USE OF CASE SURVEY TECHNIQUE TO DETECT ORIGIN OF *Blastomyces* INFECTIONS

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ALTHOUGH *Blastomyces dermatitidis* is related in many respects to the soil-grown, spore-spread *Histoplasma capsulatum* and *Coccidioides immitis*, its ecology defies understanding. The geographic nidus of *B. dermatitidis* remains a disturbing mystery.

The problem of establishing its endemic boundaries is complicated because skin testing techniques which have been used so successfully in mapping areas of histoplasmosis and coccidioidomycosis are totally ineffective in blastomycosis. Unavailability of suitable antigens has likewise precluded effective use of such other serologic techniques as complement fixation and immunodiffusion tests.

Other factors also contribute to the difficulty of precisely understanding the nature of this fungus. First, its sporadic incidence, coupled with delayed diagnoses, makes establishing an epidemiologic pattern difficult. In many cases the diagnosis is not made until long after onset. Second, consistent isolation of the organism from the soil or any other natural habitat has not been realized. There has been one report of growing *Blastomyces* from the soil under a shed where a dog is reported to have died of blastomycosis. This experiment could not be confirmed on repeated attempts by others (*1*).

We became interested in North American blastomycosis (NAB) in this coccidioidal area, California, after discovering a patient whose illness had long been misdiagnosed. A carefully recorded and evaluated history convinced us that our patient acquired his infection in another State. Yet, we continued to wonder if NAB is acquired in California, and if so, under what circumstances.

References in the standard literature were vague and in disagreement as to the established endemic areas. Blastomycosis is confined to the North American continent with most cases occurring in eastern United States (*2–4*). Furcolow, however, believes that scattered cases are found in Europe, Africa, South America, and even Australia (*5*). A recent report from a Veterans' Administration study carried the statement that this disease is found in "The Atlantic, South Central, Ohio-Mississippi River Valley States" (*6*). As late as July 1967, Sen and associates reported that blastomycosis is endemic in the southern, southeastern, and midwestern regions of the United States (*7*).

Campbell, on the other hand, is totally dissatisfied with these confining labels and states that medical mycologists are trying to delete the "North American" from blastomycosis. She refers to autochthonous cases from South America as well as several African nations (letter, March 28, 1967, from Charlotte C. Campbell, associate professor of medical mycology, Harvard University School of Public Health).

The grim reality seems to be that a solution to the problem-rent dilemma of *Blastomyces* epidemiology will have to turn to painstaking details of searching out and making direct examination of every case history, going back to the circumstances surrounding the onset of each case. This was demonstrated in our patient. We were able to trace several years of his travels, going back to a visit to Arkansas where his primary pulmonary symptoms began. Recog-

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nizing the potential of this method, we decided to conduct a survey to determine how many cases of NAB have been diagnosed in California and where they originated (*8*).

Survey Methods

Our initial survey included the large hospitals and clinics and practicing dermatologists in California. We later expanded the survey to include members of the thoracic groups (*9*).

As with any mail survey, one very difficult problem is to insure a response. We met this challenge by sending a short introductory letter defining our objective and inclosing a stamped postcard which simply required the reporter to check a yes or no box after the question, "Have you seen cases of NAB during your practice in California?" A signature was not required since identification was established by prenumbering the cards.

The success of this preliminary contact was astonishing. We sent 1,146 letters: 300 to dermatologists, 25 to hospitals and clinics, and 821 to thoracic specialists. We received replies from 1,000 or 88 percent.

The initial reply obviated further contact with all except 105 respondents who answered affirmatively. To these we sent thank-you letters and a data sheet requesting facts about their patients (see box).

Response to these letters was more difficult to obtain. Sometimes it required followup letters, phone calls, and often visits to the physicians or hospitals. In some cases it was necessary to obtain permission to review medical records in detail. There was duplication in 75 instances in which physicians described patients who had been reported by other respondents.

Data Sheet

Please provide us information about patients in your practice who have been diagnosed as having North American blastomycosis.

1. Case: Patient's initials, file number, or any other identification which will specifically identify patient so that duplications will not occur from other physician or hospital: (a) Hospital admissions where treatment for North American blastomycosis may have been given and (b) names of other known physicians who may have seen or treated this patient for North American blastomycosis.

2. Site of infection at the time you were seeing patient: (a) Specific skin area, (b) lungs (if involved), and (c) dissemination to other tissue.

3. Method by which you first made your diagnosis. Mark with the number *1* after the test and *2, 3,* etc., for subsequent positive findings. Mark 0 if test was negative and X if not done: (a) Clinical, (b) autopsy, (c) direct smear, (d) culture, (e) histopathological, (f) skin test, and (g) complement fixation.

