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Geographic distribution of human blastomycosis cases in Milwaukee, Wisconsin, USA: Association with urban watersheds

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Abstract

Most studies of endemic blastomycosis and outbreaks have involved rural areas. Case homesites in rural Northern Wisconsin have been associated with waterways and sand soils. ARC-GIS was used to geocode addresses and to observe geographic features of homesites from 45 State-mandated reports of human blastomycosis in urban Milwaukee County, Southeastern Wisconsin 2000–2004. Each case property was directly observed, and houses and duplexes ($N = 38$) were compared with 151 same-street control homesites. Categorical data was analyzed using a chi-square or Fisher's exact test; continuous variables by Kruskal–Wallis test. One case cluster was seen on Milwaukee's North side where the estimated annual incidence was 2.8/100,000 compared to 0.96/100,000 for the entire county. Cases were less common in the most urbanized watersheds (0.49/100,000/yr) versus Lake Michigan shores (0.85) versus remaining three open watersheds (1.4) [$P < 0.01$]. Case homesites averaged 1067 m to waterways and none were on sand soils. (Comparison is made to a Northern Wisconsin community where case homesites averaged 354 m to waterways, 24/25 were on sand soils and annual incidence was 74/100,000.) No unique features of case homesites were identified in Milwaukee County. In this urban area of Wisconsin, relatively low incidence rates may be explained, in part, by lower density of inland waterways and lack of sand soils, however, blastomycosis cases appear to be associated with open watersheds.

Key words: *Blastomyces dermatitidis*, blastomycosis, geographic information systems, lung infections, mycoses

Introduction

Blastomycosis is a potentially fatal systemic and cutaneous fungal infection that affects humans, dogs, and other animals. *Blastomyces dermatitidis*, the dimorphic etiologic agent, exists as a mold in nature and is generally acquired through the inhalation of spores that transform to the yeast forms in the lungs [1, 2]. Its precise ecological niche is unknown, yet studies of clustered cases and outbreaks have frequently involved sites that contain decaying wood and other organic material, including bird or animal excreta, forested podzolic or sandy soils, waterways, changing water levels, elevations typically 30–600 m above sea level, and remarkable climatic differences over all seasons [2–7]. However, most recent studies of endemic regions and outbreaks have involved rural areas [1, 5, 6, 8–13].

Blastomycosis is highly endemic in Northern Wisconsin with consistent estimated annual incidence rates of 40/100,000 for Vilas County, which includes the only incorporated city, Eagle River [5, 8]. Studies of this area have revealed an association

between blastomycosis cases and habitation along waterways, excavation [5, 6, 8] and sand soils [9]. Sands contain less organic matter, are more prone to drought and the loss of mineral content. However, sands near shoreline environments acquire organic material as a result of shoreline wash up and from animal excrements. This rapidly changing environment may also promote the growth or propagation of *B. dermatitidis* [1, 7, 9].

Studies have suggested that blastomycosis in humans may be most commonly acquired at one's homesite, which is the location where most people presumably spend the largest amount of time. In Northern Wisconsin repeat infections occur at the same homesite, sometimes among different families [14]. The geographic distribution of human cases, by homesite, also remains consistent over time [5, 8], and a correlation between the distribution of human and canine cases is seen, despite obvious differences in the range of their geographic exposures [5, 6, 8, 9]. In addition, several studies have failed to implicate specific occupational or recreational activities with acquisition of *B. dermatitidis* [6, 12, 15–17]. Case reports in urban areas suggest acquisition of blastomycosis by animals and people without likely exposure elsewhere [14, 18, 19]. Three urban Wisconsin case reports have involved older homes with front porches [14, 19].

This present study investigates the environmental and homesite features of cases of human blastomycosis in urban Milwaukee County, Wisconsin (pop. 940,000; 249 km^2; 1500 people/km^2). Comparison is made to cases within the incorporated limits of Eagle River, Wisconsin (pop. 2000; 5.2 km^2; 386 people/km^2), a highly endemic rural community located 323 km north.

