Superficial tuberculous lymphadenitis in Merseyside: 1969–1984

By E. G. L. WILKINS and C. ROBERTS

Public Health Laboratory, Fazakerely Hospital, Lower Lane, Liverpool, L9 7AL

SUMMARY

The aetiology, epidemiology and clinical presentation of 137 bacteriologically confirmed cases of superficial mycobacterial lymphadenitis identified at the Liverpool Public Health Laboratory between 1969 and 1984 were reviewed. Despite a fall in pulmonary and total extrapulmonary isolates, the annual recovery of mycobacteria from lymph nodes remained relatively constant. *Mycobacterium tuberculosis* was the cause of infection in 121 patients (88·3 %), *M. bovis* in 6 and the remaining 10 isolates were atypical mycobacteria. In European patients (68·6 %) the highest incidence was in the elderly, whereas in non-Europeans (31·4 %) the disease almost exclusively occurred in the third and fourth decades. The proportion of isolates from non-Europeans reflected the size of the immigrant population and increased during the period of study.

INTRODUCTION

'Scrofula' is a disease of antiquity and was common until the twentieth century, when it was said to have been 'once an accepted feature of British life' (Lethem, 1955), reflecting the then widespread custom in England and Scotland of drinking raw milk. Originally synonymous with the expression 'King's Evil' in describing 'strumous' swellings of the neck (many of which were probably non-tuberculous in origin), the term scrofula is now reserved for superficial tuberculous lymphadenitis, particularly if it involves the cervical region (Grange, Collins & Yates, 1982).

Today, tuberculosis still remains an important cause of superficial lymphadenitis in Great Britain. It is recognized to be particularly common among two populations: Asian immigrants, where it is the most frequently encountered form of extrapulmonary tuberculosis (Grange, 1980) and elderly Europeans, in whom it probably represents a recrudescence of past primary disease (Monie *et al.* 1982). To determine the epidemiological distribution of bacteriologically confirmed cases in Merseyside, we retrospectively examined the records at the Liverpool Public Health Laboratory back to 1969. We also reviewed the changing nature of superficial mycobacterial lymphadenitis over the last 50 years.

MATERIALS AND METHODS

One hundred and thirty-seven cases of superficial mycobacterial lymphadenitis were identified between January 1969 and September 1984 inclusive. The isolates were either from initial culture in this laboratory (42 %) or were subcultures from

Table 1. *Mycobacterial isolates* 1969–1984

| Mycobacterial species | Pulmonary (%) | Extra pulmonary (%) | | Total (%) |
		Lymph node	Other	
M. tuberculosis	2150 (93·7)	121 (88·3)	438 (85·9)	2588 (92·3)
M. bovis	24 (1·1)	6 (4·4)	57 (11·2)	81 (2·9)
Atypical	120 (5·2)	10 (7·3)	15 (2·9)	135 (4·8)
Total	2294	137	510	2805

Table 2. *Site of origin of mycobacterial isolates*

| Lymph node site | Mycobacterial species | | | Total |
	M. tuberculosis	*M. bovis*	Atypical	
Cervical	90	5	8	103
Axillary	13	—	1	14
Inguinal	5	—	1	6
'Other'	2	—	—	2
Unspecified	11	1	—	12
Total	121	6	10	137

isolates submitted from neighbouring hospitals for identification and susceptibility testing (58 %). Isolates were identified by the standard methods in practice at the time, the number of differentiating tests increasing during the period under study. Prior to 1977 all isolates other than *Mycobacterium tuberculosis* were referred to the Tuberculosis Reference Laboratory at Cardiff for confirmation of identification as well as sensitivity testing to appropriate anti-tuberculosis drugs. Since 1977, acid-fast bacilli have been screened in this laboratory by cultural methods (pigment production, growth at 25 °C, 43 °C and in the presence of p-nitrobenzoic acid, and of thiosemicarbazone) and by determining niacin production and nitrate reduction after three weeks incubation. If indicated, further tests are undertaken to identify atypical mycobacteria as previously described (Wolinsky, 1979). Sensitivity testing to rifampicin, isoniazid, streptomycin and ethambutol have been performed on all samples.

M. bovis was originally differentiated from *M. tuberculosis* by its dysgonic growth, with enhancement on pyruvate-supplemented media, and by its resistance to pyrazinamide. More recently, failure to reduce nitrate or synthesize niacin and susceptibility to thiopen-2-carboxylic acid hydrazide (TCH) have been used as confirmatory tests.

Details concerning the anatomical site of the lymph node and the age, sex and name of the patient were recorded. For the purposes of this study, the names have been classified as European, Asian or other (African, Chinese or Far Eastern).