4. Circumstances surrounding exposure to North American blastomycosis: (a) Date of diagnosis, (b) probable date of infection, (c) geographic area where infection may have occurred, and (d) areas of travel or visits in the past 10 years: (1) Visits, (2) military, (3) work, and (4) other visits to a possible endemic area.

5. Results or outcome: (a) Treatment, (b) recovery (complete) (pending) (uncertain) (failed), (c) prognosis, (d) died, or (e) chronic.

Results

A total of 37 cases of North American blastomycosis were thus obtained after instances of duplication, wrong diagnoses, and inadequate information were eliminated. We now feel that these cases represent nearly all diagnosed cases of North American blastomycosis in California over the past 40 years, which is not very many in comparison to the population of the State.

As can be seen in table 1, 33 of the reported cases could be traced to visits to other States and to areas believed to be endemic for North American blastomycosis.

Insufficient data in three cases precluded more than a speculation as to where and when infection occurred. One patient had died, leaving no clues about family or friends, and in two other cases clinical histories were incomplete and the patients could not be located.

The only case in which the patient definitely acquired the infection in California occurred in an accidentally self-inoculated autopsy assistant.

The 37 case reports which accrued from our survey are too lengthy to be included in this report, but are available to interested investigators on request to the authors. Tables 1 and 2

Table 1. Cases of North American blastomycosis in California by source of case report, years' duration, year of diagnosis, probable locality of acquisition, and basis for excluding California as endemic area

Case No.	Source of case report	Years' duration	Year of diagnosis	Probable locality of acquisition	Basis for excluding California as endemic area
1	Veterans' Administration Hospital, Fresno.	4+	1963	Arkansas	Symptoms of pulmonary disease developed after visit to endemic area, but no specific reference to blastomycosis.
2	University of California Medical Center, Los Angeles.	5+	1961	Chicago	Symptoms of dermal disease when patient entered California.
3	Veterans' Administration Hospital, Long Beach.	2+	1955	Arkansas	Pulmonary disease developed before patient came to California.
4	Dermatologist, Bakersfield	1—	1953	do	History of pulmonary disease before coming to California; dermal lesions developed while in California.
5	do	6+	1954	Oklahoma	Visited endemic area near time of onset, but no specific reference to blastomycosis.
6	Dermatologist, San Jose	25+	1939	Texas or Arizona.	Symptoms of dermal disease when patient entered California.
7	do	28	1930	Unknown	Complete history unavailable.
8	Veterans' Administration Hospital, San Fernando.	19	1952	Texas	Pulmonary disease developed before patient came to California.
9	University of California Medical Center, San Francisco.	10+	1942	North Dakota.	Visited endemic area near time of onset, but no specific reference to blastomycosis.
10	do	1+	1937	Arkansas	Do.
11	Dermatologist, Riverside	1—	1950	Nebraska	Complete history unavailable; history of pulmonary disease before coming to California; dermal lesions developed while patient was in California.
12	Los Angeles County General Hospital.	1—	1954	Los Angeles County General Hospital.	Acquired in California; accidently inoculated.
13	Veterans' Administration Hospital, Oakland.	1+	1956	Illinois	Diagnosed and treated before the patient came to California.
14	Dermatologist, Los Angeles	1—	1951	North Carolina.	Pulmonary disease developed before patient came to California; dermal lesions developed while patient was in California.
15	Los Angeles County General Hospital.	4+	1951	Texas	Patient lived in another State when condition was diagnosed; pulmonary disease developed before patient came to California.
16	Dermatologist, Long Beach	1+	1949	Iowa	Visited endemic area near time of onset, but no specific reference to blastomycosis.
17	Veterans' Administration Center, Los Angeles.	35+	1940	Wyoming or Iowa.	Dermal and pulmonary disease diagnosed and treated while the patient lived in another State before he came to California.
18	Veterans' Administration Hospital, Long Beach.	1—	1954	Rhode Island.	Symptoms of pulmonary disease developed after the patient visited an endemic area.
19	Dermatologist, Los Angeles	7+	1962	Wisconsin	Pulmonary disease developed before patient came to California; had symptoms of dermal disease when he came to California.
20	University of California Medical Center, San Francisco.	1+	1948	Minnesota	Complete history unavailable; dermal lesions developed while patient was in California; history of pulmonary disease before coming to California.

