GEOGRAPHIC VARIATION IN ALLERGIC FUNGAL RHINOSINUSITIS

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The widely accepted pathophysiologic basis of allergic fungal rhinosinusitis (AFRS) is an allergic response by a predisposed individual to inhaled mould spores.[4] The presence of mould spores are a necessary condition. Mould spores are ubiquitous, yet outdoor mould spore counts vary widely, geographically and seasonally. Another source of mould exposure is from the indoors, including damp basements, bathrooms, humidifiers, and possibly air conditioning units.

A wide variety of fungi are associated with AFRS, and in some cases, more than one fungus may be cultured. The pathophysiologic process, histopathologic findings, and clinical picture appear to be the same irrespective of the fungus cultured.[12] The most common fungi associated with the process are the dematiaceous moulds, particularly the *Bipolaris* species.[12]

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Most large series of AFRS have come from the south.[11,15] This study was undertaken to determine if there are differences in the incidence of AFRS relative to geography.

MATERIALS AND METHODS

Forty-five otolaryngologists across the United States were contacted and asked to fill out a survey detailing the total number of sinus surgeries from July 1, 1997 through June 30, 1998, and from July 1, 1998 through May 30, 1999. The survey also requested the total number of cases diagnosed with AFRS over each of the two time periods. This allowed for evaluation of differences in AFRS over two time periods. The definition of AFRS provided for the otolaryngologists was histopathologic evidence of allergic mucin with presence of fungi, either histopathologically or on fungal culture.

The otolaryngologists were requested to supply information regarding fungal culture data on the patients with AFRS.

Seven reviews in the literature provided total number of sinus surgeries along with the total number of cases of AFRS (Table 1).[1,3,5–8,14]

The Mould and Spore Catalogue of 1997, published by the American Academy of Allergy, Asthma and Immunology was used to determine mould counts in geographic locations close to the surveyed otolaryngologists.[2] Mould data was specifically extracted for peak mould counts at each reporting center for *Alternaria, Bipolaris, Helminthosporium, Dreschlera, Curvularia,* and *Aspergillus.* Mould counts for *Helminthosporium* and *Dreschlera* were grouped with *Bipolaris* (Table 2). The mould counts of smuts, ascospores, *Cladosporium,* basidiospores, cercospora, algae, rusts, myxomycetes, *Botrytis,* epicoccum, *Oidium,* or *Pithomyces* were not included.

Table 1. GEOGRAPHIC INCIDENCE OF ALLERGIC FUNGAL RHINOSINUSITIS BY LITERATURE REVIEW

Reference	Location	Years Collected	Cases of AFS	Total Cases	Percentage
Allphin[1]	Cleveland, OH	1985–1990	3	176	1.7
Cody[3]	Rochester, Minnesota	1984–1992	28 cases in 25 patients	789	3.9
Corey[5]	Chicago, IL	NR	0	99 patients CRS	0
Deshpande[6]	Bombay, India	4 years	7	85	8.2
Ence[7]	San Antonio, TX	1985–1990	14	205	6.8
Katzenstein[8]	St. Louis, MO	1977–1981	7	113 cases	6.2
Ramadan[14]	Morgantown, WV	1991–1995	8	580 patients	1.4

*CRS = chronic rhinosinusitis; NR = not reported.

