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Source: Journal of Wildlife Diseases, 17(2) : 191-196

Published By: Wildlife Disease Association

URL: https://doi.org/10.7589/0090-3558-17.2.191

THE ROLE OF BATS IN THE PROPAGATION AND SPREAD OF HISTOPLASMOSIS: A REVIEW

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EPIZOOTIOLOGY

Histoplasmosis is a mycotic infection of man and animals caused by *Histoplasma capsulatum* a dimorphic fungal soil saprophyte that produces mycelium-borne infective spores. Inhalation of airborne spores invariably is the route of infection. When suitable microclimatic conditions are present and soils harboring *H. capsulatum* become enriched with animal feces, the environment is favorable for proliferation of the fungus.[19] Avian habitats are considered to be especially suitable for the proliferation of *H. capsulatum;* however, infection has never been documented in birds probably because of their high body temperature.[37] While the yeast form of *H. capsulatum* has been found in a number of mammalian species only the Chiroptera are considered to play significant roles in the epizootiology of this mycosis.[19,25,26]

An acute, febrile respiratory disease, referred to as cave sickness, had long been recognized in individuals who worked in or visited caves in various parts of the world.[3,5,19] Epidemiological studies demonstrated that cave sickness was histoplasmosis, with the fungus being recovered from soil, guano, and bats inhabiting many of the caves. However, caves were not the only harborhages of bats which were associated with human histoplasmosis. Bat guano and soil from in and around roosting trees, houses, bridges and other structures also have yielded *H. capsulatum.*[3,5]

DISTRIBUTION

H. capsulatum has a worldwide distribution. In the United States an endemic area has been determined by histoplasmin skin testing of man and animals. This area includes the central portion of the country, particularly the Ohio River and Mississippi River valleys, extending eastward into Virginia and Maryland.[26] Almost 90% of all reported cases of human histoplasmosis in the United States come from this area. In Florida, which is outside the endemic area, investigation of reported human histoplasmosis has revealed that all autochthonous cases since 1955 were derived from exposure to caves inhabited by bats (Table 1). This observation is supported by histoplasmin skin test surveys that revealed 71% reactivity rate in cave explorers as opposed to a 2% or lower rate for non-cave exploring, life-long residents of the state.[13]

Table 2 summarizes the reported isolations of *H. capsulatum* from bats. These isolations have been overwhelmingly from colonial species. The only isolation from a solitary species was from a *Pipistrellus subflavus* collected by the authors.[20] *H. capsulatum* also was recovered from 37 of 307 *Myotis austroriparius* and 3 of 10 guano specimens collected in the same cave from which the *P. subflavus* was obtained. The fact that colonial species are easier to capture may be a factor in the paucity of *H. capsulatum* isolates from

TABLE 1. Bat associated histoplasmosis in Florida, 1955-1979.

Year	Number of Human Cases	Positive Bat Species	Positive Soil Samples	Reference
1955	1	N.T.*	N.T.	32
1966	1	*Myotis austroriparius*	YES	14
1972	3	*Myotis austroriparius*	YES	unpubl.
1973	23	*Myotis austroriparius* *Pipistrellus subflavus*	YES	21

*N.T. = none tested

solitary species. Only two studies reported the results of the examination of a significant number of solitary bats, 461 aggregate, and all were negative.[7,45] However, there is wide variation in rates of infection among colonial species, even among those sharing the same harborhage, among different colonies of the same species, and within the same colony over time.[28] Consequently, the involvement of solitary species in the epizootiology of *H. capsulatum* remains undetermined.

In addition to the bats listed in Table 2, other chiropteran species have been incriminated in the histoplasmosis cycle based on isolation of the fungus from guano under roosting colonies.[3,5] However, attempts to demonstrate infection of these bats were not attempted and

TABLE 2. Reported isolations of *Histoplasma capsulatum* from bats.

Species	Country	Reference
Artibeus jamaicensis	El Salvador	14
Carollia perspicillata	Colombia/Panama	4, 11, 17, 28, 35
Desmodus rotundus	Colombia/Panama	4, 28, 35
Eptesicus brasiliensis	Colombia	35
Eptesicus fuscus	U.S.A.	10, 34
Glossophaga soricina	Colombia/Panama	4, 9, 11, 17, 28
Leptonycteris sanborni	U.S.A.	7
Lonchophylla robusta	Panama	28
Lonchorhina aurita	Panama	4, 28
Micronycteris megalotis	Panama	17, 18
Molossus major	Panama	15, 17
Molossus sp.	Panama	11, 28
Myotis austroriparius	U.S.A.	7, 13, 20, 34
Myotis grisescens	U.S.A.	34
Myotis lucifugus	U.S.A.	34
Myotis sodalis	U.S.A.	34
Noctilio labialis	Panama	28
Nycticeius humeralis	U.S.A.	34
Phyllostomus discolor	Panama/El Salvador	14, 28
Phyllostomus hastatus	Panama	11, 17, 28
Pipistrellus subflavus	U.S.A.	20
Pteronotus rubiginosa	Panama	4, 11, 12, 17, 28, 29, 30
Pteronotus suapurensis	Panama	28
Tadarida brasiliensis	U.S.A.	1, 2, 6, 34
Tadarida yucatanica	Panama	11, 28
Tonatia bidens	Panama	28

the validity of the association could not be established. The level of recoverable *H. capsulatum* from the soil and guano in a given cave is influenced by microgeological cycles within the cave environment.[27] Hence roosting bats may be positive or negative for histoplasmosis, while at the same time the soil and guano beneath the bats may or may not contain detectable *H. capsulatum*. Also, the bats in the cave at the time of sampling may not be responsible for the fungi recovered in the soil and guano. Consequently, isolation of *H. capsulatum* from the tissues of bats is preferrable to isolations from guano or soil.

