung-cell monolayers of the WI-38 strain (BioWhittaker, Walkersville, Md.). Viral isolates were identified as rhinoviruses by their characteristic cytopathic effect and acid lability.[9]

Nasal Mucosal Transport

Nasal mucociliary clearance was determined by a modification of a previously described method.[10-12] Fifteen microliters of a test solution was placed on the mucosa of each nostril in the anterior part of the nasal cavity below the inferior meatus. The test solution consisted of 8 mg of indigo carmine per milliliter, 3 mg of saccharin per milliliter, and 45 mg of sorbitol per milliliter (pH adjusted to 7.4). The subjects reported the first occurrence of a sweet taste, and then the pharyngeal cavity was examined for the appearance of the blue dye. Repeated inspections of the pharynx were made at 30-second intervals for 30 minutes or until dye was observed on each side. The combined clearance time was defined as the time elapsed from the introduction of the test solution to the first report of a sweet taste. Separate clearance times for the right and left nasal passages are not reported. For the combined clearance time, the occurrence of a sweet taste 20 minutes or more after the introduction of the solution was considered abnormal.

CT Scans of the Upper Airway

CT scans of the nasal passages, ostiomeatal complex, and paranasal sinuses were obtained in 33 (30 percent) of the 110 subjects. Two subjects were excluded from the analysis because of bony changes in the maxillary antra, which were thought to be the result of chronic sinus disease. Twenty-eight subjects underwent CT scanning within 24 hours after enrollment, and three within 48 hours after enrollment. Subjects were selected for CT scanning primarily on the basis of scheduling considerations; the severity of illness was not a factor in selection. Fifteen to 20 images were obtained in a direct coronal plane that included the nasal passages and sinuses (GE-9800 Quick scanner, General Electric, Schenectady, N.Y., or Picker PQ-2000 scanner, Picker International, Cleveland). Fourteen subjects with abnormalities of the sinuses on the initial CT scans had repeat scans and repeat studies of nasal mucosal transport and airway resistance 8 to 15 days later. All scans were read independently by two radiologists who had no clinical information on the subjects; the radiologists compared their readings and resolved any differences in interpretation.

Results

Characteristics of the Study Subjects

Subjects were enrolled in the study between June 9 and October 9, 1992. Of the 31 subjects who had CT scans, 21 were women and 10 were men; 25 were white and 6 were nonwhite. Their ages ranged from 19 to 35 years, with a mean of 24 years. Of the 79 subjects who did not have CT scans, 50 were women and 29 were men; 69 were white and 10 were nonwhite. Their ages ranged from 18 to 55 years, with a mean of 23.5 years.

Illnesses in both groups were typical common colds. Rhinorrhea and nasal stuffiness were the most prominent respiratory symptoms, followed by cough and sore throat. Total symptom scores over six days ranged from 28 to 236 for the subjects who had CT scans and from 53 to 333 for those who did not (Table 1). The mean total scores (±SD) were 132±50 and 156±63 for the respective groups (P = 0.07 by Student's t-test). The greater severity of illness in the group without CT scans was attributable mainly to the systemic symptoms of lethargy, myalgia, chilliness, and headache.

Table 1. Symptoms, Delayed Mucosal Transport, and Abnormal Nasal-Airway Resistance in 110 Adults with Naturally Acquired Colds.*

Subject Group	Symptom						Delayed Mucosal Transport	Abnormal Nasal-Airway Resistance
	Rhinorrhea	Nasal Stuffiness	Sore Throat	Cough	Headache	Total†		
	score						no. of days	
With CT scans (n = 31)	22±11.5	21±11.5	17±10	18±15	11±10	132±50	2.1±2	4.2±2
Without CT scans (n = 79)	20±9	24±9	15±12	21±15	16±13	156±63	3.3±2	4.4±2

*Values are means ±SD.

†The total symptom score is the sum of the daily scores for symptoms of sneezing, rhinorrhea, nasal stuffiness, sore throat, cough, headache, feverishness, chilliness, myalgia, and lethargy or fatigue, over a period of six days.

Viral Cultures

Viral cultures of nasal secretions yielded rhinovirus isolates in 24 of 90 subjects (27 percent): 7 of 17 subjects who had CT scans (41 percent) and 17 of 73 who did not (23 percent) (P = 0.2 by Fisher's exact test). The total six-day symptom scores for the 24 rhinovirus-positive subjects ranged from 53 to 247 (mean, 152±53). Thus, the colds that were associated with rhinovirus tended to be in the middle range of severity for the group as a whole.