Table 2. MOULD COUNTS BY LOCATION FROM THE 1997 POLLEN AND SPORE REPORT

Location	*Alternaria* Range*	*Bipolaris* Range*	*Curvularia* Range*	*Aspergillus* Range*
Tucson, Arizona	1–100	1–20		
Los Angeles, California	9–200			10–10,000
Pleasantville, California	0.5–300			0.5–500
Roseville, California	0.5–100			
Santa Barbara, California	0.5–500			0.5–2,000
Vallejo, California	0.5–400			0.5–1,000
Colorado Springs, Colorado	0.5–500	0.5–10		
Sarasota, Florida	9–300	10–200		
Tallahassee, Florida	9–200	0.5–100	0.5–100	
Atlanta, Georgia	5–100			
De Kalb, Illinois	0.5–60			
Indianapolis, Indiana	0.5–900			
Lexington, Kentucky	0.5–500			
Louisville, Kentucky	0.5–200			
Lafayette, Louisiana	0.5–20	0.5–20	0.5–80	
Grand Rapids, Michigan	0.5–900	0.5–200		
Rochester, Minnesota	0.5–100			
Cape Girardeau, Missouri	0.5–200			
Kansas City, Missouri	0.5–2,000	0.5–800		
St. Louis, Missouri	0.5–700			8–1,000
Omaha, Nebraska	0.5–1,000			
Cherry Hill, New Jersey	0.5–20			
Newark, New Jersey	0.5–300			
Olean, New York	0.5–200			
Fargo, North Dakota	0.5–3,000	0.5–200		
Dayton, Ohio	0.5–1,000			
Oklahoma City, Oklahoma	9–1,000	0.5–200		
Philadelphia, Pennsylvania	0.5–80			
Pittsburgh, Pennsylvania	0.5–1,000	0.5–200		
Knoxville, Tennessee	10–200		0.5–100	
Waco, Texas	0.5–200 (100)	0.5–80 (10)		
Washington, DC	1–800	0.5–80		
Seattle, Washington	0.5–10 (1)			
Vancouver, Washington				0.5–900
Appleton, Wisconsin	9–500	0.5–300		

*Spores per cubic meter.

Results

Twenty of 45 otolaryngology practices surveyed (44%) provided information regarding the incidence of AFRS. No significant difference in incidence for the year July 1, 1997 through June 30, 1998, and from July 1, 1998 through May 30, 1999 was found in most practices. The Dallas, Texas reporting center with Mabry and Marple did double their AFRS patients, going from 6 of 75 cases (8%) in the first year, to 16 of 72 cases (22%) in the second year. The data were combined from the 2 years for

each practice to give a percentage of cases of AFRS relative to all endoscopic surgical cases performed (Table 3). The fungi cultured from each site are listed in Table 4.

The geographic incidence of AFRS is mapped in Figure 1. The highest percentage of cases occurred in the southern United States and along the Mississippi basin. There was no correlation with mould counts for *Alternaria, Aspergillus, Bipolaris,* or *Curvularia* by scatter plot analysis. Nevertheless, the available mould counts are quite spotty and most of the mould-reporting centers are not in the exact location of the otolaryngology practices. The mould center closest to the AFRS site and in the same state was used to prepare Table 5, which shows the peak mould count for *Bipolaris* and *Alternaria* next to the AFRS reporting sites. For example Waco, Texas mould counts were used in the correlation with the AFRS incidence from Dallas, Texas.

The literature provides information regarding incidence of AFRS relative to all sinus surgeries (see Table 1). The highest reported incidence in the literature is in Bombay, India, with an incidence of 8.2% of all sinus cases. The trend toward an increased incidence in the south and in the Mississippi basin area in the current survey is supported by the literature. The highest incidence of AFRS reported in the literature from the United States is in San Antonio, Texas, (6.8%)[14] and St. Louis, Missouri (6.2%).[8]

DISCUSSION

The first to report the incidence of AFRS was Katzenstein[8] in 1983, with an incidence of 6.2% from St. Louis, Missouri, which lies along the central Mississippi River. The highest level reported in the survey was from Memphis, Tennessee, at 23%, which lies on the other side of the Mississippi River a few hundred miles downstream. Both by literature review and analysis of the current survey, it appears that cases of AFRS do occur more frequently in the southern central United States. Texans refer to this as the I-35 corridor of AFRS. I-35 is the interstate highway that begins down in Laredo, Texas, extends through San Antonio, Waco, and Dallas, and continues through Oklahoma City, Kansas City, and on up to Minneapolis, Minnesota.

Marple cautioned that the high incidence of AFRS in Dallas, Texas, might in part be accounted for by referral patterns. Recognized as expert in the treatment of AFRS, their institution may see a disproportionate number of AFRS cases.