MORBIDITY AND MORTALITY

Morbidity and/or mortality attributable to *H. capsulatum* has been demonstrated only by intraperitoneal inoculation of *Tadarida brasiliensis*.[33] An 80% mortality rate was observed 7 to 34 days post-infection. Morbidity was evident one to several days prior to death with signs consisting of irritability, lethargy, refusal to eat, emaciation and diarrhea. Eight of the 16 bats which died and 3 of the 4 surviving bats shed the organism in their feces. Eighty-three percent of the fecal isolates were recovered between 10 and 30 days post-infection, with only a single isolate recovered prior to day 14.

In contrast, experimental studies utilizing *Artibeus lituratus* and *Pteronotus suapurensis*[22,23,31] resulted in infection but no morbidity or mortality.

PATHOGENESIS

Bats are probably infected with *H. capsulatum* via the respiratory tract with the infection spreading from the pulmonary system to other organs. This has been demonstrated by intranasal infection of *A. lituratus* with as few as 100 viable yeast cells.[22] Recovery of *H. capsulatum* from various organs of free-flying bats is well documented, with most studies relying on cultures from the liver, spleen and lung.[5] Demonstration of tissue infection by histologic techniques correlates poorly with the success of cultural procedures and no cellular response to tissue infection has been noted.[12]

If bats are to serve as active disseminators of *H. capsulatum* in the environment then shedding of viable yeast cells in the feces is paramount. Passive transit of ingested *H. capsulatum* is probably of little significance outside the immediate harborhage. Bats have an extremely short intestinal transit time of 15 min,[16] and would quickly clear any fungi from the intestinal tract. Active multiplication of yeast cells in extralumenal tissues and shedding of these cells into the intestinal lumen has been demonstrated by histologic examination of free-flying bats[12,17] and by experimental studies.[22,33] These observations suggest that in at least some bat species natural exposure may result in a chronic, controlled infection which allows the bat to excrete viable fungi over a long period of time.[22]

Unfortunately, while intestinal shedding of *H. capsulatum* is important, attempts to culture the fungus from feces of free-flying bats have produced inconsistent results.[9,12,15,17] The reason for the inconsistency of intestinal or fecal cultures may be variance within and between species of bats in the number of organisms present. Naturally infected *Pteronotus rubiginosa* and *Micronycteris megalotis* shed 10 to 2,000 yeast cells/fecal content and 10 to 100 yeast cells/fecal content respectively.[17]

IMMUNITY

Most investigators are concerned with the demonstration of *H. capsulatum* infection in bats and few studies have investigated the antibody response. Serologic surveys of bats from Arizona, Minnesota and Panama have been

conducted,[5,17,24] and reactors were detected in the bats in Arizona and Minnesota. Eight culturally positive bats from Panama were serologically negative. Experimental studies using *A. lituratus* indicated that complement-fixing antibodies develop to detectable levels at 3 weeks post-infection and precipitating antibodies at 3 to 5 weeks post-infection.[22,23] A significant delayed hypersensitivity reaction to histoplasmin was noted 2 to 4 weeks post-infection, but this hypersensitivity waned by 9 weeks post-infection. Thus, delayed hypersensitivity appears to be a sensitive, but transient, indicator of active histoplasmosis in bats.

COMMENT

The available evidence indicates that certain bat species play a role in the epizootiology of *H. capsulatum*. Their feces serve source of nutrients to fungi in the soil and other litter and the bats serve as potential active disseminators of the organism in the environment. This does not infer that all bats have histoplasmosis or are capable of its dissemination, as data are lacking for most species. Theoretically, though, the migrating habits of bats could greatly enhance the distribution of *H. capsulatum* far from a natural focus, although there is no data to support or disprove this hypothesis.

The actual role of bats in human histoplasmosis is probably limited given the high infection rates observed in bats in areas where there are low rates of human infection.[6] Emmons has hypothesized that bats dwelling around houses could be involved in sporadic rural or urban cases of human histoplasmosis.[8] However, the majority of bat associated cases of human histoplasmosis have been traced to harborhages such as caves and trees where exposure to fungi laden soil and guano can be more intense. Further studies are needed to assess the role bats play in disseminating *H. capsulatum* from one harborhage to another and to determine the susceptibility of various bat species to histoplasmosis.

Acknowledgements

The authors would like to thank Dr. C.R. Freeble, St. Petersburg, Florida and Mr. D. Peterson, U.S. Fish and Wildlife Service, Jacksonville, Florida for their epizootiologic investigative assistance, and to thank Dr. L. Ajello, Center for Disease Control, Atlanta, Georgia and Dr. L. Selby, University of Missouri, Columbia, Missouri for their review and comments of the manuscript.

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Received for publication 25 April 1980