A Case Control Study of Nontuberculous Mycobacteria in Oklahoma

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A case control study was performed to determine the association of environmental factors with the occurrence of *Mycobacterium avium-interacellulare* complex and *M. kansasii* in patients from Oklahoma. Statistically significant differences were found between the cases and controls for the following: life-time exposure for males to dogs, horses and pigs; for females to horses, pigs, cattle, and frequency of drinking milk.

INTRODUCTION

It is fairly well established that *Mycobacterium tuberculosis* and the nontuberculous mycobacteria (NTM) differ significantly in their mode of transmission to man. The former is transmitted directly person-to-person through respiratory droplet inhalation whereas NTM are thought to be acquired from the environment. This environmental source concept has become central to NTM research. It is not clear how a disease, such as that seen with NTM in which oropharyngeal droplets have been ruled out as a significant route of infection, can occur in the lower respiratory tract.

This problem has led to the formulation of several hypotheses concerning the modes and mechanisms of human infection by NTM. Parker *et al.* (1) have proposed the 'bubble-burst jet-drop' theory in which NTM existing in natural fresh water are concentrated into tiny droplets that are ejected into the atmosphere by bursting air bubbles rising to the water surface. Upon desiccation of the droplets, the organisms therein are freed for inhalation. Chapman, on the other hand, has suggested that milk, both raw and processed, may be a significant medium through which oral infection occurs (2). Other reports have implicated animals, as in the report in which piggery workers were found to possess the same strains of NTM as those found in the pigs they attended (3).

The purpose of this study was to determine whether a significant association could be detected between some of the hypothesized environmental factors and the occurrence of the two most common NTM, *M. avium-intracellulare* complex and *M. kansasii,* in patients. This was accomplished with a case control study.

MATERIALS AND METHODS

Laboratory records of acid-fast bacilli (AFB) isolates housed at the Oklahoma State Department of Health (OSDH) were reviewed to identify individuals who had positive AFB cultures. This review covered the period between January, 1978 and May, 1983. All individuals whose culture report indicated at least one isolate of either *M. avium-interacellulare* complex or *M. kansasii* were identified. There were 743 such patients. Among the information that was extracted from these records was the name and address of the attending physician. This was used to obtain his/her consent to follow up with a questionnaire. By this means 203 patients were contacted and asked to complete a questionnaire. Only 103 (51%) responded, of which 89% were 50 years or older and all of whom were white. Over 50% were 65 years or older. There is a preponderance of the 50 + age group because these infections are chronic and tend to occur in older individuals.

A control group consisting of 190 men and women, without a history of NTM infection,

were also questioned. Since it was desirable to obtain a control group that matched the case group with respect to race (all white) and age (equal to or older than 50 years), controls were sought from specific target groups that were most likely to yield the desired individuals. These target groups included six senior citizens centers in Oklahoma City and Tulsa and three fraternities of Veterans of Foreign Wars (VFW) in Oklahoma City, which included their female auxiliary consorts.

The questionnaire. Both cases and controls were mailed the same questionnaire. The purpose of the questionnaire was to obtain information from the respondents on the following areas: a) life-time exposure to dogs, cats, horses, cattle, pigs, and sheep. Life-time exposure was defined as an estimate of the total time a respondent had been in contact with these animals since childhood. Other questions concerned b) the frequency of both raw and processed milk consumption; c) frequency of participation in the water-related activities of fishing, boating, swimming, skiing, and lakeside camping; d) occupational history, including the nature of duties during tenure; and e) biographical information. Responses to these questions were compared between cases and controls to determine the relationship between NTM and these environmental factors.

RESULTS

Tables 1 and 2 represent median scores of lifetime exposures by male cases to dogs and horses, respectively. In both cases, the respondents, who were stratified by age groups, show a significant case vs. control difference in the 65 + years age group. Table 3 shows median scores of lifetime exposure to horses by females and a significant case vs. control difference is demonstrated in the 50-64 years age group. Tables 4 and 5 represent median scores of lifetime exposure to pigs of males and females respectively. Males show a significant case-control variance in median scores in the 65 + years age groups, whereas the females show significance in both the 50-64 and 65 + years age groups. Table 6 demonstrates a significance in the 65 + years age group of female exposure to cattle. Table 7 represents the distribution of female cases and controls by frequency of milk drinking. The chi-square test shows a significant difference in the distributions between cases and controls.

TABLE 1. Median scores (number of points above median) of lifetime exposure to *dogs* by age in *male* cases and controls.

Age (years)	Group	N	Sum of scores	Expected under HO	Std dev under HO	X^2	*P* value
<50	Cases	7	2.00	3.23	0.94	1.7	0.19
	Controls	6	4.00	2.77	0.94		
50-64	Cases	16	7.00	7.85	1.69	2.5	0.61
	Controls	37	19.00	18.15	1.69		
65 +	Cases	19	13.00	9.32	1.76	4.3	0.03
	Controls	34	13.00	16.68	1.76		

TABLE 2. Median scores (number of points above median) of lifetime exposure to *horses* by age in *male* cases and controls.

