

Increase in *Mycobacterium avium* complex Isolations Among Patients Admitted to a General Hospital

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THE *Mycobacterium avium* complex is a group of closely related strains that cannot be reliably separated on the basis of cultural characteristics (1). The complex contains 28 serovars (2), virtually all of which have been associated with human disease (3). The organisms are known to be ubiquitous in soil and have been recovered from avian, bovine, and porcine sources (3-5). Neither animal-to-man nor man-to-man transmission has been documented, however, and the mode of acquisition of human infection remains obscure (6,7). Skin test data indicate that infection is more common among residents of the South Atlantic and Gulf Coast States than elsewhere in the United States (8). Uniformly collected epidemiologic information about cases of disease are not available, but clinical reports generally corroborate the suggestion that exposure and disease are more common in the Southeast (2). A few areas such as Milwaukee, however, apparently have high rates of disease caused by *M. avium* complex even though they lie outside of the Southeast (9). This observation suggests that local factors may be important in the prevalence of infection and disease.

M. avium complex has been implicated as the causative agent of cervical adenitis (mainly in chil-

dren) and of pulmonary disease (mainly in adults) clinically indistinguishable from that caused by *Mycobacterium tuberculosis*. However, these organisms also have been isolated from the sputum of other persons in whom their role as a pathogen is unclear, including persons with other pulmonary diseases such as chronic obstructive disease, malignancies, and bronchitis and those lacking clinical or radiographic evidence of any pulmonary disease (7).

In early 1979, the laboratory director of a general hospital in southwestern Illinois reported that an increased number of patients had had cultures positive for *M. avium* complex during 1978 (see chart). To establish the extent and epidemiologic character of this reported outbreak, an investigation was initiated.

Background

The 449-bed general hospital is in an industrial community (estimated population of 44,400 in 1977) on the east bank of the Mississippi River. Several heavy industries located there are known to produce large quantities of airborne pollutants. According to the Illinois Environmental Protection Agency, the community has more total suspended particulate matter and lead in its air than any other city in the State. It is second only to Chicago in the levels of airborne photochemical oxidants and carbon monoxide. The hospital's administrators estimated that approximately two-thirds of all newly admitted patients reside in the community, and the other one-third live in the surrounding two counties on the Illinois side of the Mississippi.

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Before April 1979, the hospital did not process mycobacterial cultures in its laboratory but referred them to a series of private reference laboratories (see chart). For many years and until June 1976, the cultures were referred to laboratory A in another hospital. From June 1976 until May 1977, the hospital referred mycobacterial cultures to a private reference laboratory, laboratory B. From May 1977 until April 1979, the hospital referred all mycobacterial cultures to a third institution, laboratory C. The increase in cultures positive for *M. avium* complex began several months after laboratory C became the referral laboratory (see chart). All specimens sent to laboratory C were processed by the same technician who used the same techniques in performing the cultures. Confirmation and susceptibility testing of mycobacterial isolates grown by laboratory C were performed by the Missouri State Chest Hospital Laboratory.

Methods

The epidemiologic investigation was restricted to the period January 1, 1976–December 31, 1978. Before that interval, mycobacterial culture data were irretrievable, and after it, the laboratory director purposefully intensified the search for mycobacterial organisms.

Review of the hospital's laboratory log books for specimens referred for mycobacterial culture yielded the following numbers on a monthly basis: mycobacterial cultures referred, cultures positive for any *Mycobacterium* species, cultures positive for *M. avium* complex, patients cultured, patients positive for any *Mycobacterium*, and patients positive for *M. avium* complex. Similar data were compiled on specimens received at laboratory C from all hospitals for the period May 1, 1977–December 31, 1978. Officials of all six other hospitals in the two-county region were also questioned concerning recovery rates of *M. avium* complex.

The charts of study hospital patients identified by the laboratory record review as having positive mycobacterial cultures were examined, and the following data were extracted: age, sex, place of residence, millimeters of induration of a Mantoux test if one had been performed, the presence or absence and diagnosis (if available) of known pulmonary disease, chest X-ray findings, the date and source of the culture material, the number of positive cultures, and the species of *Mycobacterium* grown. The number of colonies present on a positive culture was not available.

Statistical methods included the use of the Student *t*-test for comparison of means and the Chi square or

Fishers exact test (two tailed) for comparison of proportions.

Results

Laboratory record review at the hospital revealed 7 patients with a specimen positive for *M. avium* complex in 1976, 8 in 1977, and 36 in 1978; patients positive for other mycobacterial species numbered 16, 13, and 17 respectively for these 3 years (see chart). Only one culture grew more than one species, that from a patient in 1978 whose specimen grew *M. avium* complex and *M. tuberculosis*. Only one patient had positive cultures in 2 different years—1976 and 1978. That patient is counted in both years.