Allergic bronchopulmonary aspergillosis (ABPA) is the pulmonary equivalent of AFRS. The only case of AFRS or APBA in which the source of fungal infestation was identified occurred in a 76-year-old man who developed ABPA following exposure to ground mulch which contained *Aspergillus fumigatus,* the source of his ABPA.[9]

Mould counts do not seem to correlate with incidence of AFRS in the present analysis. The lack of mould spore data for the relevant moulds (*Alternaria, Aspergillus, Bipolaris,* and *Curvularia*) from locations proximate

Table 3. GEOGRAPHIC INCIDENCE OF ALLERGIC FUNGAL RHINOSINUSITUS PER TOTAL NUMBER OF SINUS SURGERIES

Name	City	State	Total Number of Sinus Surgeries 7/1/97–6/30/98	Number Diagnosed with AFRS	Total Number of Sinus Surgeries 7/1/98–5/31/99	Number Diagnosed with AFRS	Percent of Cases with AFRS over 2 Years
Morgan, A	Culman	AL	10	1	10	1	10.0
Krouse, J	Ormond Beach	FL	300*	5*			1.7
Kuhn, F	Savannah	GA	162	17	114	20	13.4
Graham, S	Iowa City	IA	53	0	27	3	3.7
Gordon, B	Cape Cod	MA	26	1	21	1	4.2
Terrell, J	Ann Arbor	MI	100	3	80	2	2.8
Cook, P	Columbia	MO	161	2	114	2	1.4
DeWitt, W	Missoula	MT	23	0	16	1	2.6
Yonkers, A	Omaha	NB	202*	2*			1.0
Clark, C	Durham	NC	100	2	59	0	1.2
Brown, D	Santa Fe	NM	24	0	21	2	4.4
Bernstein, J	Amherst	NY	43	0	36	0	0
Levine, H	Cleveland	OH	250	6	250	8	2.8
Ferguson, BJ	Pittsburgh	PA	331	2	135	2	0.9
Osguthorpe, J	Charleston	SC	93	5	79	3	4.6
Rain, M	Memphis	TN	176	37	126	32	22.8
Marple, B	Dallas	TX	75	6	72	16	15.0
Skedros et al†	Salt Lake City/ Bountiful	UT	176	0	192	1	0.2
Manning, S	Seattle	WA	—	0	—	0	0
Ramadan, H	Morgantown	WV	90	3	108	2	2.5

*Data not provided by separate year, represents 7/97–5/99.
†Includes a total of four separate practices from area.

Table 4. FUNGI CULTURED IN ALLERGIC FUNGAL RHINOSINUSITIS BY LOCATION

State	City	Number of Cases	Fungal Cultures
Alabama	Cullman	2	*Aspergillus flavus* 1, *Candida albicans* 1
Florida	Ormond Beach	5	*Curvularia* 3, NG 2
Missouri	Columbia	4	Zygomycosis 1, *Aspergillus* 1, NG 1, NA 1
Nebraska	Omaha	2	NG 2
New Mexico	Santa Fe	2	NG 2
South Carolina	Charleston	8	*Aspergillus* 3, *Bipolaris* 2, *Dreschlera* 1, NG 2
Texas	Dallas	22	*Bipolaris* 9, *Curvularia* 3, *Alternaria* 2, *Exserohilum* 1, NG 7

*Fungal culture information was not available from the other sites.
NA = not available; NG = no growth

to the reporting AFRS sites makes conclusions regarding lack of correlation of AFRS incidence with mould counts unsupportable with the present analysis. Mould peak levels were used in this analysis. It is not clear which is more significant, the mean or peak levels.

Other limitations of this study include the requirement for histopathologic evidence to make the diagnosis of AFRS. This approach may underrepresent the true incidence of AFRS, but it does provide objective evidence for the diagnosis. Patients with AFRS often have a multiyear history and have undergone multiple surgical procedures. AFRS is a chronic disease, in which the patient may present after several months or even years of progressively increasing symptoms. It is possible that the survey of the mould count in just the year 1997 does not reflect the actual exposure. Before analysis of several years of mould data can begin, one must first have a more comprehensive reporting of mould counts for the moulds of particular interest in AFRS.

Manning and Holman reported a male predominance in patients with AFRS of 1.6.[10] It is possible that males are out of doors more than females. If outdoor exposure to mould counts is greater than indoor exposure to moulds, then this may explain the increased male predominance.

