

ALLERGIC FUNGAL SINUSITIS

David R. Nash, MD, and Philip Fireman, MD

Allergic fungal sinusitis is a recently recognized form of fungal sinusitis that both clinically and histopathologically resembles allergic bronchopulmonary aspergillosis (ABPA). Allergic fungal sinusitis (AFS) is increasingly diagnosed as an important type of chronic sinusitis. Reviews in the otolaryngologic literature have found between 5% and 10% of patients with chronic sinusitis meet the criteria for allergic fungal sinusitis.^{13, 16, 29}

AFS must be distinguished not only from chronic bacterial sinusitis but also from other forms of fungal sinusitis. Although fungal infections of the paranasal sinuses have been a diagnosed clinical entity for the past 100 years, it is only recently that there has been an attempt to classify the different manifestations of fungal sinusitis. Fungal sinusitis can be categorized as invasive and noninvasive and subdivided into four distinct clinicopathologic entities (Table 1): (1) acute/fulminant, (2) chronic/indolent, (3) mycetoma, and (4) allergic fungal sinusitis.^{11, 26}

Invasive sinus disease includes acute/fulminant and chronic/indolent sinusitis. Acute fulminant sinusitis is most commonly seen in immunocompromised individuals and diabetics; it is rapidly progressive and without treatment can frequently result in death. Fungi belonging to the *Mucoraceae* family, which includes *Rhizopus*, *Mucor*, and *Absidia*, are most frequently involved. Chronic or indolent sinusitis is most commonly seen in immunocompetent, nonatopic individuals with a history of chronic sinusitis. It is a slowly progressive disease characterized by granuloma-

Supported in part by NIH Grant AI19262.

From the Division of Allergy, Immunology, and Infectious Diseases, Department of Pediatrics, University of Pittsburgh School of Medicine; and Children's Hospital of Pittsburgh, Pittsburgh, Pennsylvania

similar to ABPA and proposed the term *allergic aspergillosis of the paranasal sinuses*.²⁵

In 1983 Katzstein reviewed 119 surgically excised sinus specimens and encountered six patients with sinus histologic findings that were indistinguishable from the mucoid impaction of the bronchi seen in ABPA.^{16, 17} The histologic findings consisted of clumps of eosinophils and other cellular debris within a background of pale eosinophilic-to-basophilic amorphous mucin and was termed *allergic mucin*. Throughout the 1980s case reports showed that fungi in the *Dematiaceae* family, rather than *Aspergillus*, were more commonly associated with AFS.^{7, 12, 23} Consequently, the more generic term *allergic fungal sinusitis* has become widely accepted.

CLINICAL PRESENTATION

Although allergic fungal sinusitis has only recently been characterized as a disease entity, its clinical presentation has been well described in numerous case reports and large series of patients (Table 2).^{1, 4, 7, 12, 13, 18, 19, 23, 30, 32} Patients tend to be young adults who present with a long-standing history of nasal obstruction that is poorly responsive to antibiotics. The average age of patients with allergic fungal sinusitis is in the late 20s with a range from 8 years old to 71 years old. Patients typically have had at least two and frequently more than a half dozen surgical procedures before a diagnosis of AFS is made.

The most common presenting complaint is nasal obstruction. Nasal polyps are an almost universal finding. Orbital involvement also occurs in a surprisingly high percentage of patients. deShazo et al reported two out of seven patients presenting with proptosis and observed that both patients were less than 16 years of age.^{10, 11} They hypothesize that in young patients with AFS sinus structures have not fully calcified, predisposing patients to proptosis as a result of impingement of the lamina papyracea of the ethmoid bone or from compression of the roof of the maxillary sinus. Although the larger series of patients, like deShazo's, report orbital symptoms or findings in a third of patients with AFS, an examination of individual case reports suggest an even higher percentage of orbital involvement.^{5, 6, 14}

Another co-morbid condition frequently seen with AFS is asthma (see Table 2). The published reports that include larger numbers of patients with AFS demonstrate that one third to half of patients also have asthma. Although asthma is commonly seen in AFS, it is rare for ABPA to be present. The literature only identifies five cases of AFS complicated by ABPA.^{1, 28, 31} Even though ABPA does not commonly co-exist with AFS, the reciprocal may not be true. It is worth noting that in reviews of ABPA, up to 10% of patients complain of chronic nasal plugs from which *A. fumigatus* has been frequently cultured.²⁴ Because *Dematiaceae* and not *Aspergillus* are the predominant fungi in AFS, it

Table 2. CLINICAL SYMPTOMS IN ALLERGIC FUNGAL SINUSITIS

Author	N	Average Age	Average of Surgeries	Nasal Obstruction	Orbital Symptoms/Findings	Asthma	ABPA	ASA	Polyps
Alphin	3	29 (9-42)	2			2/3	1/3	1/3	3/3
Bent	15					8/15			15/15
Cody	26	34 (14-66)	2.5			8/26		5/26	26/26
deShazo	7	32 (7-64)	1.7		2/7	1/7	0/7		5/7
Kinsella	25	28 (8-59)		25/25	1/25	8/25		2/25	25/25
Manning	18	26 (9-46)							14/18
Torres	16	25 (8-71)		16/16	5/16	1/16			
Waxman	15	29 (13-56)	4	14/15		11/15	0/15	1/15	14/15
Ence	14	31 (11-58)	2.1			6/14			14/14

remains to be determined if the sinus disease affecting patients with ABPA meets the diagnostic criteria for AFS.