Nasal-Airway Resistance

Rhinomanometric studies showed abnormal nasal-airway resistance on 1 or more days in 29 of the 31 subjects with CT scans (94 percent); the number of days ranged from 1 to 6 (mean, 4.2±2). The subjects with the 10 highest symptom scores had abnormal airway resistance on an average of 4.1 days, as compared with an average of 3.8 days for those with the 10 lowest symptom scores. None of the 6 subjects with abnormal airway resistance on two or fewer days had CT evidence of swelling of the turbinates or thickening of the nasal wall, as compared with 9 of the 16 subjects (56 percent) with abnormal airway resistance on all six days (P = 0.05 by Fisher's exact test).

Mucosal Transport

A delay in mucosal transport was noted on one or more days in 19 of the 31 subjects (61 percent) who had CT scans and in 63 of the 79 (80 percent) who did not (P = 0.08 by Fisher's exact test) (Table 1). The mean number of days of abnormal mucociliary clearance was 2.1±2.2 for the subjects who had CT scans and 3.3±2.2 for those who did not (P = 0.01 by Student's t-test). These results, like the data on symptoms, suggest that illnesses were somewhat more severe in the group of subjects who did not have CT scans.

Mucosal-transport times correlated with the severity of illness as indicated by the six-day symptom scores. In the group with CT scans, the transport time was abnormal on one or more days in 8 of the 10 subjects with the highest total symptom scores but in only 2 of the 10 subjects with the lowest total scores ($P = 0.02$ by Fisher's exact test). The mean number of days on which measurements were abnormal in these groups was 3 and 0.5, respectively ($P = 0.005$ by Student's t-test).

CT Scans

Twenty-two of the 31 subjects with CT scans (71 percent) reported nasal or head congestion, and 9 did not. Of the subjects with congestion, 21 (95 percent) had occlusion of the ethmoid infundibulum, as compared with 3 of the 9 subjects without congestion (33 percent) ($P = 0.001$ by Fisher's exact test). All 22 subjects reporting congestion had abnormalities of one or more sinuses, as compared with 5 of the 9 subjects (56 percent) who did not report congestion ($P = 0.004$ by Fisher's exact test).

Twenty-four of the 31 subjects with CT scans (77 percent) had occlusion of the ethmoid infundibulum (Table 2). In 16 of these subjects (67 percent) the occlusion was bilateral. All 24 subjects with unilateral or bilateral infundibular occlusion had abnormalities of one or more sinuses, whereas only 3 of the 7 subjects without infundibular occlusion (43 percent) had abnormalities of the sinuses ($P = 0.002$ by Fisher's exact test). None of the four subjects with normal sinus cavities had infundibular occlusion.

Twenty-seven of the 31 subjects with CT scans (87 percent) had abnormalities of one or both maxillary sinuses; the abnormalities were bilateral in 23 subjects (85 percent) and unilateral in 4 (15 percent). Twenty of the 31 subjects (65 percent) had abnormalities of the ethmoid sinuses, and in 12 of the 20 (60 percent) the abnormalities were bilateral. Abnormalities of the maxillary sinuses were present in all subjects who had ethmoid abnormalities and in seven of those who did not. Frontal-sinus abnormalities were present in 10 of the 31 subjects (32 percent), and sphenoid-sinus abnormalities were present in 12 (39 percent).

The abnormal findings consisted of radiopaque material in the sinus cavity that had the density of soft tissue or fluid. These changes have traditionally been interpreted as mucosal swelling, except when an air–fluid level is present. However, the nonuniform areas of opacity suggested the presence of thick secretions. A definite air–fluid level was observed in the sphenoid and frontal sinuses in one subject and in the maxillary and sphenoid sinuses in another. The thickness of the abnormal material in the maxillary sinuses ranged from 2 to 15 mm and averaged 4.6 mm on the right and 4.4 mm on the left. The mean thickness of abnormal material in the other sinuses was 2.7 and 3.0 mm in the right and left frontal sinuses, respectively; 3.1 and 3.2 mm in the right and left ethmoid sinuses, respectively; and 3.8 mm in the sphenoid sinus. The extent and degree of abnormality in the sinus cavities tended to be greater in the subjects with higher symptom scores than in those with lower scores (i.e., milder illnesses), but these associations were inexact. Unilateral or bilateral infundibular occlusion was present in 6 of 7 subjects with rhinovirus (86 percent) and in 18 of 24 without rhinovirus (75 percent), and sinus-cavity abnormalities were detected in 6 subjects (86 percent) and 21 subjects (88 percent), respectively.

Table 2. CT Findings in 31 Adults with Naturally Acquired Colds.

