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Incidence and nature of human tuberculosis due to *Mycobacterium africanum* in South-East England: 1977–87

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SUMMARY

A total of 210 new cases of tuberculosis due to *Mycobacterium africanum* were registered at the South-East Regional Centre for Tuberculosis Bacteriology, Dulwich, between 1977 and 1987 inclusive. This represented 1·25% of bacteriologically-confirmed cases of tuberculosis in South-East England, an incidence slightly higher than that of disease due to *M. bovis*. Two variants were identified: 150 strains were typed as African I (a type associated with East Africa) and 60 as African II (a type more prevalent in West Africa). Over half the patients infected with African I strains were of Indian subcontinent ethnic origin; patients of African ethnic origin predominated in the African II group while about a fifth of patients infected with either type were of European origin. The European patients with tuberculosis due to *M. africanum* were notably younger than those in the same region with disease due to other tubercle bacilli. The distribution of lesions due to *M. africanum* was similar to that due to other tubercle bacilli in the various ethnic groups, except that genito-urinary tuberculosis was uncommon. The importance of a clinical awareness that *M. africanum* is a highly pathogenic and transmissible tubercle bacillus rather than an opportunist or 'atypical' mycobacterium is stressed.

INTRODUCTION

The *Mycobacterium tuberculosis* group or complex consists of four very closely related clusters of strains which are now usually known by separate species names: *M. tuberculosis* (the human tubercle bacillus), *M. bovis* (the bovine tubercle bacillus), *M. microti* (the vole tubercle bacillus) and *M. africanum*. The latter name was given to a group of strains isolated from man in equatorial Africa (1, 2). The name *M. africanum* is really one of convenience as it does not represent a true new species but a rather heterogeneous group of strains with properties intermediate between those of *M. tuberculosis* and *M. bovis*.

An extensive taxonomic study (3) of *M. africanum* showed that the strains

formed two main clusters: those phenetically related to the human tubercle bacillus, which were usually nitratase positive and found in West Africa, and those more like the bovine tubercle bacillus which were usually nitratase negative and from more easterly African countries such as Rwanda and Burundi. Most isolates of *M. africanum* have been from man but an animal reservoir is suggested by its occasional isolation from zoo or laboratory chimpanzees and other apes shipped from Africa to Europe (4, 5).

Bacteriological surveys in many countries of West Africa showed that *M. africanum* is widely distributed in that region: depending on the country, from 15–90% of isolated tubercle bacilli were of this type (6). Strains of *M. africanum* were isolated from African expatriates living in the Paris region (7) and from an Asian lady of Ugandan origin living in Scotland (8). The first cases occurring in indigenous white Europeans were reported in Germany (5): 8 of 32 isolates were from Africans resident in that country but the remainder were from indigenous German patients. The source of these infections was unknown. We have also previously noted that some patients in South-East England with tuberculosis due to *M. africanum* had European names (9).

The purpose of this study was to report the incidence of tuberculosis due to *M. africanum*, relative to that due to *M. tuberculosis* and *M. bovis*, in South-East England over the 11-year period 1977–87 inclusive and to determine the ethnic groups of patients involved and the anatomical distribution of the lesions caused by the disease.

MATERIALS AND METHODS

About 95% of mycobacteria isolated in South-East England are referred to the South-East Regional Centre for Tuberculosis Bacteriology at Dulwich. Since 1977, all mycobacteria identified at that Centre as tubercle bacilli have been divided into five variants for epidemiological purposes by means of four simple tests, i.e. oxygen preference (aerobic or microaerophilic), nitratase activity, susceptibility to thiophen-2-carboxylic acid hydrazide (TCH) and susceptibility to pyrazinamide (10, 11). These five variants are summarized in Table 1. This system permits the identification of 'African' strains (*M. africanum*) and their division into two groups according to nitratase activity, with African I corresponding to the predominent East African type and African II corresponding to the West African type.

Information on the age and sex of the patients, and the anatomical sites from which the tubercle bacilli were isolated, were supplied by the referring clinician or microbiologist. The patients were divided into those of apparent European, African and Indian Subcontinent (ISC) origin on the basis of their names.

Statistical analyses were performed with the Chi-squared and Student's *t* tests where appropriate.