The presence of chronic sinus symptoms, nasal polyps, and asthma has led many investigators to examine the role of salicylate sensitivity in AFS (see Table 2). Corey et al⁸ report that there is no increased salicylate sensitivity. deShazo and Swain's review of 99 case reports of AFS only identified one patient with salicylate sensitivity.¹² In contrast to the previous reports, Cody et al⁷ reported salicylate sensitivity in 5 out of 26 patients and in an additional 16% of the AFS cases they reviewed in literature. It is worth noting that many reports of AFS have not included an evaluation for salicylate sensitivity, and the reports that did evaluate for ASA sensitivity did not discuss the criteria for diagnosing ASA sensitivity. The published reports, including relatively large numbers of patients with AFS, found only nine cases of salicylate sensitivity out of 139 patients (see Table 2). The association of AFS and salicylate sensitivity appears to be relatively rare.

LABORATORY RESULTS

Investigators have focused laboratory studies of allergic fungal sinusitis on those parameters identified as abnormal in ABPA. These include elevated eosinophil counts, elevated total serum IgE, elevated specific IgE antibody, cutaneous sensitivity to relevant fungal antigens, and the presence of specific serum IgG and serum precipitins. Laboratory findings in AFS show trends that resemble ABPA; however, no particular laboratory finding is pathognomonic for AFS (Table 3). Elevated eosinophil counts greater than 600/mm³ are seen in 50% of patients. Eosinophil levels presumably fluctuate with disease activity as has been seen in patients with ABPA. Unfortunately, much of the published data for eosinophil counts in patients with AFS does not indicate the timing of the blood count in relationship to disease activity.

Most patients with AFS have elevated total serum IgE levels greater

Table 3. LABORATORY FINDINGS IN ALLERGIC FUNGAL SINUSITIS

Author	N	EOS > 600/mm ³ or 7%	IgE > 100 ng/mL	IgE > 1000 ng/mL or High	RAST ≥ Class 2 or Cutaneous Test
Allphin	3	1/1	1/3	2/3	3/3
Bent	15	6/15	2/7	7/7	5/5
Cody	26	8/22	8/11*		12/15
deShazo	7	5/5	3/3*		
Kinsella	25	12/25			
Waxman	15				6/10
Mabry	16		8/16	6/16	15/16
Manning	16		15/16	3/16	16/16
Ence	15	1/8	4/8	3/8	8/8

*Level not specified—only reported as high.

EOS = eosinophils; RAST = radioallergosorbent tests.

remains to be determined if the sinus disease affecting patients with ABPA meets the diagnostic criteria for AFS.

The presence of chronic sinus symptoms, nasal polyps, and asthma has led many investigators to examine the role of salicylate sensitivity in AFS (see Table 2). Corey et al⁸ report that there is no increased salicylate sensitivity. deShazo and Swain's review of 99 case reports of AFS only identified one patient with salicylate sensitivity.¹² In contrast to the previous reports, Cody et al⁷ reported salicylate sensitivity in 5 out of 26 patients and in an additional 16% of the AFS cases they reviewed in literature. It is worth noting that many reports of AFS have not included an evaluation for salicylate sensitivity, and the reports that did evaluate for ASA sensitivity did not discuss the criteria for diagnosing ASA sensitivity. The published reports, including relatively large numbers of patients with AFS, found only nine cases of salicylate sensitivity out of 139 patients (see Table 2). The association of AFS and salicylate sensitivity appears to be relatively rare.

LABORATORY RESULTS

Investigators have focused laboratory studies of allergic fungal sinusitis on those parameters identified as abnormal in ABPA. These include elevated eosinophil counts, elevated total serum IgE, elevated specific IgE antibody, cutaneous sensitivity to relevant fungal antigens, and the presence of specific serum IgG and serum precipitins. Laboratory findings in AFS show trends that resemble ABPA; however, no particular laboratory finding is pathognomonic for AFS (Table 3). Elevated eosinophil counts greater than 600/mm³ are seen in 50% of patients. Eosinophil levels presumably fluctuate with disease activity as has been seen in patients with ABPA. Unfortunately, much of the published data for eosinophil counts in patients with AFS does not indicate the timing of the blood count in relationship to disease activity.