Materials and methods

Milwaukee County is located in Southeastern Wisconsin along the shores of Lake Michigan. The average high/low temperatures are −3 °C/−12 °C in January and 26 °C/17 °C in July. Eagle River is located in Northern Wisconsin, where the average high/low temperatures are −6.7 °C/−17.5 °C in January and 26 °C/13.8 °C in July. Both Milwaukee County and Eagle River have a similar annual precipitation of approximately 84 cm.

State-mandated reports of blastomycosis were used to investigate features of case homesites in urban Milwaukee County. Cases were examined individually by home address and by comparing estimated annual incidence by zip (postal) code to determine the geographic and population distribution within the county. While all case addresses were used to determine incidence rates and association with respective geographical features in the community such as soils and waterways, only homesites that contained a private outside entrance (houses and duplexes) were used to compare features of individual homesite properties. We wished to examine potential house/duplex homesite differences including presence of a front porch (defined as a roofed, partially open home entrance with potential crawl space beneath), size and type of lot (middle versus corner), driveway and foundation materials, presence of adjacent empty lot or garage, and proportion and type of trees present (hardwood versus softwood), without confounding regarding proximity to waterways and soil type. Thus, for each Milwaukee County house or duplex, the four numerically closest same street address domiciles were entered into a control group ($N = 151$).

Forty-five cases (38 houses/duplexes) were recorded from the City of Milwaukee Health Department 2000–2004 (and 151 house/duplex controls were identified). Comparison was made regarding these same geographic features with 25 cases (17 houses/duplexes) from the Vilas County Health Department (1984–2004). Beginning time periods were chosen based on the first year of reliable consecutive case recording for each area. As the small land area of incorporated Eagle River did not allow analysis of geographic features by postal zone or watershed, 57 random number city homesites were selected from the 2001 Vilas County tax records for comparison; in addition to 65 same street controls selected in a fashion identical to that of the Milwaukee County control group.

Power analyses were performed using Epi-Info software. For evaluation of house/duplex features, we were interested in meaningful differences between cases and controls. Therefore, the inclusion of 38 cases and 151 controls resulted in 99% power to detect a 40% difference at $P = 0.05$ for Milwaukee County. In Eagle River, 25 cases and

57 random controls were estimated to have 90% power to detect a 40% difference at $P = 0.05$.

Each case and control homesite was directly observed. Due to age of cases in Eagle River (up to 21 years), every attempt was made to insure that observed physical features of the homesite were as old as the date of the involved case of blastomycosis. Home style and age were estimated based on knowledge of neighborhood age, observation of style and material utilized, and a reference text [20]. The physical features of the homesite were recorded and analyzed using MINITAB (Minitab, State College, PA) software. Categorical data was analyzed using a chi-squared (Yates corrected for 2×2 tables) or Fisher's exact test; continuous variables by Kruskal–Wallis test. Street addresses were geocoded using ARC-GIS software (ESRI, Redlands, CA). A cluster analysis amongst the Milwaukee County case homesite locations was performed using CrimeStatII with four points per cluster and $P = 0.05$ (Ned Levine & Associates, Houston, TX). Resultant maps were generated and incidence rates were calculated for each zip code in Milwaukee County. The distribution of blastomycosis cases was analyzed with respect to geographical features: waterways, parks, soil surface type (USDA database); and for Milwaukee County, watersheds (www.wisconline.com/greenmap), deep tunnel storm sewage collections system, toxic waste sites and median household income by zip code (2000 US Census). Aurora Health Care Institutional Review Board deemed these studies exempt from human subjects review.

Results

Cases averaged 1067 m to waterways in Milwaukee County ($N = 45$), and 354 m to waterways in Eagle River both among cases ($N = 25$) and random controls ($N = 57$). None of the 15 categorized Milwaukee County homesites were on sand soils; 12 were on silt loams, two silty clay loams, one loam. Except for the immediate Lake Michigan beaches, there are no sand soils in Milwaukee County, <1% of county soils are sandy soils and 35% of soils are unmapped/urbanized. In Eagle River 24/25 case homesites were on sands; the remaining case on a sandy loam. This compares to 42/57 random control homesites on sands ($P = 0.03$).