RESULTS

During the period 1977–87, 210 new cases of tuberculosis due to *M. africanum* were registered at Dulwich: 150 were typed as African I and 60 as African II. During the same period, 16452 new cases of tuberculosis due to *M. tuberculosis* and 201 due to *M. bovis* were registered. Thus, *M. africanum* was responsible for 1·25%

Table 1. *Characteristics of tubercle bacilli used for epidemiological subdivision*

	Oxygen preference	Nitratase	Sensitivity	
			TCH	PZA
Classical human (*M. tuberculosis*)	A	+ve	R	S
Asian human (*M. tuberculosis*)	A	+ve	S	S
African I (*M. africanum*)	M	−ve	S	S
African II (*M. africanum*)	M	+ve	S	S
Bovine (*M. bovis*)	M	−ve	S	R

TCH, thiophen-2-carboxylic acid hydrazide; PZA, pyrazinamide; A, aerobic; M, microaerophilic; S, sensitive; R, resistant.

Table 2. *Annual numbers of new cases of tuberculosis due to human, African I and II and bovine tubercle bacilli*

Year	Human	African			Bovine	Percentage of total due to African
		I	II	total		
1977	1597	17	2	19	20	1·16
1978	1777	22	7	29	27	1·58
1979	1647	23	8	31	22	1·82
1980	1788	9	6	15	23	0·82
1981	1683	15	3	18	20	1·05
1982	1483	12	6	18	18	1·78
1983	1522	18	4	22	19	1·41
1984	1298	11	9	20	15	1·50
1985	1308	12	6	18	10	1·35
1986	1185	6	7	13	13	1·07
1987	1164	5	2	7	14	0·59
Total	16452	150	60	210	201	1·25

Table 3. *Age of patients according to their ethnic origin and type of bacillus*

Ethnic origin	African I				African II			
	No.	Mean	S.D.	Range	No.	Mean	S.D.	Range
African	32	26·3	10·9	15–81	26	26·7	12·2	8–66
ISC	65	37·3	18·2	17–78	22	32·0	12·3	20–69
European	35	40·9	21·1	6–84	12	43·1	18·2	19–78
Other	4	33·3	10·8	23–49	0	—	—	—

S.D., standard deviation.

of new cases of tuberculosis, slightly more than were due to *M. bovis* (1·2%). The annual isolation rate of both types of *M. africanum* are listed in Table 2. This annual isolation rate was somewhat erratic and no predictive trends were apparent. There was a slight excess of male patients in both groups: 74 of 146 (51%) in the African I group and 34 of 59 (58%) in the African II group.

The ages of the patients in the ethnic groups are shown in Table 3. These do not differ significantly between the two bacterial groups but the African patients were

Table 4. *Age of patients according to site of lesion and type of bacillus*

Site	African I				African II			
	No.	Mean	S.D.	Range	No.	Mean	S.D.	Range
Lung	79	34·8	18·6	10–84	36	30·2	16·9	8–78
Lymph node	23	37·8	20·9	23–81	12	32·4	8·6	20–49
Bone and joint	19	33·6	15·6	19–61	8	35·4	11·1	23–56
Genito-urinary	6	56·0	16·9	41–82	1	—	—	26
Abdominal	6	29·5	8·7	21–44	2	—	—	28, 66
CNS	2	—	—	6, 18	1	—	—	22
Other*	2	—	—	32, 38	0	—	—	—

* 1 breast, 1 miliary. S.D., standard deviation.

Table 5. *Site of lesion according to ethnic origin of the patient*

Site	African I					African II				
	Afr	ISC	Eur	Oth	Total	Afr	ISC	Eur	Total	Total
Lung	18	45	22	1	86	15	10	11	36	122
Lymph node	9	15	1	3	28	4	7	1	12	40
Bone and joint	5	9	4	—	18	4	4	—	8	26
Genito-urinary	—	4	3	—	7	—	1	—	1	8
Abdominal	1	4	1	1	7	1	1	—	2	9
CNS	—	—	2	—	2	1	—	—	1	3
Other*	—	—	2	—	2	—	—	—	—	2
Total	33	77	35	5	150	25	23	12	60	210

* 1 breast, 1 miliary.
Afr, African; ISC, Indian subcontinent; Eur, European; Oth, other ethnic groups.

significantly younger than the European patients ($P < 0{\cdot}001$). The ISC patients were younger than the European patients (but not significantly so) and older than the African patients, significantly so in the case of those infected with African I strains ($P < 0{\cdot}001$).