Table 1. Cases of North American blastomycosis in California by source of case report, years' duration, year of diagnosis, probable locality of acquisition, and basis for excluding California as endemic area—Continued

Case No.	Source of case report	Years' duration	Year of diagnosis	Probable locality of acquisition	Basis for excluding California as endemic area
21	University of California Medical Center, San Francisco.	5+	1947	Nebraska	Patient lived in another State when condition was diagnosed.
22	Dermatologist, Fresno	1—	1958	Arkansas	Visited endemic area near time of onset, but no specific reference to blastomycosis.
23	San Diego County General Hospital.	3+	1958	----do	Visited endemic area near time of onset, but no specific reference to blastomycosis; pulmonary disease developed before the patient came to California; dermal lesions while in California.
24	Los Angeles County General Hospital.	2—	1954	Unknown	Complete history unavailable; patient died.
25	Veterans' Administration Center, Los Angeles.	3+	1955	Arkansas	Visited endemic area near time of onset, but no specific reference to blastomycosis; symptoms of pulmonary disease developed following visit to endemic area.
26	Dermatologist, Berkeley	13?	1943	Texas	Complete history unavailable; history of pulmonary disease before coming to California; dermal lesions developed while the patient was in California.
27	Los Angeles County General Hospital.	2+	1947	Illinois	Complete history unavailable; pulmonary disease developed before patient came to California; dermal lesions developed while patient was in California.
28	Veterans' Administration Center, Los Angeles.	[1]1+	1959	Louisiana	Complete history unavailable; patient had history of pulmonary disease when he came to California; dermal lesions developed after patient came to California.
29	Los Angeles County Harbor General Hospital.	4+	1957	Maine	Patient had pulmonary disease before he came to California.
30	St. John's Hospital, Santa Monica.	1—	1957	Georgia	Visited endemic area near time of onset, but no specific reference to blastomycosis; symptoms of pulmonary disease developed following visit to endemic area.
31	Los Angeles County Harbor General Hospital.	1—	1953	Mississippi	Pulmonary disease developed before patient came to California.
32	Good Samaritan Hospital, Los Angeles.	2+	1948	Wisconsin	Patient lived in another State when condition was diagnosed.
33	LeVina Hospital and Sanatorium, Altadena.	[1]5	1966	New Jersey	Visited endemic area near time of onset, but no specific reference to blastomycosis.
34	Santa Barbara General Hospital, Santa Barbara.	[1]	1964	Unknown	Complete history unavailable.
35	City of Hope Medical Center, Duarte.	[1]5	1954	Illinois	Visited endemic area time of onset, but no specific reference to blastomycosis.
36	Los Angeles County General Hospital.	5	1967	Louisiana	Do.
37	Veterans' Administration Hospital, Palo Alto.	[1]8	1964	Indiana	Complete history unavailable; history of pulmonary disease before coming to California; dermal lesions developed after the patient came to California.

[1] Time not precise.

Table 2. Positive results of laboratory procedures used in diagnosing 37 cases of

Case No.	Mycological diagnosis					Histological examination of tissues					
	Sputum		Biopsy of lung material			Skin			Other tissues		
	Smear	Culture	Smear	Culture	Tissue section	Smear	Culture	Tissue section	Smear	Culture	Tissue section
1	+	+				+	+	+			
2	+	+				+	+	+			
3	+	+				+	+	+			
4						+		+			
5						+	+	+			
6						+	+	+			
7						+	+	+			
8									+	+	+
9									+	+	+
10								+			
11								+			
12						+	+	+			
13	+	+	+	+	+						
14						+	+	+			
15									+	+	+
16						+	+	+			
17						+	+	+			
18			+	+	+			+			
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21						+	+	+			
22						+	+	+			
23								+	+	+	+
24		+							+	+	+
25		+				+	+	+	+	+	+
26						+	+	+			
27							+	+			
28						+	+	+			
29					+						
30					+						
31			+	+	+				+	+	+
32		+			+						
33							+				
34					+						
35					+						
36										+	+
37					+						+

summarize much of the data obtained from them. Table 1 gives nine of the bases by which the probability of infection occurring in California was reduced. The table also includes the area more likely to have been the source of infection. Table 2 shows the bases for the diagnoses of the 37 cases. Basically, these included one or more positive results for smear, culture, or histology report. Serology and skin test results were supportive but were not the primary bases for diagnosis.

Discussion and Conclusion

We feel quite comfortable in the conclusion that this survey excludes California as a natural site of infection. Cases are acquired elsewhere and diagnosed in California. We conclude also that because of the lack of more specific measures, such as isolation of the organism from nature or immunological procedures, it would seem that a workable alternative would be to conduct retrospective case surveys. If the surveys are painstakingly done in areas where followup visits and record reviews can be made, the endemicity of North American blastomycosis will soon be much more understood.