One case cluster was observed on Milwaukee's North side between two zip codes (Figure 1), where the estimated annual incidence was 2.8/100,000 compared to 0.96 for all of Milwaukee County (versus 74/100,000 for Eagle River). In Milwaukee County, cases were less common in the predominately urbanized watersheds (waterways which are confined by retaining walls, have their streambeds and shorelines replaced by concrete, or run underground), namely the Menomonee and Kinnickinnic River watersheds, (0.49/100,000/yr) than along Lake Michigan shores (0.85) or in the remaining three watersheds typified by open waterways, the Milwaukee River, Root River, and Oak Creek (1.4) [$P < 0.01$, chi-squared test for trend]. Of the 45 Milwaukee County cases, the nearest waterway was an open stream or pond lagoon for 35, an urbanized waterway for 5, the junction of an open and urbanized stream for 2, and Lake Michigan for 3 case sites.

Figure 2 is a faithful representation of the distribution of the 45 individual homesites of blastomycosis cases in Milwaukee County and relationships to geographic features. With respect to the United States Health Insurance Portability and Accountability Act of 1996, actual homesite locations are not shown. Instead, individual actual (dot) map locations were subjected to random displacement within their same US census track (area representing 1500–8000 persons). Over the 5 years, no cases were reported east of the Milwaukee River, an area with a population of nearly 100,000 (Figure 2), and no apparent relationships of cases to toxic waste sites or parks, apart from waterways were seen.

Utilizing census data, there was no correlation between incidence rates and median household income by zip code in Milwaukee County. The median age of case houses/duplexes was 63 years (range 5–110), and there were no gross differences between age of housing in postal zones with and without blastomycosis cases. Table 1 details homesite features of blastomycosis cases, compared to their respective control groups, for houses and duplexes in Milwaukee County and Eagle River. All homes had basements or the equivalent (two Eagle River same street controls were bi-level type homes), and all homesites had driveways except one Milwaukee case. In Milwaukee County, only 15/38 homes had a front porch versus 48/151 same street controls ($P = 0.48$). Only 9/38 cases