Data for 1976 and 1977 were similar and were therefore pooled. The results for the mycobacterial cultures referred by the hospital were as follows:

Monthly means of—	1976 + 1977	1978
Mycobacterial cultures referred.....	59.2	60.2
Cultures positive for <i>M. avium</i> complex..	¹ 0.6	¹ 4.8
Cultures positive for other mycobacteria..	1.6	1.6
Patients with specimens cultured.....	31.0	31.6
Patients with specimens positive for		
<i>M. avium</i> complex.....	¹ 0.6	¹ 2.8
Patients with specimens positive for other		
mycobacteria.....	1.2	1.4

¹*P* < .001.

As the preceding table and chart indicate, the mean monthly values for 1976 and 1977 combined do not differ significantly from the means for 1978 with respect to the number of cultures referred and the number of patients with specimens cultured. However, the mean number of cultures and patients with specimens positive for *M. avium* complex were significantly (*P* < .001) greater for 1978 than for 1976 and 1977. No other hospitals in the area showed similar differences.

Data from laboratory C from May 1977 through 1978 corroborated the data from the study hospital's records. When the hospital's submissions to laboratory C for 1978 were compared with submissions from all other hospitals, a significantly greater proportion (*P* < .001) of cultures and patients were positive for *M. avium* complex, but the proportion of cultures and patients with specimens positive for all other mycobacteria did not differ (table 1).

The patients with positive mycobacterial cultures for whom charts were reviewed (48 of the 51 patients with *M. avium* complex isolates, all 46 patients with other mycobacteria isolated) were compared (table 2). First, all patients positive for *M. avium* complex were compared with all patients positive for any other *Mycobacterium* for the entire study period. One significant (*P* < .05) difference was

Table 1. Comparison of mycobacterial culture results at laboratory C by hospital, 1978

Comparisons	Study hospital	All other hospitals
Ratio of positive cultures to total cultures	'0.11	'0.04
Ratio of <i>M. avium</i> complex positive cultures to total cultures	'0.09	'0.01
Ratio of cultures positive for all other mycobacteria to total cultures	0.02	0.03
Ratio of <i>M. avium</i> complex patients to total patients with positive cultures	'0.76	'0.34

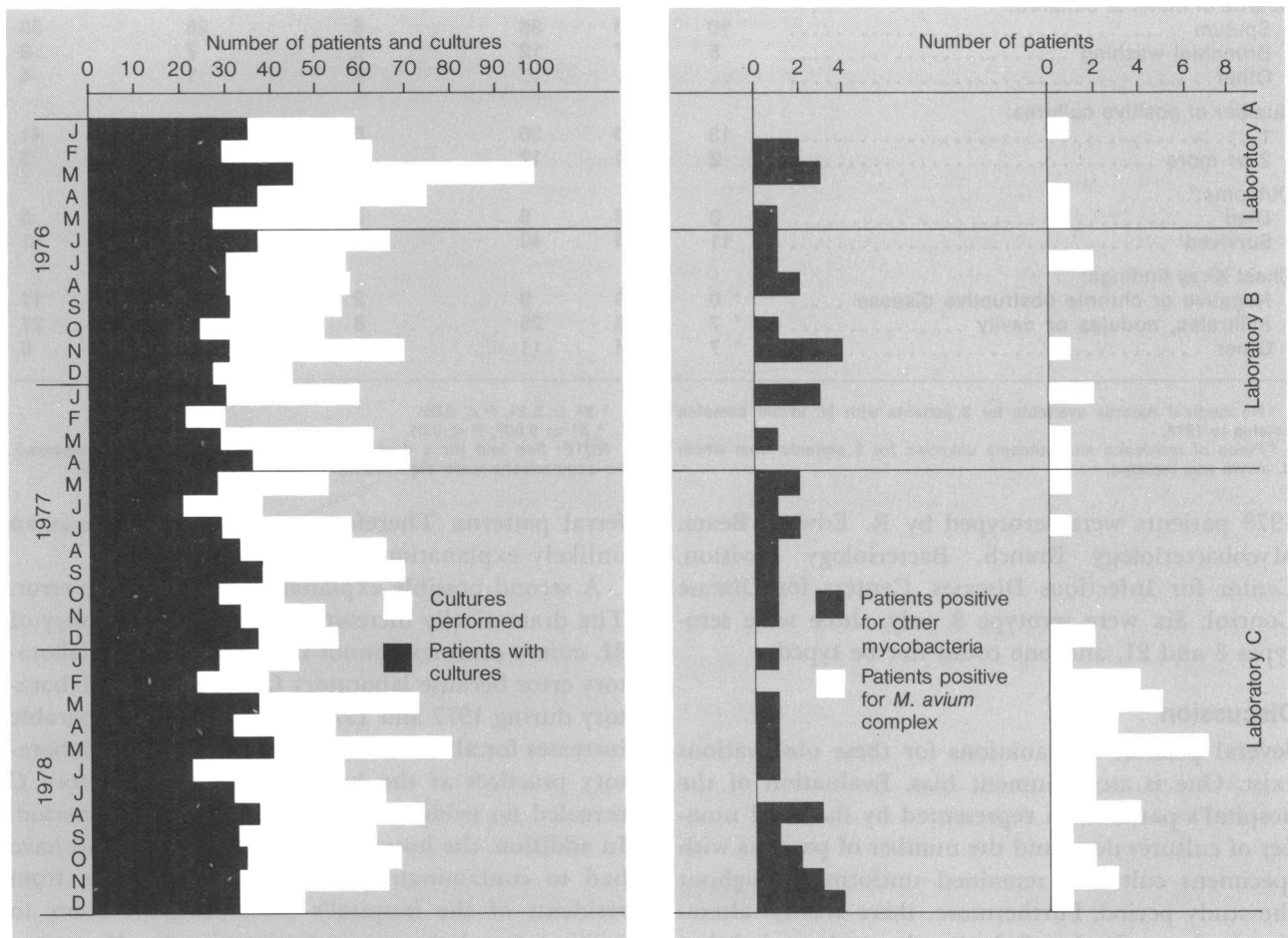
'P < .001.