Most patients with AFS have elevated total serum IgE levels greater

Table 3. LABORATORY FINDINGS IN ALLERGIC FUNGAL SINUSITIS

Author	N	EOS > 600/mm ³ or 7%	IgE > 100 ng/mL	IgE > 1000 ng/mL or High	RAST ≥ Class 2 or Cutaneous Test
Allphin	3	1/1	1/3	2/3	3/3
Bent	15	6/15	2/7	7/7	5/5
Cody	26	8/22	8/11*		12/15
deShazo	7	5/5	3/3*		
Kinsella	25	12/25			
Waxman	15				6/10
Mabry	16		8/16	6/16	15/16
Manning	16		15/16	3/16	16/16
Ence	15	1/8	4/8	3/8	8/8

*Level not specified—only reported as high.

EOS = eosinophils; RAST = radioallergosorbent tests.

than 100 ng/mL, and a subset of patients have very high IgE levels greater than 1000 ng/mL. As noted in discussing eosinophil counts, IgE levels also vary with disease activity. Again, the published data on IgE levels is not presented within the context of disease activity.

Only a few studies have demonstrated either positive cutaneous allergy test or serum IgE antibody to a specific fungus identified in sinus culture. The difficulty in diagnosing specific IgE sensitivity in the form of cutaneous tests or radioallergosorbent test (RAST) levels to fungal antigens is complicated by the lack of availability and standardization of fungal antigens. Almost all patients have demonstrated IgE antibody to common inhaled aeroallergens and fungal antigens in the form of either positive cutaneous allergy tests or by RAST that demonstrate serum reactivity greater than or equal to Class 2.

There is very little information available about the presence of either serum precipitins or specific IgG for fungal antigens. A few reports have found increased specific IgG and serum precipitins to the specific fungus identified in culture.^{1,5} The data is only available for a few patients, and it is difficult to draw definitive conclusions. The limited information on serum precipitins and specific IgG is predominately due to the lack of suitable commercial reagents.

MYCOLOGY

The clinical presentation and associated laboratory findings will frequently suggest the possibility of allergic fungal sinusitis. The presence of fungus by either culture or staining combined with the histological appearance of the mucosa, however, is necessary to make a definitive diagnosis of AFS. Initially, the first descriptions of allergic fungal sinusitis involved only the *Aspergillus* genus. Early reports of AFS relied on hematoxylin-eosin (HAE) and Gomori-methenamine silver stain (GMS) to morphologically classify fungi. Unfortunately, GMS and HAE stain, although useful in identifying fungi, do not aid in distinguishing *Dematiaceae* fungi from *Aspergillus*. Although not used in many of the reports of AFS, Fontana-Masson stain identifies the pigmented fungi and can be used to distinguish the pigmented *Dematiaceae* fungi from all *Aspergillus* species except *A. niger*.

More recent reports of AFS have utilized culture to facilitate proper identification of fungal species. Increasingly, the *Dematiaceae* family is recognized as the most important pathogen in AFS. Until the recognition of AFS as a clinical entity, the *Dematiaceae* fungi were seldom considered to be pathogens. The *Dematiaceae* are common soil saprophytes and include the following genera: *Alternaria*, *Bipolaris*, *Curvularia*, *Drechslera*, *Exserohilum* and *Helminthosporium*. Distinguishing these different genera has been hampered by both changing taxonomy and morphologic similarities. If only published reports with organisms identified by culture are analyzed, then 59 out of 73 cultures grew either *Bipolaris* or *Curvularia* (Table 4).

Table 4. CULTURE AND FUNGAL STAINING IN ALLERGIC FUNGAL SINUSITIS

Author	Fungal Stain	Cultures	Alternaria	Aspergillus	Bipolaris	Drechslera	Curvularia	Other
Alphin	3/3	5/3		2/3			1/3	
Bent	15/15	11/15	1/11	3/11	3/11		4/11	2/11
Cody	26/26	13/19	6/19	1/19	1/19	2/19	11/19	
deShazo	2/7	5/7		1/7			5/7	1/7
Kinsella	25/25	NA		1/10	3/10		3/10	
Manning		19/22	1/22	1/22	10/22	3/22	2/22	2/18
Torres	15/16	NA			1/6	1/6	1/6	3/6
Ence		11/12	2/12	1/12	6/12		7/12	1/12

Culture identification of fungal organisms has been complicated by both the difficulty in properly identifying fungal species and in successfully growing these fastidious organisms. Further, many of the fungi responsible for AFS were not identified as pathogens because they were assumed to be only laboratory contaminants. Ence et al¹³ speculated that eosinophil-derived major basic protein may be toxic to fungi leading to difficulty in sustaining cultures. Another possibility is that the pathologic process of AFS may only require a few organisms, thereby making successful culture difficult.⁴

An alternative diagnostic approach is to employ in situ hybridization (ISH) techniques that allow almost immediate identification of the fungus. ISH uses a labeled DNA probe that binds to a complementary ribosomal RNA sequence from a specific fungus. Only one study has been undertaken to examine the role of ISH in diagnosing fungal sinus disease.²⁷ All patients with culture-proven *Aspergillus* fungal sinusitis were identified using this technique. The exact role for ISH techniques in AFS remains to be fully elucidated. ISH clearly has a role in further elucidating the pathogenesis of AFS. However, at this time, identifying the specific fungus in AFS does not affect the treatment plan, is a relatively expensive technique, and may not be any more helpful than appropriate histologic staining.