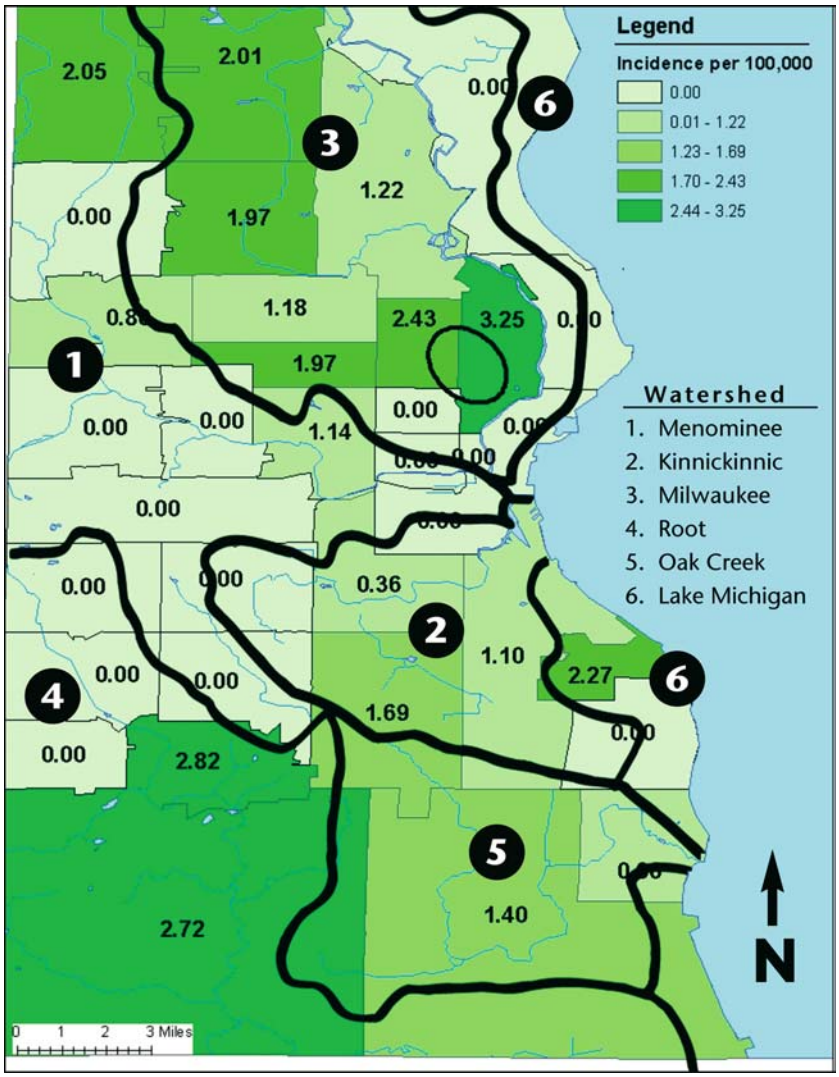

Figure 1. Annual incidence of human blastomycosis, by postal code, Milwaukee County, with urban watersheds indicated. Note that upper Menomonee River system is open where cases occurred, far lower Milwaukee is urbanized. Oval represents single cluster with CrimeStatII nearest-neighbor analysis at 4 points/cluster, $P = 0.05$.

had a front porch with fully or partially open crawlspace beneath where small mammals and other animals could potentially live or leave excrements [21]. Front porches were more common among case houses and duplexes, compared to controls, in Eagle River. Interpretation of data regarding porches is limited due to the potential for unintentional bias in subjective interpretation of ambiguous home entrances. Overall, due to the range in age of occurrence of cases in Eagle River, data regarding homesite features should be interpreted with caution.

Discussion

Blastomycosis incidence rates and geographic associations differ between these two contrasting Wisconsin cities. No evidence of significant clustering around individual waterways was found for Milwaukee County, yet we did see a relationship with waterways, namely differences in incidence rates among the types of urban watersheds. A preponderance of cases were seen in watershed areas having open waterways, suggesting that perhaps associations with open waterways are