Age (years)	Group	N	Sum of scores	Expected under HO	Std dev under HO	X^2	*P* value
<50	Cases	7	3.00	3.77	0.94	0.6	0.41
	Controls	6	4.00	3.23	0.94		
50-64	Cases	16	6.00	7.85	1.69	1.2	0.27
	Controls	37	20.00	18.15	1.69		
65 +	Cases	19	6.00	9.32	1.76	3.5	0.05
	Controls	34	20.00	16.68	1.76		

No statistical difference was detected between the following factors: females and dogs, cats, fishing, boating, swimming and dust exposure; males and cats, cattle, sheep, drinking milk, fishing boating, swimming, lakeside camping and dust exposure. The lack of data yielded statistically inconclusive results for: males and raw milk consumption or water skiing; females and raw milk consumption, water skiing, or lakeside camping.

DISCUSSION

Results from this study note statistically significant differences between the cases and controls for the following: lifetime exposure for males to dogs, horses and pigs; and for females to horses, cattle, pigs and frequency of drinking milk, Several points should be mentioned here. The study was based on the assumption that OSDH isolates probably reflect the distribution (not necessarily disease) of NTM in Oklahoma. The data analysis showing significant differences between cases and controls suggests that cases have more isolates than controls. We believe that this study is important as a screening mechanism for detecting environmental sources of NTM in Oklahoma. The OSDH organism/isolate data are obtained from patients throughout the state and are probably representative of the distribution of NTM. This is the only statewide study of the potential role of these environmental factors in the epidemiology of NTM organisms, to the best of our knowledge. Several questions remain unanswered. Why was there a difference for males and not females with dogs? What is the significance of the finding relative to pigs in both males and females? This is the only consistent finding by sex and age over 65. We hope to answer some of these questions in future studies which should expand on the positive results noted here.

This study suggests that pigs, horses, dogs and milk may harbor or be involved with the transmission of NTM.

REFERENCES

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TABLE 3. Median scores (number of points above median) of lifetime exposure to *horses* by age in *female* cases and controls.

Age (years)	Group	N	Sum of scores	Expected under HO	Std dev under HO	X^2	*P* value
<50	Cases	7	0.00	0.89	0.66	1.8	0.18
	Controls	7	4.00	3.11	0.66		
50-64	Cases	16	14.00	11.08	1.56	4.1	0.06
	Controls	23	13.00	15.92	1.56		
65 +	Cases	40	26.00	27.93	2.57	0.6	0.45
	Controls	76	55.00	53.07	2.57		

TABLE 4. Median scores (number of points above median) of lifetime exposure to *pigs* by age in *male* cases and controls.

Age (years)	Group	N	Sum of scores	Expected under HO	Std dev under HO	X^2	*P* value
<50	Cases	7	6.00	5.25	0.89	0.9	0.40
	Controls	5	3.00	3.75	0.89		
50-64	Cases	16	8.00	9.06	1.69	0.4	0.53
	Controls	37	22.00	20.94	1.69		
65 +	Cases	19	6.00	9.68	1.76	4.3	0.04
	Controls	34	21.00	17.32	1.76		

TABLE 5. Median scores (number of points above median) of lifetime exposure to *pigs* by age in *female* cases and controls.

Age (years)	Group	N	Sum of scores	Expected under HO	Std dev under HO	X^2	*P* value
<50	Cases	7	2.00	1.11	0.66	0.9	0.18
	Controls	7	3.00	3.89	0.66		
50-64	Cases	16	15.00	12.31	1.56	0.4	0.08
	Controls	23	15.00	17.69	1.56		
65 +	Cases	40	26.00	31.03	2.57	4.3	0.05
	Controls	76	64.00	58.97	2.57		

TABLE 6. Median scores (number of points above median) of lifetime exposure to *cattle* by age in *female* cases and controls.

Age (years)	Group	N	Sum of scores	Expected under HO	Std dev under HO	X^2	*P* value
<50	Cases	2	2.00	1.33	0.66	0.1	0.31
	Controls	7	4.00	4.67	0.66		
50-64	Cases	16	13.00	10.67	1.56	1.2	0.13
	Controls	23	15.33	18.15	1.56		
65 +	Cases	40	23.00	28.28	2.57	1.7	0.04
	Controls	76	59.00	53.72	2.57		

TABLE 7. Distribution of *female* cases and controls by frequency of milk drinking.

Frequency	Cases	Controls	Total
Light	22	23	45
Moderate	12	22	34
Heavy	23	60	83
Total	57	105	162

$X = 5.7$; $P = 0.05$