Interestingly, Manning noted many cases of AFRS while in Dallas, Texas, but in 2 years has failed to note any cases of AFRS in Seattle, Washington. The mould counts in Seattle are significantly lower than the mould counts in Dallas. Manning has speculated that AFRS may be caused by mould exposure from air conditioning units. Air conditioning is much more common in the areas of highest incidence. To date, this theory remains unproven. Noble and colleagues in Georgia reported that the predominant fungi recovered from air samples in selected patients' residences included the same species isolated from the mucin of its inhabitants. Eight of the species implicated in AFRS were found to colonize the surfaces of indoor construction other than the residence of the patient.[13]

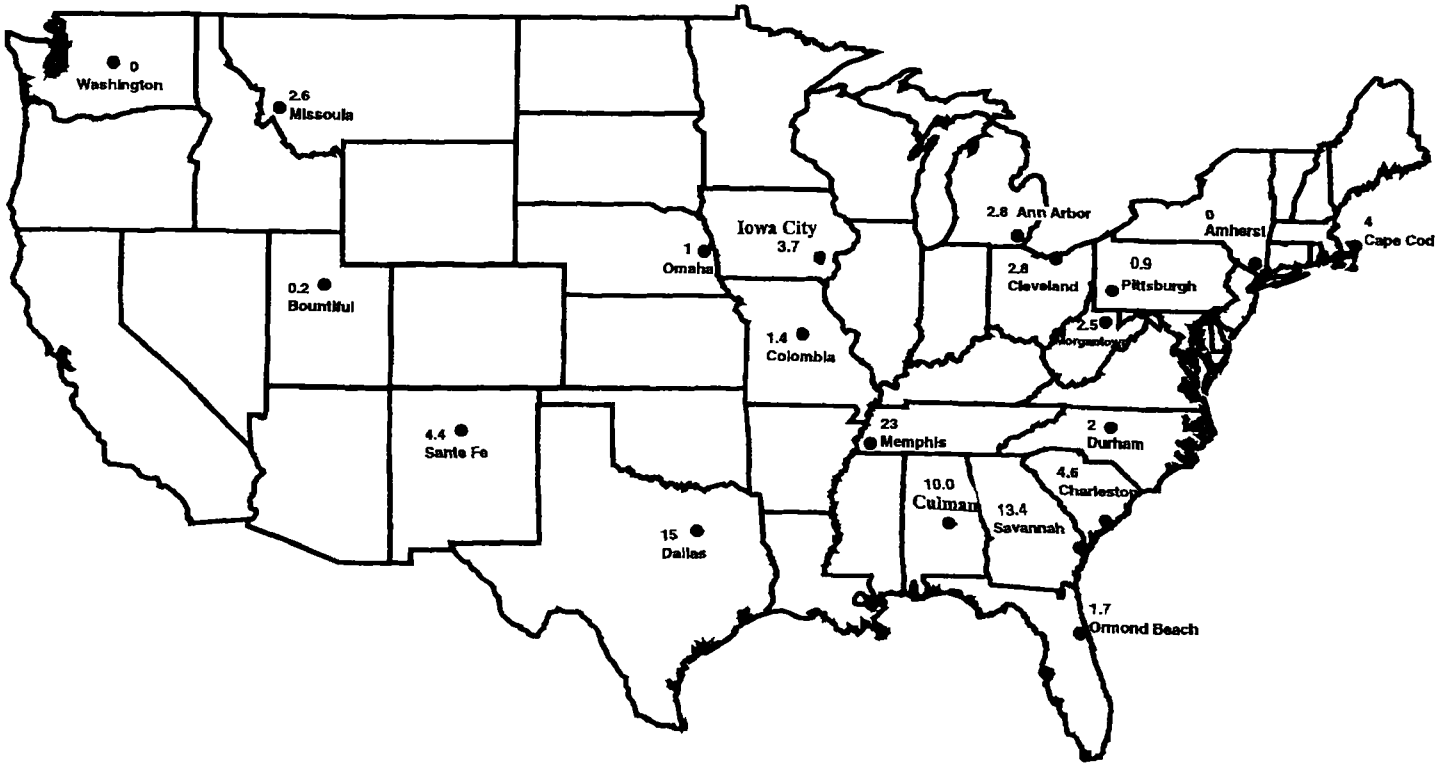

Figure 1. The number beside each bulleted location represents the percentage of allergic fungal rhinosinusitis cases present per total number of sinus surgeries performed by the reporting practice from July 1997 through May 1999. Note the higher incidence in the southern central states relative to the rest of the country.