RADIOGRAPHIC FINDINGS

Even before culture results and histology allow for the definitive diagnosis of AFS, radiographic findings can be effectively utilized to support a clinical diagnosis of AFS. The most commonly recognized radiographic feature of AFS is the involvement of multiple sinuses (Table 5). Approximately 50% of patients show evidence of bone erosion or thinning of the sinus walls, nasal turbinates, or septum on either plain radiographs or computed tomography (CT). It is important to recognize that the presence of bony erosion is consistent with AFS and does not necessarily mean there is tissue invasion. CT scans of patients with

Table 5. RADIOLOGIC FINDINGS IN ALLERGIC FUNGAL SINUSITIS

Author	Multiple Sinuses	Bony Erosions
Alphin	3/3	1/3
Bent		12/15
Cody	26/26	10/44*
deShazo	7/7	3/7
Manning	18/18	7/18
Torres		12/16
Waxman	14/16	≥2/16
Ence	14/14	7/14

*Includes some patients with AFS-like syndrome without evidence of fungus.



Figure 1. Increased soft-tissue density within the nasal cavity and maxillary and ethmoid sinuses. There is bony erosion of the medial maxillary sinus walls, nasal septum, and inferior and middle nasal turbinates. Hyperdense regions are seen in the nasal and ethmoidal masses.

fungal disease have been noted to show relatively specific findings with the involved sinuses showing areas of high attenuation centrally (Fig. 1). The high attenuation areas may take on a variety of different patterns ranging from a “starry sky” pattern to a serpiginous pattern.²² The high attenuation areas on CT scan appear as a hypointense signal on T1-weighted magnetic resonance (MR) images.^{22, 33} Additional MR imaging findings include higher signal characteristics in the periphery of involved sinuses corresponding to inflamed mucosa. On MR T2-weighted images, a central signal void corresponds with the areas of high attenuation seen on CT.^{22, 33}

Unfortunately, the previous delineated CT and MR imaging findings do not readily distinguish AFS from other chronic fungal diseases. Subtle aspects of radiographic findings may, however, lead more in the direction of AFS than other fungal sinus diseases. The presence of tissue invasion such as intracerebral abscess, involvement of the dura, or optic nerve infiltration rules out allergic fungal sinus disease and suggests invasive acute/fulminant sinusitis. The involvement of only one sinus is very consistent with mycetoma and is less consistent with AFS disease.

HISTOLOGY

Ultimately, the diagnosis of AFS is based on histologic and microbial examination. Katzstein initially described mucoid impaction of the paranasal sinuses that was indistinguishable from that seen in ABPA. The mucoid impaction was termed *allergic mucin* and has become the

defining characteristic of AFS. The mucoid material is grossly the consistency of peanut butter and of a yellow, brown, or green color. Microscopically, clumps of necrotic eosinophils and other cellular debris is found within a background of eosinophilic to basophilic amorphous mucin. The mucin is arranged in multilayered rows with Charcot-Leyden crystals appearing either hexagonal if seen in cross-section, or bipyramidal if seen in longitudinal section (Fig. 2). Unlike mycetomas, in which fungal elements are frequently seen, hyphae are relatively rare in AFS. Fungal elements must be either visualized by staining methodology or seen in culture in order to make a diagnosis of AFS (Fig. 3). If the presence of fungal elements cannot be confirmed, then AFS cannot be definitively diagnosed. No evidence of either bony or soft tissue invasion should ever be seen in allergic fungal sinusitis.

PATHOPHYSIOLOGY

The exact pathophysiologic mechanism of AFS is still not fully elucidated. The principal theory surrounding the pathogenesis of AFS is derived from the studies of ABPA. Immunologic over-responsiveness mediated by IgE (Gell-Combs type I) and immune complexes (Gell-Combs type III) are postulated to be the main pathways for the induction of the inflammatory process seen in AFS.