Since we began our survey, similar projects have been reported in West Virginia (*10*), Wisconsin (*11*), and North Carolina (*7*). All three of these projects establish high endemicity within the borders of their respective States. Our survey is the first so far to suggest that nonendemicity of blastomycosis can be established on the basis of survey techniques.

Complement fixation tests			Skin tests	
Blasto-myces	*Histo-plasma*	*Coccidi-oides*	*Blasto-myces*	*Histo-plasma*
+			+	+
			+	
+	+			
+			+	
			+	
+				
+	+		+	
+	+		+	
			+	
			+	
+			+	
+	+			
+				
				+
+		+		

It has been suggested that the survey procedure introduces a bias which tends to show greater incidence of disease diagnoses near sophisticated diagnostic centers. For example, McDonough (*11*) states in his survey in Wisconsin, "There is a grouping of cases in the southeastern (one of the most populated) and northwestern (one of the least populated) parts of the State. These groupings may not indicate the true picture of distribution during the period. The notification of cases depends to a large extent upon the Wisconsin State Laboratory of Hygiene located at Madison, and physicians, microbiologists, technicians, etc., located mainly in the vicinity of Milwaukee." He further states, "Minneapolis-St. Paul, Minnesota, are adjacent to this part of Wisconsin and it would seem logical to assume that the patients residing in the area would attend the excellent hospitals in these cities where the diagnosis and laboratory confirmation would be made." He states further, "No doubt, some of the difference was caused by the writer being located in the Milwaukee region and, therefore, being more easily informed of the diagnosis." In the West Virginia survey (*10*) Pfister and Hamaty state, "The lack of cases in northern and eastern parts of the State could well be due to referral to medical centers outside the State." Such a bias could not be operating in our study since all cases came from areas far from the base for our investigation.

Summary

Available literature shows that North American blastomycosis is one of few infectious diseases for which the ecology remains unknown. Because of antigenic nonspecificity, the immunological techniques which were successful in mapping the endemicity of histoplasmosis and coccidioidomycosis have been of no help in blastomycosis. The problem is further complicated by the sporadic incidence of this disease, the ofttimes long delays in diagnosis, and the inability to isolate the fungus from its natural habitat.

An extensive survey revealed that in 37 cases of North American blastomycosis observed in California, 33 patients were infected elsewhere. The survey provides strong evidence that this fungus is not a natural inhabitant of California.

Similar surveys have been conducted recently in West Virginia, Wisconsin, and North Carolina—States known to be endemic for North American blastomycosis. We suggest that the survey method be used widely as a means of more precisely establishing *Blastomyces* endemicity.

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Survey of High Schools for Radiation-Producing Equipment

A joint State-Federal survey to assess health implications in the use of radiation-producing electronic equipment in high school science classes began in April in selected schools throughout the nation. In some high schools, X-ray and other radiation equipment is being used for scientific demonstrations in an unsafe manner.

The survey was conducted in one metropolitan area in each of the nation's nine Public Health Service regions. About 20 high schools in each area were selected for the study for a national total of about 200 institutions. Electronic equipment studied for radiation hazard potential included X-ray machines, Van de Graaf accelerators, and microwave and laser devices.

Arrangements for the survey as a State-Federal effort were initiated by the Environmental Control Administration's Bureau of Radiological Health following reports of the potentially hazardous use of radiation-generating electronic equipment in high schools in several States. In one school, health authorities found unshielded X-ray units were used frequently. Hand-held fluoroscopes, long recognized as dangerous, were observed in the same school. Thirty-one junior and senior high schools in another State were registered as users of radiation-producing equipment.

The survey was conducted under provisions of the new Radiation Control for Health and Safety Act. Survey findings will be reported to Congress. A major objective of the survey was to establish an informational basis for recommendations for safe practices in the use of radiation-generating equipment in educational institutions.

Two-man teams of State and Federal radiological health specialists conducted the survey. They made radiation measurements of electronic equipment operating under conditions of simulated or actual classroom use. They also (*a*) identified types and listed quantities of equipment which actually or potentially may emit radiation, (*b*) estimated the number of students in each of the survey schools who use or could be exposed to radiation equipment, and (*c*) determined if communications between school administrations and radiological health agencies effectively fostered radiation protection.

Metropolitan areas chosen for the survey were Boston, Mass.; Philadelphia, Pa.; Raleigh-Durham, N.C.; selected areas in Florida; Chicago, Ill.; Kansas City, Mo.; Dallas-Fort Worth, Tex.; Denver, Colo.; and San Francisco, Calif.