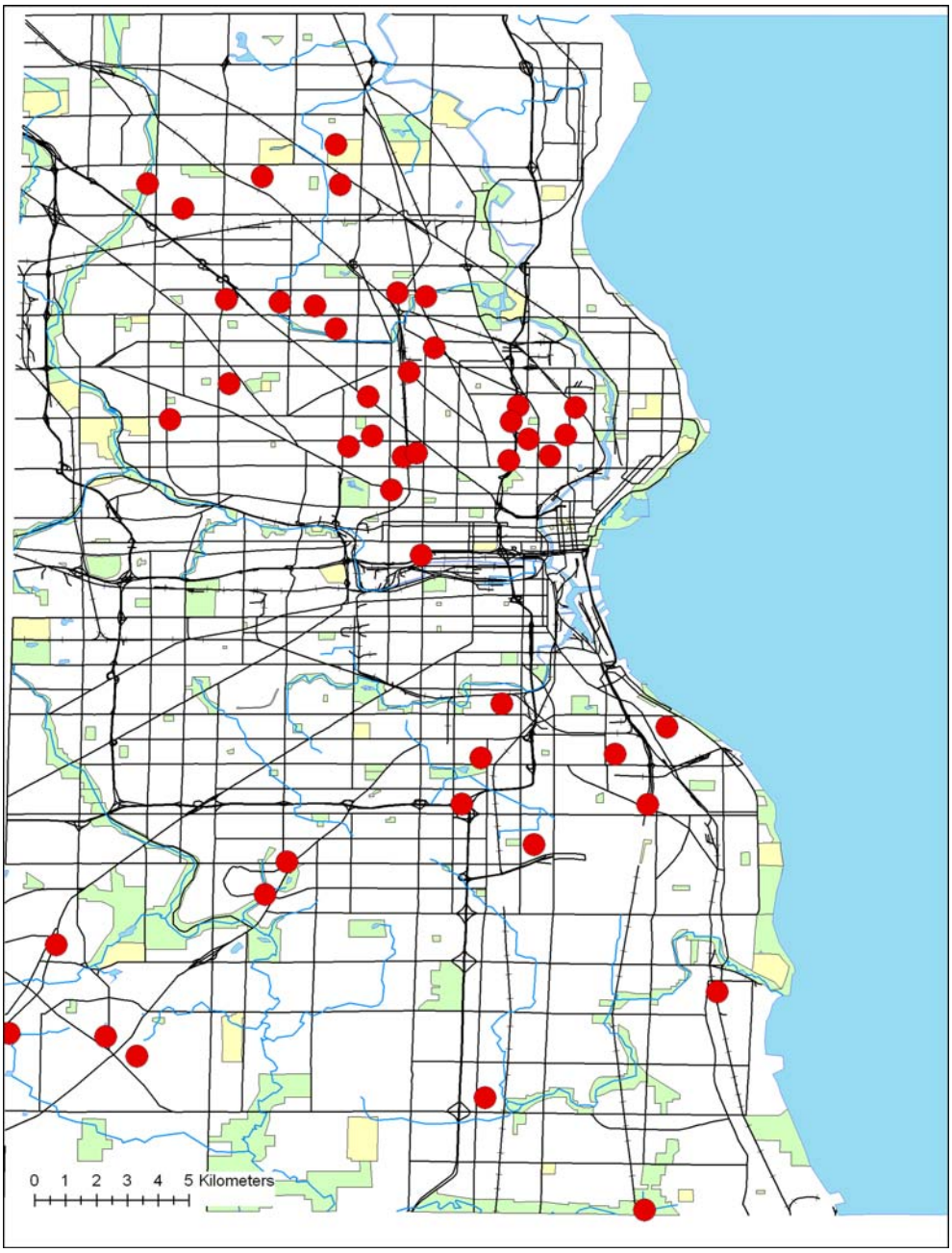

Figure 2. Distribution of homesite locations of 45 cases of human blastomycosis, Milwaukee County, WI, 2000–2004, subjected to random displacement within their individual census track to protect subject privacy. Features shown include waterways, parks and major streets.

important for acquisition of *B. dermatitidis* even in significantly less prevalent urban areas.

The association of cases with open waterways, without close proximity to these streams and lagoons, suggests the possibility of passive or active spread of the fungus from stream bank to homesites. Thus far, investigation of bats, beavers, wood lice (*Isopoda*) and two species of shrews have shown no evidence of spread by these animals [22]. A wide variety of birds and terrestrial animals and

Table 1. Features of houses and duplexes associated with human blastomycosis, Milwaukee County and City of Eagle River, WI

	Milwaukee County cases ($N=38$)	Milwaukee County controls ($N=151$)	*P* Value*	Eagle River cases ($N=17$)	Eagle River random controls ($N=52$)	*P* Value*	Eagle River same-street controls ($N=65$)	*P* Value*
Median age of home (y)	63	60	1.0**	45	40	0.6**	45	0.8**
Number of stories								
1	36%	33%	0.06	41%	67%	0.1	62%	0.2
2	42%	58%		59%	33%		38%	
3	21%	8%		0%	0%		0%	
House style (20)								
Bungalow	60%	64%	0.7	82%	90%	0.6	77%	0.5
Stick/Eastlake	26%	18%		0%	2%		11%	
Colonial	5%	6%		6%	2%		3%	
Other	7%	10%		12%	6%		9%	
Foundation								
Concrete	52%	54%	0.9	82%	90%	0.6	83%	0.6
Stone	34%	29%		12%	8%		16%	
Brick	13%	15%		6%	2%		1%	
Front Porch	39%	32%	0.5	59%	29%	0.06	25%	0.02
Trees shading ≥½ of lot	36%	42%	0.7	59%	54%	0.9	43%	0.4
Lots with hardwoods only	37%	38%	0.9	6%	8%	1.0***	6%	1.0***
Empty lot adjacent	23%	17%	0.5	41%	48%	0.8	29%	0.5
Lot size >2500 ft^2	24%	23%	0.9	29%	46%	0.4	20%	0.5***
Corner lot	16%	15%	0.9	29%	31%	0.8	42%	0.5
Driveway material								
Concrete	88%	78%	0.6	6%	12%	0.7	8%	0.1
Asphalt	12%	16%		59%	65%		45%	
Gravel	0%	5%		24%	17%		46%	
Dirt	0%	1%		12%	6%		1%	
Garage present	82%	93%	0.5	88%	83%	0.7***	72%	0.2***
If garage, attached	19%	22%	0.9	40%	51%	0.7	25%	0.3***