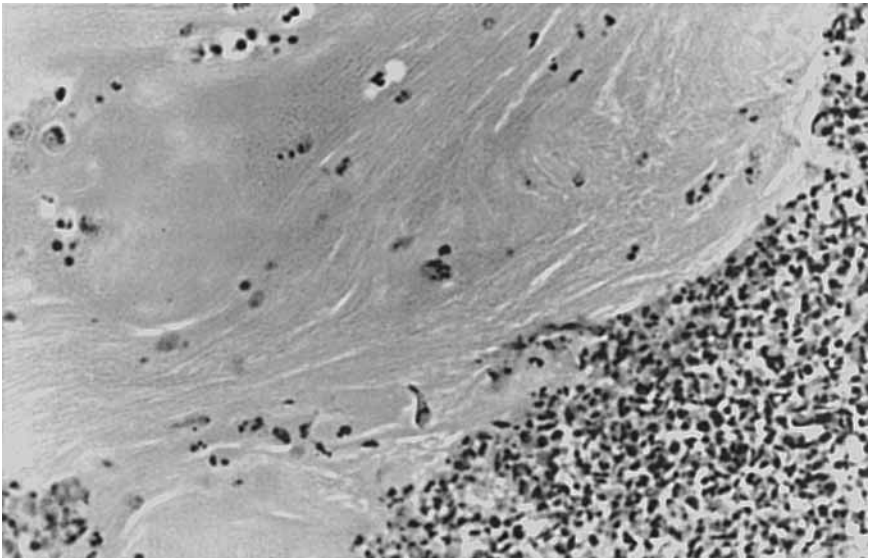


Figure 2. Multilayered rows of allergic mucin with eosinophils (hematoxylin-eosin, original magnification $\times 400$).

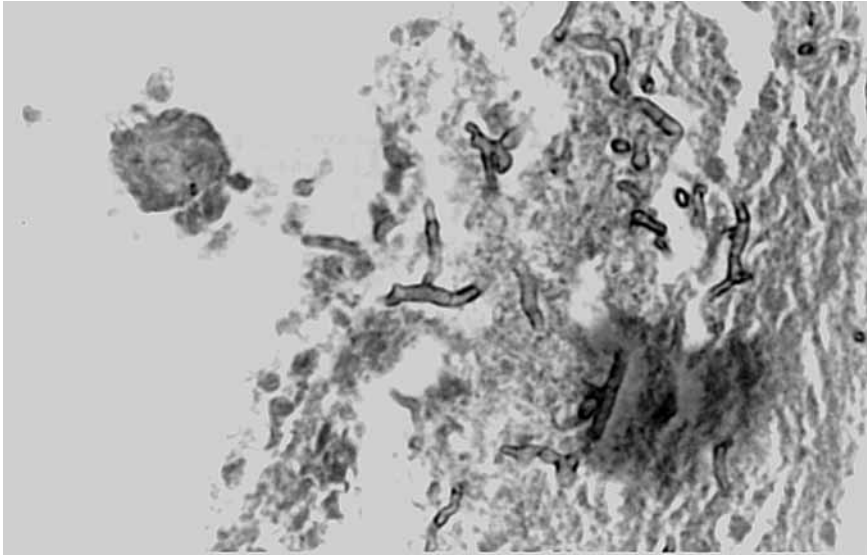


Figure 3. Fungal hyphae. The acute angle branching of the hyphae and the presence of septum suggest *Aspergillus*. A definitive identification will require fungal culture (Grocott stain, original magnification $\times 400$).

To date, the data generated strongly support the role for IgE-mediated hypersensitivity. Virtually every patient has demonstrated one of the following markers indicating IgE-mediated hypersensitivity: positive cutaneous skin tests for fungal allergens or other aeroallergens, elevated specific IgE for fungal allergens, or the presence of elevated total serum IgE. It is important to recognize that there are many patients that demonstrate only one of the above markers for IgE-mediated hypersensitivity. Further support for the role of type 1 hypersensitivity is found in the histologic demonstration of eosinophils and eosinophil-derived Charcot-Leyden crystals. Finally, a few studies have examined the response of total or specific IgE or RAST levels to treatment protocols. In most cases, treatment has led to decreased IgE or RAST levels.^{5, 21} IgE clearly seems to play a role in the pathophysiology of AFS.

The role of Type 3-mediated hypersensitivity driven by IgG immune complexes is more debatable. To date, there has been absolutely no demonstration of immune complexes in the development of AFS. In fact, examination for specific IgG or serum precipitins has only been undertaken in a handful of studies. The paucity of studies demonstrating the presence of serum precipitins or elevated specific IgG is due to the lack of commercially available tests for the *Dematiaceae* fungi. No study has examined the effect of treatment protocols on levels of specific IgG or serum precipitins. In addition to the need for studies to further elucidate the role for IgG in AFS, examination of cytokine profiles may

also further our understanding of the pathophysiologic mechanisms involved in AFS.

At this point, the pathophysiologic mechanisms involved in AFS can best be viewed as a combination of factors related to an individual's atopic predisposition, sinus and nasal anatomy, and their local fungal environment. Presumably, a fungal antigen initially triggers an inflammatory response mediated through IgE. A combination of factors, the initial atopic response, the patient's nasal anatomy, or a concurrent infection then leads to sinus blockage. The fungal antigen continues to elicit an IgE response and possibly an IgG response in the now blocked sinus cavity. If natural drainage is not quickly restored, a self-perpetuating cycle of inflammation is initiated.