Site	No. of Patients (%)
Nasal passages	
Septal deviation	6 (19)
Engorged turbinate	
Right	7 (23)
Left	7 (23)
Thickened nasal wall	13 (42)
Ostiomeatal complex	
Infraorbital cells	
Right	11 (35)
Left	14 (45)
Ethmoid bullosa	
Right	6 (19)
Left	6 (19)
Concha bullosa	
Right	10 (32)
Left	6 (19)
Infundibular occlusion	
Right	20 (65)
Left	20 (65)
Sinus Thickness	**mm (Mean ±SD)***
Frontal	
Right	2.7±5
Left	3±7
Ethmoid	
Right	3.1±9
Left	3.2±9
Maxillary	
Right	4.6±3
Left	4.4±3
Sphenoid	3.8±2.3

*Means were calculated from abnormal values only.

Preexisting, fixed anatomical variations in the 31 subjects who had CT scans included marked septal deviation in 6 (19 percent), infraorbital air cells (Haller cells) in 14 (45 percent), enlarged ethmoid bullae in 6 (19 percent), and concha bullosa (air cells of the turbinate) in 11 (35 percent) (Table 2). Acute, reversible changes included engorged turbinates in 7 subjects (23 percent) and mucosal thickening of the nasal walls in 13 (42 percent). Eighteen of the 24 subjects with ethmoid infundibular occlusion (75 percent) had anatomical variations, as did 6 of the 7 subjects without infundibular occlusion (86 percent). Fourteen of the subjects with occlusion (58 percent) and none without it had engorged turbinates or thickened nasal walls ($P = 0.03$ by Fisher's exact test). Also, none of the 4 subjects without sinus abnormalities had engorged turbinates or thickened nasal walls, as compared with 14 of the

27 subjects with sinus abnormalities (52 percent) ($P = 0.2$ by Fisher's exact test).

Follow-up Evaluations

Fourteen subjects with abnormalities on CT scanning underwent a follow-up evaluation after 13 to 20 days of illness (Fig. 1 and 2). Eleven of the 14 (79 percent) reported feeling well at the time of follow-up. The mucosal-transport time had returned to normal and sinus abnormalities had resolved or markedly improved in 11 of the subjects (79 percent). Nasal-airway resistance had returned to normal in only six subjects (43 percent); however, in nine (64 percent) the flow rate was higher than the mean rate during the acute illness. All values and anatomical findings had returned to normal in only 3 of the 14 subjects at the time of follow-up.

Nasal-airway resistance remained abnormal in the three subjects with persistent symptoms; the mucosal-transport time remained abnormal in two of the three. However, the CT scans in all three subjects showed marked improvement. Three of the subjects who did not report persistent symptoms had sinus CT scans that showed residual abnormalities; two had had air–fluid levels on their initial scans. One of these three subjects had persistently abnormal nasal-airway resistance, but the mucosal-transport time had returned to normal in all three. Thus, there was not a close correlation between the resolution or persistence of the symptoms of illness and the objective findings of the other follow-up studies.

Discussion

In a group of adults with naturally acquired common colds, we found a high prevalence of ostiomeatal and sinus abnormalities on CT scans. Although the high prevalence of sinus abnormalities was surprising, their reversal without antimicrobial treatment was not, since most colds are self-limited. These findings indicate that the common cold is actually a viral rhinosinusitis.

That the abnormalities in the sinus cavities were directly or indirectly caused by a virus might be inferred from their early appearance and reversibility without antimicrobial treatment. A viral rhinitis may lead to sinus-cavity disease by obstructing sinus drainage with or without direct invasion of the sinus cavity. Respiratory viruses, including rhinovirus, unaccompanied by bacteria have been recovered directly from the sinus cavity in adults with acute sinusitis.[13] Acute bacterial sinusitis has been reported to follow the common cold in 0.5 percent[1] to 5 percent[14] of cases. In our study, 3 of 14 subjects (21 percent) had marked but resolving abnormalities on follow-up CT scans. Whether those with persistent abnormalities are more prone to secondary bacterial sinusitis is uncertain.