household pests could be investigated in this regard, although the specific distribution of cases in Milwaukee County may more suggest a terrestrial mammal such as the Virginia opossum (*Didelphis virginiana*) that is found in urban environments, is more prevalent where open streams are more prevalent, are semi-nomadic and prefer to den along vegetated stream banks [21]. These animals are not generally observed in Eagle River, however, animal vectors or environmental factors (e.g., porches, types of stream banks) important for the spread of *B. dermatitidis* may differ between endemic areas.

No specific homesite features were identified as being unique to those with blastomycosis cases in Milwaukee County. Only a minority of case homes featured a front porch conducive to small animal denning or latrine chambers [21, 23], however, multiple other potential sites of animal activity could have existed on these properties. Significant limitations of this study include the subjective nature of some of the data, the inability to examine the inside of these domiciles or the backs of the homes' yards (including rear decks or porches), to take environmental samples or to interview the patients.

Manetti [24] reported on 23 cases of human blastomycosis from the 1980s in Rockford, IL, an urban area just south of Wisconsin. The annual incidence was estimated at 1.94/100,000, and concentrations of cases in two areas of the city were seen in this report in which the investigator was similarly unable to interview subjects.

Our study of Milwaukee County suggests that even in urban areas, geographic features near one's homesite may affect risk of disease acquisition. Were this not the case, blastomycosis incidence rates would be expected to be uniform throughout the county. Cases occurred in both City of Milwaukee and suburbs and did not appear to be associated with median household income or age of homes or neighborhoods.

The premise of our manuscript is that geographic and environmental features in close proximity to one's homesite are important for the acquisition of *B. dermatitidis* and that this fact explains the variation in distribution of cases in urban areas such as Milwaukee. In the absence of case and control subject travel and recreational histories, one might suggest that urban case patients may travel to rural areas and engage in outdoor activities more commonly than subjects in control households, thus leading to misinterpretation of geographic data. This possibility indeed remains as a limitation of this study.

Other studies, however, have failed to associate specific outdoor activities with *B. dermatitidis* exposure [6, 12, 15–17]. In Eagle River, for example, where opportunities for hunting and fishing abound, only 13% of blastomycosis patients engaged in these activities in the 1990s [8]. In addition to case reports indicating likely exposure near the urban homesite of the human or animal [14, 18, 19], we are currently investigating a cluster of five blastomycosis cases among indoor domestic cats with no significant travel or non-property exposure in suburban Chicago, IL (N. Blondin, D. Baumgardner, unpublished observations).

In rural Northern Wisconsin, blastomycosis case homesites are associated with sand soils, which predominate in Eagle River. No association with sandy soils was seen in Milwaukee County, likely due to lack of such soils in the region. Features of such soils may strongly favor, but not be essential for the proliferation of *B. dermatitidis* in the environment. The relative absence of sand soils and lower density of inland waterways in Milwaukee County may explain the significantly lower incidence rates compared to the Eagle River area. Sand soils in Eagle River are the result of reddish brown sandy till deposited by glaciers 18,000–15,000 years ago [25]. In contrast, Milwaukee County is typified by brown silty and clayey till from glaciation 26,000–11,000 years ago. If indeed the presence or absence of sandy soils is a significant determinant of the environmental distribution of *B. dermatitidis* in Wisconsin, it is interesting to speculate that geologic events over 11,000 years ago may be underlying this distribution and the resultant disparities in blastomycosis incidence rates between these two areas.

Finally, even patients from low incidence areas who have suggestive symptoms should still be investigated for blastomycosis even if they have not traveled beyond central urban areas. Such urban areas may indeed have their own geographic features, which impart increased risk of acquisition of *B. dermatitidis*.

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