DIAGNOSIS

Numerous investigators have attempted to delineate specific diagnostic criteria for AFS.^{2, 4, 7, 12, 15} Many of the proposed diagnostic criteria have been modeled after the diagnostic criteria used for ABPA. Gourley et al was one of the first investigators to propose diagnostic criteria that were described as "tentative diagnostic criteria" for *Bipolaris specifera* sinusitis¹⁵:

- Atopic history and positive skin-prick test to aeroallergens.
- Pansinusitis often with nasal polyposis, unresponsive to antibiotics.
- Immediate cutaneous reactivity to *B. specifera*.
- Isolation of *B. specifera* from the sinuses.
- Typical histologic allergic mucin.
- Elevated total serum IgE.
- Serum precipitins to *B. specifera*.
- High levels of specific IgE and IgG antibodies to *B. specifera*.
- Peripheral blood eosinophilia.

The Gourley diagnostic criteria were derived from a combination of the laboratory data from three patients with *B. specifera* and incorporating the diagnostic criteria for ABPA. The essential laboratory values for ABPA include immediate cutaneous reactivity to *Aspergillus*, elevated total serum IgE, precipitating antibodies to *A. fumigatus*, and elevated specific IgE and IgG antibodies to *A. fumigatus*. As the clinical characteristics of AFS have been further defined, it has become clear that a significant number of patients with AFS lack elevated total serum IgE and peripheral eosinophilia. Further, as previously described, data on serum precipitins and specific fungal IgG and IgE are frequently not available for patients with AFS.

In order to address the lack of certain specific laboratory data for most patients with AFS, recent investigators have modified the diagnostic criteria.^{2, 4, 12} A strong consensus seems to exist about the following criteria:

Histologic presence of allergic mucin.

Absence of any evidence of fungal invasion in the nasal mucosa or bone.

Presence of fungus by either staining techniques or culture.

Characteristic radiologic findings: sinusitis of one or more of the paranasal sinuses.

Other symptoms that are not universally acknowledged as vital for diagnosis but are seen in virtually all patients include the following signs:

Normal immunologic function and no history of immunosuppressive drugs.

Presence of nasal polyps.

Atopic predisposition determined by skin testing or serology.

The proper diagnosis has important clinical implications in terms of initiating the appropriate treatment regimen.

TREATMENT

Proper diagnosis is essential before initiating treatment. Because AFS frequently causes bony erosion, it is frequently misdiagnosed as invasive sinusitis. A histologic specimen is necessary to confirm the absence of tissue invasion. Patients demonstrating tissue invasion need aggressive antifungal therapy. Patients without tissue invasion have AFS, and it is widely believed that there is no role for systemic antifungal therapies. It is worth noting that the oral antifungal, itraconazole, has been used successfully in ABPA and reduced symptoms, IgE levels, steroid requirements and turned three out of four patient cultures negative for *Aspergillus*.¹⁰ Unfortunately, the most common pathogens in AFS, *Dematiaceae* fungi, have shown limited susceptibility to itraconazole.³ A clinical trial in either *Aspergillus* or itraconazole-sensitive *Dematiaceae*-induced AFS will be worthwhile. One potentially novel antifungal therapy involves topical application in effort to eliminate the fungus. No studies have yet examined this approach, but Bent and Kuhn have suggested the need for clinical trials utilizing sinus irrigation with amphotericin B or ketoconazole.³

The mainstay of AFS treatment is surgical debridement and aeration using endoscopic techniques. It is important to realize that the optimal surgical approach has not been studied, and currently an individualized approach based on the extent of disease and the surgeon's expertise is recommended. Surgical goals improve the natural drainage pattern and remove the inflammation-generating fungal debris.

Unfortunately, there is a very high rate of disease relapse following surgery. Bent et al³ have treated 50 patients with AFS and concluded that there are no long-term cures. Other investigators have identified a small percentage of patients who seem to have a sustained disease-free

CONCLUSION

AFS is an increasingly recognized cause of chronic sinusitis. It appears to be the explanation for chronic sinusitis in approximately 7% of cases. Patients with AFS have certain characteristic clinical features, including atopy, asthma and nasal polyps, along with rather characteristic radiographic findings that should heighten suspicion for this clinical entity. It is important to distinguish AFS from other causes of fungal sinus disease. The appropriate diagnosis has very important therapeutic implications such as the avoidance of unnecessary systemic antifungal therapy. Further, the recognition of AFS indicates the need for surgery followed by corticosteroid therapy. Additional therapeutic and prophylactic therapies need to be identified and studied to advance the clinical treatment of AFS.