Anatomical variations, as well as reversible abnormalities of the nasal passages and ostiomeatal area,

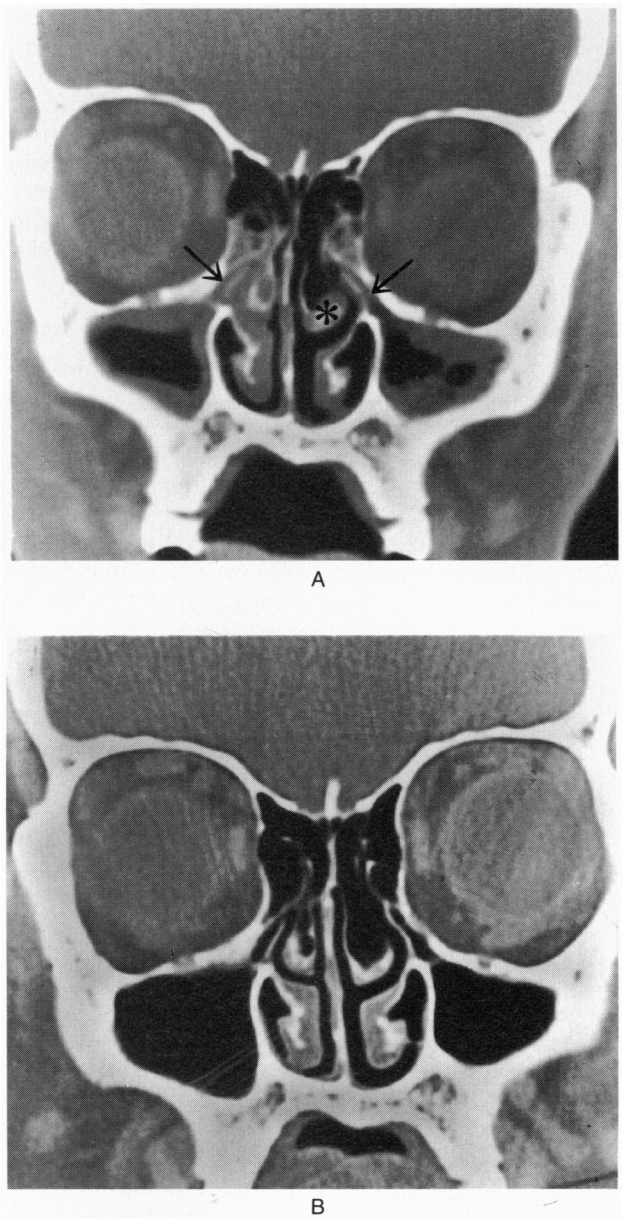

Figure 1. Initial and Follow-up Sinus CT Scans in an Untreated Adult (Subject 1) with the Common Cold.

The initial scan, obtained on day 4 of illness (Panel A), shows bilateral occlusion of the ethmoid infundibulum (arrows), the passage draining the maxillary sinus; abnormalities of the ethmoid sinuses (right, 4 mm; left, 4 mm) and maxillary sinuses (right, 4 mm; left, 7 mm); and bilateral pneumatization of the middle turbinate (concha bullosa [asterisk]). The scan obtained on day 13 (Panel B) shows minimal residual infundibular occlusion and a residual abnormality of the right maxillary sinus (2 mm).

were present in many of our subjects: septal deviation in 19 percent, infraorbital air cells in 45 percent, and concha bullosa in 35 percent. In the general population, the reported prevalence of these abnormalities is 19.5 percent, 45 percent, and 11 to 16 percent, respectively.[15-17] However, it was the reversible abnormalities — thickened nasal walls, engorged turbinates, and