Table 5. ALLERGIC FUNGAL RHINOSINUSITIS REPORTING SITE WITH PEAK MOULD DATA FROM NEAREST REPORTING POLLEN AND MOULD REPORTING SITE IN 1997 POLLEN AND SPORE REPORT

City	State	*Bipolaris* Peak*	*Alternaria* Peak*
Ormond Beach	FL	200	300
Savannah	GA		
Cape Cod	MA		
Ann Arbor	MI	200	900
Colombia	MO	200	2000
Missoula	MT		
Omaha	NB		1000
Durham	NC		
Santa Fe	NM		
Amherst	NY		200
Cleveland	OH		1000
Pittsburgh	PA	200	1000
Charleston	SC		
Memphis	TN		200
Dallas	TX	80	200
Culman	AL		
Salt Lake City/Bountiful	UT	10	500
Seattle	WA		10
Morgantown	WV	50	1000

*Spores per cubic meter.

CONCLUSION

This survey of geographic distribution of practices across the United States reveals that differences exist. The highest incidence exists along the Mississippi basin and the southern United States, including both the Southwest and the Southeast. To date, no correlation with mould counts has been established. Shortcomings of the present analysis include insufficient information on mould counts important in AFRS from sites proximate to the otolaryngologic reporting sites.

References

1. Allphin AL, Strauss M, Abdul-Karim FW: Allergic fungal sinusitis: Problems in diagnosis and treatment. Laryngoscope 101:815–820, 1991
2. The American Academy of Allergy, Asthma and Immunology: The 1997 Pollen and Spore Report. Milwaukee, Wisconsin, American Academy of Allergy, Asthma, and Rhinology, 1997
3. Cody DT, Neel HB, Ferreiro JA, et al: Allergic fungal sinusitis: The Mayo Clinic experience. Laryngoscope 104:1074–1079, 1994
4. Corey JP, Delsupehe KG, Ferguson BJ: Allergic fungal sinusitis: Allergic, infectious, or both? Otolaryngol Head Neck Surg 113:110–119, 1995
5. Corey JG, Romberger CF, Shaw GY: Fungal diseases of the sinuses. Otolaryngol Head Neck Surg 103:1012–1015, 1990
6. Deshpande RB, Shukla A, Kirtane MV: Allergic fungal sinusitis; Incidence and clinical and pathological features of seven cases. Journal of the Association of Physicians of India 43:98–100, 1995
7. Ence BK, Gourley DS, Jorgensen NL, et al: Allergic fungal sinusitis. Am J Rhinol 4:169–178, 1990

8. Katzenstein AA, Sale SR, Greenberger PA: Allergic Aspergillus sinusitis: A newly recognized form of sinusitis. J Allergy Clin Immunol 72:89–93, 1983
9. Krasnick J, Patterson R, Roberts M: Allergic bronchopulmonary aspergillosis presenting with cough variant asthma and identifiable source of *Aspergillus fumigatus*. Ann Allergy Asthma Immunol 75:344–345, 1995
10. Manning SC, Holman M: Further evidence for allergic pathophysiology in allergic fungal sinusitis. Laryngoscope 108:1485–1496, 1998
11. Manning SC, Mabry RL, Schaefer SD, et al: Evidence of IgE-mediated hypersensitivity in allergic fungal sinusitis. Laryngoscope 103:717–721, 1993
12. Manning SC, Schaefer SD, Close LG, et al: Culture-positive allergic fungal sinusitis. Arch Otolaryngol Head Neck Surg 117:174–178, 1991
13. Noble JA, Crow SA, Ahearn DG, et al: Allergic fungal sinusitis in the southeastern USA: Involvement of a new agent *Epicoccum nigrum* Ehrenb Ex Schlecht. 1824. Journal of Medical and Veterinary Mycology 35:405–409, 1997
14. Ramadan HH, Quaishi HA: Allergic mucin sinusitis without fungus. Am J Rhinol 11:145–147, 1997
15. Schubert MS, Goetz DW: Evaluation and treatment of allergic fungal sinusitis. I. Demographics and diagnosis. J Allergy Clin Immunol 102:387–394, 1998

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