observed: *M. avium* complex patients were more likely to have been residents of the hospital's city than were patients positive for any other mycobacterial species. Second, patients positive for *M. avium* complex in 1976 and 1977 were compared to the 1978 *M. avium* complex patients. The distribution of chest film abnormalities differed significantly ($P < .05$) between the two groups. The proportion of patients with infiltrates, nodules, or cavities was nearly the

same for both groups, but patients from 1978 had more films read as normal or consistent with chronic obstructive pulmonary disease (COPD) and fewer films read as having other abnormalities. Third, all patients positive for *M. avium* complex were compared with all 10 patients with specimens positive for *M. tuberculosis* (2 in 1976 and 4 each in 1977 and 1978). There were no significant differences.

Ten *M. avium* complex isolates preserved from

Cultures for *Mycobacterium avium* complex and other mycobacteria among patients of a general hospital performed at 3 referral laboratories, by month, 1976-78



NOTE: 3 patients are omitted because the dates of their positive cultures are unknown. In 1976 1 patient was positive for *M. avium* complex and 1 patient was positive for other mycobacteria; in 1978 1 patient was positive for *M. avium* complex.

Table 2. Distribution of patients according to clinical or epidemiologic parameters and mycobacteria isolated

Characteristic	Mycobacterium avium complex			All years		Total
	1976-77	1978	Total	Mycobacterium tuberculosis	All other Mycobacteria	
Age (years):						
0-40	3	5	8	1	3	4
41-60	8	11	19	3	16	19
61 or older	4	17	21	6	17	23
Sex:						
Male	8	18	26	5	23	28
Female	7	15	22	5	13	18
Place of residence: ²						
Hospital community	11	27	38	6	21	27
Other	3	5	8	4	15	19
Induration if tuberculin skin test performed:						
0	4	13	17	4	8	12
1-9 millimeters	1	1	2	1	0	1
10 millimeters	1	4	5	1	7	8
Pulmonary disease:						
None or no symptoms	4	4	8	2	5	7
Acute infection	5	15	20	6	22	28
Chronic obstructive disease	4	13	17	1	15	16
Malignancy	2	5	7	1	5	6
Source of material cultured:						
Sputum	10	26	36	5	28	33
Bronchial washing	5	7	12	2	7	9
Other	3	1	4
Number of positive cultures:						
1	13	23	36	8	33	41
2 or more	2	10	12	2	3	5
Outcome: ²						
Died	3	3	6	0	5	5
Survived	11	29	40	10	31	41
Chest X-ray findings:						
Negative or chronic obstructive disease	* 0	* 9	9	2	9	11
Infiltrates, nodules or cavity	* 7	* 18	25	8	19	27
Other	* 7	* 4	11	0	6	6

¹ No medical records available for 3 patients with *M. avium* complex isolates in 1978.