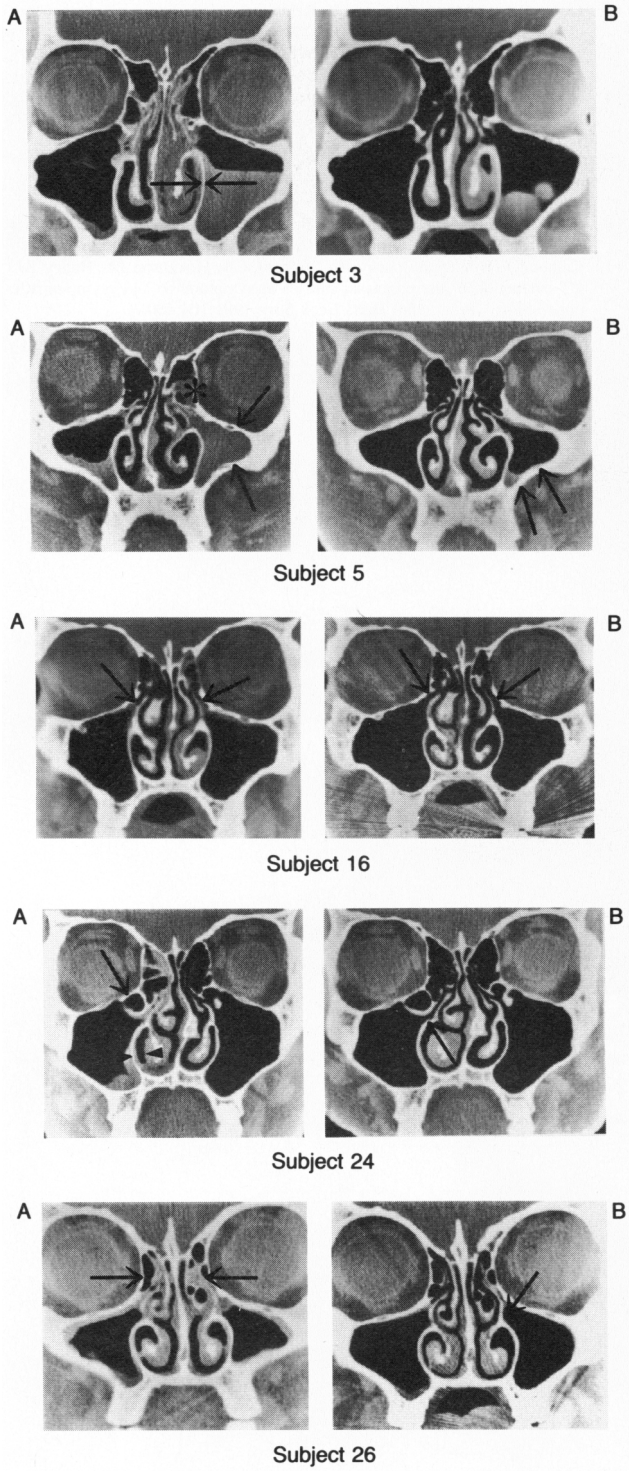

Figure 2. Initial and Follow-up Sinus CT Scans Shown in Descending Order of the Severity of Illness, According to the Total Symptom Score, in Five Untreated Subjects.

In Subject 3 the initial scan, obtained on day 5 of illness (Panel A), shows thickened nasal walls (arrows), bilateral ethmoid infundibular occlusion, and abnormalities of the ethmoid sinuses (right, 3 mm; left, 3 mm) and maxillary sinuses (right, 3 mm; left, air–fluid level). The scan obtained on day 18 of illness (Panel B) shows patent infundibula and residual abnormalities of the maxillary sinuses (right, 4 mm; left, 11 mm). In Subject 5 the initial scan, obtained on day 5 of illness (Panel A), shows bilateral ethmoid infundibular occlusion and abnormalities of the ethmoid sinuses (left, 5 mm [asterisk]) and maxillary sinuses (right, 10 mm; left, 15 mm [arrows]). On day 15 of illness (Panel B), the scan shows partial resolution of the infundibular occlusion and marked clearing of the sinus abnormalities, with a residual abnormality of the left maxillary sinus (3 mm [arrows]). In Subject 16 the initial scan, obtained on day 6 of illness (Panel A), shows bilateral ethmoid infundibular occlusion (arrows) and abnormalities of the left ethmoid (2 mm) and right maxillary (2 mm) sinuses. On day 14 of illness (Panel B), the scan shows patent infundibula (arrows) and resolution of the sinus abnormalities. In Subject 24 the scan obtained on day 4 of illness (Panel A) shows bilateral infraorbital air cells (arrow) and thickened nasal walls (arrowheads), occlusion of the right ethmoid infundibulum, and abnormalities of the ethmoid (right, 3 mm) and maxillary (right, 3 mm; left, 1 mm) sinuses. On day 19 of illness (Panel B), some thickening of the nasal wall persisted, and the right infundibulum was patent (arrow). There was a minimal residual abnormality of the left maxillary sinus (not shown). In Subject 26 the scan obtained on day 3 of illness (Panel A) shows thickened nasal walls and bilateral ethmoid infundibular occlusion, with abnormalities of the ethmoid sinuses (right, 4 mm; left, 4 mm [arrows]) and maxillary sinuses (right, 4 mm; left, 5 mm). On day 14 of illness (Panel B), the scan shows partial resolution of the bilateral infundibular occlusion (arrow) and a residual abnormality of the right maxillary sinus (3 mm).

infundibular occlusion — that appeared to be more clinically important in our group of subjects.

The current study shows that the common cold is an illness with broader anatomical involvement in the upper airway than previously recognized. These findings help improve our understanding of the pathogenesis of both the common cold and acute bacterial sinusitis and may even help us find better treatment for the cold. Although CT scanning is obviously not appropriate for the clinical evaluation of patients with colds, it is useful in research on the pathogenesis and treatment of this illness, which at some time afflicts virtually every human being.

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