References

1. Allphin AL, Strauss M, Abdul-Karim F: Allergic fungal sinusitis. *Laryngoscope* 101:815, 1991
2. Bartynski JM, McCaffrey TV, Frigas E: Allergic fungal sinusitis secondary to dermatiaceous fungi—*Curvularia lunata* and *Alternaria*. *Otolaryngol Head Neck Surg* 103:32, 1990
3. Bent JP, Kuhn FA: Antifungal activity against allergic fungal sinusitis organisms. *Laryngoscope* 106:1331, 1996
4. Bent JP, Kuhn FA: Diagnosis of allergic fungal sinusitis. *Otolaryngol Head Neck Surg* 111:580, 1994
5. Brummund W, Kurup VP, Harris GJ, et al: Allergic sino-orbital mycosis. *JAMA* 256:3249, 1986
6. Chang WJ, Shields CL, Shields JA, et al: Bilateral orbital involvement with massive allergic fungal sinusitis. *Arch Ophthalmol* 114:767, 1996
7. Cody DT, Neel HB, Ferreiro JA, et al: Allergic fungal sinusitis: The Mayo Clinic experience. *Laryngoscope* 104:1074, 1994
8. Corey JY, Delsupehe KG, Ferguson BJ: Allergic fungal sinusitis: Allergic, infectious, or both? *Otolaryngol Head Neck Surg* 113:110, 1995
9. Corey JY, Romberger CF, Shaw GY: Fungal diseases of the sinuses. *Otolaryngol Head Neck Surg* 103:1012, 1990
10. Denning DW, Wye JE, Lewiston NJ, et al: Adjunctive therapy of allergic bronchopulmonary aspergillosis with itraconazole. *Chest* 100:813, 1991
11. deShazo RD, Chapin K, Swain RE: Fungal sinusitis. *N Engl J Med* 337:254, 1997
12. deShazo RD, Swain RE: Diagnostic criteria for allergic fungal sinusitis. *J Allergy Clin Immunol* 96:24, 1995
13. Ence BK, Jorgensen NL, Parsons DS, et al: Allergic fungal sinusitis. *Am J Rhinol* 4:169, 1990
14. Friedman GC, Hartwick WJ, Ro JY, et al: Allergic fungal sinusitis. *Clin Microbiol* 96:368, 1991
15. Gourley DS, Whisman BA, Jorgensen NL, et al: Allergic *Bipolaris* sinusitis: Clinical and immunopathologic characteristics. *J Allergy Clin Immunol* 85:583, 1990
16. Katzstein AA, Sale SR, Greenberger PA: Allergic *Aspergillus* sinusitis: A newly recognized form of sinusitis. *J Allergy Clin Immunol* 72:89, 1983
17. Katzstein AA, Sale SR, Greenberger PA: Pathologic findings in allergic *Aspergillus* sinusitis: A newly recognized form of sinusitis. *Am J Surg Pathol* 7:439, 1983
18. Kinsella JB, Bradfield JJ, Gourley WK, et al: Allergic fungal sinusitis. *Clin Otolaryngol* 21:389, 1996

CONCLUSION

AFS is an increasingly recognized cause of chronic sinusitis. It appears to be the explanation for chronic sinusitis in approximately 7% of cases. Patients with AFS have certain characteristic clinical features, including atopy, asthma and nasal polyps, along with rather characteristic radiographic findings that should heighten suspicion for this clinical entity. It is important to distinguish AFS from other causes of fungal sinus disease. The appropriate diagnosis has very important therapeutic implications such as the avoidance of unnecessary systemic antifungal therapy. Further, the recognition of AFS indicates the need for surgery followed by corticosteroid therapy. Additional therapeutic and prophylactic therapies need to be identified and studied to advance the clinical treatment of AFS.