² Place of residence and outcome unknown for 2 patients from whom *M. avium* was isolated.

³ $\chi^2 = 5.24, P < 0.05$.

⁴ $\chi^2 = 9.607, P < 0.01$.

NOTE: See text for a description of how categories were compared. No comparisons were significantly different except where noted.

1978 patients were serotyped by R. Edward Beam, Mycobacteriology Branch, Bacteriology Division, Center for Infectious Diseases, Centers for Disease Control. Six were serotype 8 only, three were serotypes 8 and 21, and one could not be typed.

Discussion

Several possible explanations for these observations exist. One is ascertainment bias. Evaluation of the hospital's patients, as represented by the total number of cultures done and the number of patients with specimens cultured, remained uniform throughout the study period. Furthermore, there was no alteration in the medical staff during the study period that would have fostered a change in diagnostic or re-

ferral patterns. Therefore, ascertainment bias is an unlikely explanation for the increase.

A second possible explanation is laboratory error. The dramatically increased frequency of recovery of *M. avium* complex cannot be explained by a laboratory error because laboratory C, the reference laboratory during 1977 and 1978, did not have comparable increases for all other submitters. A review of laboratory practices at the hospital and at laboratory C revealed no evidence of changes during this period. In addition, the hospital or laboratory C would have had to contaminate preferentially specimens from residents of the hospital's community in order to account for their preponderance in the *M. avium* complex group. Such actions seem unlikely.

A third possibility is increased numbers of persons colonized with *M. avium* complex. A source of exposure within the city would explain the excess number of patients from the city and would be consistent with the increased proportion of patients whose chest films were read as normal or consistent with COPD. Unfortunately, the patients were not geographically clustered within the city, and no point source of environmental contamination is apparent. In addition, the increased proportion of patients with normal chest films or abnormalities consistent with COPD is accompanied by a decrease in the proportion of those with other abnormalities (mostly pleural disease) but no apparent change in the proportion of those with infiltrates, nodules, or cavities. One would have expected the decrease to have affected all abnormal chest film categories equally.

A final explanation is that the incidence of disease due to *M. avium* complex increased. The serotyping data support this explanation. Virtually all the isolates are serotype 8, a serotype which has frequently been associated with human disease (3). The clinical data currently available are insufficient to meet the rigorous criteria for a definite diagnosis of disease due to non-tuberculous Mycobacteria (6); therefore, this explanation remains speculative.

The data suggest that the increased recovery of *M. avium* complex from patients admitted to the hospital is not due to ascertainment bias or laboratory error but reflects pulmonary colonization or disease caused by these strains. Presently, we feel that the most likely explanation is that persons living in the community in which the hospital is located experi-

enced an increased rate of exposure to and colonization by *M. avium* complex. It seems likely that some of the persons so colonized also became diseased. In an effort to elucidate the nature of the "outbreak" and to identify risk factors associated with the acquisition of *M. avium* complex, the Illinois Department of Public Health and the University of Illinois School of Public Health plan to compare the clinical course and environmental exposures of patients who had a positive culture for *M. avium* complex with patients for whom the culture was negative.

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SYNOPSIS

WIESENTHAL, ANDREW W. (Centers for Disease Control, Springfield, Ill.)
POWELL, KENNETH E., KOPP, JOSEPH, and SPINDLER, JAMES E.: *Increase in Mycobacterium avium complex isolations among patients admitted to a general hospital. Public Health Reports, Vol. 97, January-February 1982, pp. 61-65.*

In early 1979, an official of an Illinois hospital reported an increase in the number of patients from whom *Mycobacterium avium* complex recently had been recovered. Over the preceding 3 years specimens from a total of 51 patients were culture positive for *M. avium* complex: 7 in

1976, 8 in 1977, and 36 in 1978. Nine of 10 serotyped isolates were serotype 8.

The increase was not attributable to an increase in the number of mycobacterial cultures performed. No other area hospitals had similar increases in rates of recovery of *M. avium* complex. Patients with *M. avium* complex were significantly more likely than patients with other mycobacteria to have been residents of the city where the hospital is located. The distribution of abnormalities in patients' chest films differed significantly between patients with *M. avium* complex in 1978 and pa-

tients with *M. avium* complex in 1976-77; in 1978, patients although equally likely to have infiltrates, nodules, or cavities, were more likely to have no abnormalities or abnormalities consistent with chronic obstructive pulmonary disease, and less likely to have other abnormalities. The data suggest that the increased rate of recovery of *M. avium* complex from patients could not be attributed to ascertainment bias or laboratory variation but may be due to an increase in the incidence of disease or colonization among persons living in the community where the hospital is located.