Table 4 shows the ages of the patients according to the site of the lesion. There was a tendency for those with genito-urinary disease to be older than those with other forms of tuberculosis ($P < 0{\cdot}05$) and three patients with meningitis were relatively young.

The distribution of the isolates according to the ethnic origin of the patient, the type of *M. africanum* and the anatomical site of isolation of the organism is shown in Table 5. The distribution of patients according to their ethnic origin in the two bacterial groups was significantly different ($P < 0{\cdot}025$). Over half the African I isolates were from patients of ISC ethnic origin with only 22% being from those of African origin, while 25 of 60 (42%) of African II strains were from patients of African origin. Both bacterial groups contained a number of isolates from individuals with European names (23·5% and 20% of African I and II isolates respectively). Within each ethnic group, the anatomical sites of the lesions were similar in each bacterial group. When patients in the two bacterial groups were

combined, the anatomical sites of lesions in the African and ISC patients were similar but both differed significantly from those of European patients ($P = 0{\cdot}032$ and 0·023 respectively). The lung (sputum, bronchial and gastric washings) was the most frequent site of disease in both bacterial groups and in the three main ethnic groups. Lymphadenopathy, usually cervical, was relatively more frequent in patients of African and ISC ethnic origin. There were only 8 patients with genito-urinary tuberculosis, 5 ISC and 3 European.

Resistance to antituberculous agents was detected in 4 of the 150 African I strains: 2 to isoniazid only (African patients), 1 to streptomycin only (ISC patient) and 1 to both these drugs (European patient). Four African II strains also showed resistance: 1 to isoniazid only (African patient), 1 to streptomycin only (ISC patient) and 2 to isoniazid, streptomycin and rifampicin (both ISC patients).

DISCUSSION

Strains of *Mycobacterium africanum* are responsible for 1 in 80 cases of tuberculosis in South-East England, a slightly higher incidence that that of disease due to *M. bovis*. The distribution of patients according to ethnic origin is very different to that observed with *M. bovis* infections in which, in the same region and over the same period of time, 89% of cases occurred in Europeans, 9% in ISC patients and only 2% in Africans (12).

The differences in the distribution of patients of various ethnic origins in the two bacterial groups probably reflects the pattern of migration of individuals from different parts of Africa. African I strains are likely to be of East African origin and many individuals of ISC ethnic origin now resident in South-East England are immigrants from that part of Africa. The substantial number of infections occurring in those with European names was surprising and possible explanations include: 1) some individuals may have been infected abroad, 2) some of these patients may be of Afro-Caribbean origin, amongst whom British names are common, 3) these strains may have been introduced into England in the past, possibly in colonial times, and 4) they may not be specifically of African origin but may from time to time arise by mutation from human or bovine tubercle bacilli.

Infection with *M. africanum* involved young individuals in each ethnic group. The age ranges of the ISC patients are similar to those in the same region infected with human or bovine tubercle bacilli (9, 10) but those with European names are considerably younger than those infected with the other types of tubercle bacilli. This suggests that tuberculosis due to *M. africanum* is a relatively new form of the disease in Great Britain: cases being due to recent infection rather than reactivation of old disease.

The sites of disease resemble those observed in disease due to human and bovine tubercle bacilli in the same region, i.e. a relatively high incidence of non-pulmonary disease in patients who are not of European ethnic origin. Although genito-urinary tuberculosis is a fairly frequent form of the disease due to *M. bovis* in those with European names (12), cases due to *M. africanum* were uncommon; possibly due to the younger age group involved.

Drug resistance was detected in 8 of the 210 cultures (4·2%): 3 of the patients

were of African origin, 4 of ISC origin and 1 of European origin. In the same region, drug resistant strains of *M. tuberculosis* were isolated from 8·3% of ISC patients and 2·6% of European patients (10).

From the clinical point of view, the management of tuberculosis due to *M. africanum* is identical to disease caused by *M. tuberculosis* or *M. bovis* (although strains of the latter are naturally resistant to pyrazinamide). To the best of our knowledge, *M. africanum* is as virulent and infectious as the other tubercle bacilli that cause disease in man. A serious threat to the future health of a patient and his or her contacts would arise if a physician falsely assumed that a report of the isolation of *M. africanum* implied that the cause of disease was an 'atypical' mycobacterium of low virulence and no infectivity.

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