References

1. Allphin AL, Strauss M, Abdul-Karim F: Allergic fungal sinusitis. *Laryngoscope* 101:815, 1991
2. Bartynski JM, McCaffrey TV, Frigas E: Allergic fungal sinusitis secondary to dermatiaceous fungi—*Curvularia lunata* and *Alternaria*. *Otolaryngol Head Neck Surg* 103:32, 1990
3. Bent JP, Kuhn FA: Antifungal activity against allergic fungal sinusitis organisms. *Laryngoscope* 106:1331, 1996
4. Bent JP, Kuhn FA: Diagnosis of allergic fungal sinusitis. *Otolaryngol Head Neck Surg* 111:580, 1994
5. Brummund W, Kurup VP, Harris GJ, et al: Allergic sino-orbital mycosis. *JAMA* 256:3249, 1986
6. Chang WJ, Shields CL, Shields JA, et al: Bilateral orbital involvement with massive allergic fungal sinusitis. *Arch Ophthalmol* 114:767, 1996
7. Cody DT, Neel HB, Ferreiro JA, et al: Allergic fungal sinusitis: The Mayo Clinic experience. *Laryngoscope* 104:1074, 1994
8. Corey JY, Delsupehe KG, Ferguson BJ: Allergic fungal sinusitis: Allergic, infectious, or both? *Otolaryngol Head Neck Surg* 113:110, 1995
9. Corey JY, Romberger CF, Shaw GY: Fungal diseases of the sinuses. *Otolaryngol Head Neck Surg* 103:1012, 1990
10. Denning DW, Wye JE, Lewiston NJ, et al: Adjunctive therapy of allergic bronchopulmonary aspergillosis with itraconazole. *Chest* 100:813, 1991
11. deShazo RD, Chapin K, Swain RE: Fungal sinusitis. *N Engl J Med* 337:254, 1997
12. deShazo RD, Swain RE: Diagnostic criteria for allergic fungal sinusitis. *J Allergy Clin Immunol* 96:24, 1995
13. Ence BK, Jorgensen NL, Parsons DS, et al: Allergic fungal sinusitis. *Am J Rhinol* 4:169, 1990
14. Friedman GC, Hartwick WJ, Ro JY, et al: Allergic fungal sinusitis. *Clin Microbiol* 96:368, 1991
15. Gourley DS, Whisman BA, Jorgensen NL, et al: Allergic *Bipolaris* sinusitis: Clinical and immunopathologic characteristics. *J Allergy Clin Immunol* 85:583, 1990
16. Katzstein AA, Sale SR, Greenberger PA: Allergic *Aspergillus* sinusitis: A newly recognized form of sinusitis. *J Allergy Clin Immunol* 72:89, 1983
17. Katzstein AA, Sale SR, Greenberger PA: Pathologic findings in allergic *Aspergillus* sinusitis: A newly recognized form of sinusitis. *Am J Surg Pathol* 7:439, 1983
18. Kinsella JB, Bradfield JJ, Gourley WK, et al: Allergic fungal sinusitis. *Clin Otolaryngol* 21:389, 1996

19. Mabry RL, Manning SC: Radioallergosorbent micscreen and total immunoglobulin E in allergic fungal sinusitis. *Otolaryngol Head Neck Surg* 113:721, 1995
20. Mabry RL, Manning SC, Mabry CS: Immunotherapy in the treatment of allergic fungal sinusitis. *Otolaryngol Head Neck Surg* 116:31, 1997
21. Manning SC, Mabry RL, Schaefer SD, et al: Evidence of IgE-mediated hypersensitivity in allergic fungal sinusitis. *Laryngoscope* 103:717, 1993
22. Manning SC, Merkel M, Kriesel K, et al: Computed tomography and magnetic resonance diagnosis of allergic fungal sinusitis. *Laryngoscope* 107:170, 1997
23. Manning SC, Schaefer SD, Close LG, et al: Culture-positive allergic fungal sinusitis. *Arch Otolaryngol Head Neck Surg* 117:174, 1991
24. McCarthy DS, Pepys J: Allergic broncho-pulmonary aspergillosis. *Clin Allergy* 1:261, 1971
25. Millar JW, Johnston A, Lamb D: Allergic aspergillosis of the maxillary sinuses [abstract]. *Thorax* 36:710, 1981
26. Morpeth JF, Rupp NT, Kolen WK, et al: Fungal sinusitis: An update. *Ann Allergy Asthma Immunol* 76:128, 1996
27. Perez-Jaffe LA, Lanza DL, Loevner LA, et al: In situ hybridization for *Aspergillus* and *Penicillium* in allergic fungal sinusitis: A rapid means of speculating fungal pathogens in tissues. *Laryngoscope* 107:233, 1997
28. Safirstein BH: Allergic bronchopulmonary aspergillosis with obstruction of the upper respiratory tract. *Chest* 70:788, 1976
29. Schwartz HJ: Allergic fungal sinusitis: Experience in an ambulatory allergy practice. *Ann Allergy Asthma Immunol* 77:500, 1996
30. Schweitz CA, Gourley DS: Allergic fungal sinusitis. *Allergy Proc* 13:3, 1992
31. Torres C, Ro JY, El-Naggar AK, et al: Allergic fungal sinusitis: A clinicopathologic study of 16 cases. *Hum Pathol* 27:793, 1996
32. Travis WD, Kwon-Chung KJ, Kleiner DE, et al: Unusual aspects of allergic bronchopulmonary fungal disease: Report of two cases due to *Curcularia* organisms associated with allergic fungal sinusitis. *Hum Pathol* 22:1241, 1991
33. Waxman JE, Spector JG, Sale SR, et al: Allergic *Aspergillus* sinusitis: Concepts in diagnosis and treatment of a new clinical entity. *Laryngoscope* 97:261, 1987
34. Zinreich SJ, Kennedy DW, Malat J, et al: Fungal sinusitis: Diagnosis with CT and MR imaging. *Radiology* 169:439, 1988

Address reprint requests to

David R. Nash, MD
Children's Hospital of Pittsburgh
3705 Fifth Avenue
Pittsburgh, PA 15213