RESULTS

During the 15·5 years 1969–84, the 137 isolates from lymph nodes represented 4·9 % of all mycobacterial isolates identified (Table 1). Of these, 121 were strains of *M. tuberculosis*, 6 were strains of *M. bovis* and the remaining 10 isolates were
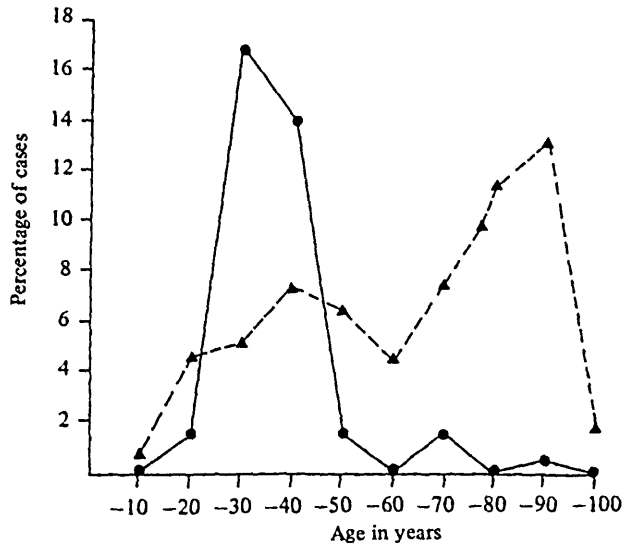
Fig. 1. Percentage of cases of mycobacteria isolates from European (▲----▲) and non-European (●—●) patients in relation to age.
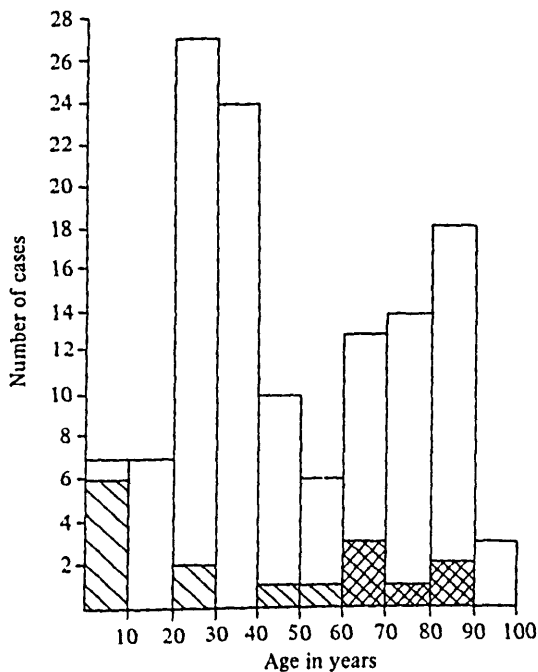

Fig. 2. Distribution of mycobacteria isolates according to age. ☐, *M. tuberculosis*; ☐, *M. bovis*; ▨, *atypical mycobacteria*.

atypical mycobacteria; 6 *M. avium intracellulare*, 2 *M. scrofulaceum* and 1 each of *M. kansasii* and *M. chelonei* var. *abscessus*. The cervical glands were most frequently affected in all forms (Table 2).

Seventy-eight of the 121 patients with *M. tuberculosis* infection had European names, 38 had Asian names and five had names identifiable as African, Chinese or Far Eastern. The strains of *M. bovis* and of the atypical mycobacteria were all

Table 3. *Percentage of total mycobacterial isolates recovered from non-European patients*

| Quinquennium* | Pulmonary | Extra pulmonary | | Total |
		Lymph node	Other	
1969–1973	5·2	22·7	9·0	5·9
1974–1978	7·0	27·5	15·9	8·5
1979–1983	7·1	39·1	19·6	9·5
1969–1983	6·3	31·4	14·3	7·7

* Isolates for 1984 not included.

recovered from European patients. The distribution of cases due to human strains of *M. tuberculosis* according to age and ethnic origin (European or non-European) is shown in Fig. 1. In European patients the highest incidence was in the elderly, whereas in the non-European group the disease was most frequent in the third and fourth decades. The male to female ratio was 1:2·2 amongst the European patients, with a 1:1 ratio in the non-European group. Age-related differences in mycobacterial aetiology are displayed in the histogram (Fig. 2).

Extrapulmonary sites accounted for 75 (34·1 %), including 43 (19·5 %), from lymph nodes from a total of 220 isolates from non-European patients. Corresponding figures for 2584 isolates from European cases showed 435 (16·8 %) were cultured from extrapulmonary sites with 94 (3·6 %) from lymph nodes.

During the period 1969–83 there has been a pronounced fall in the total number of respiratory isolates from all patients and a lesser decline in the number of cultures from extrapulmonary sites. However, during this time the proportion of the total isolates recovered from non-European patients has steadily increased (Table 3) and is highest (31·4 %) amongst patients with tuberculous lymphadenitis.

DISCUSSION

The sites of tuberculous lesions are determined by the route of infection and the degree and mode of subsequent spread of disease from the primary site. Hence cervical lymphadenitis may represent the glandular component of a primary infection originating in the tonsil, mouth, or on the face (Miller & Cashman, 1955); may arise from extension by lymphatic spread from a pulmonary primary complex (Innes, 1981) or from miliary disease (Crofton & Douglas, 1981) or may result from a haematogenous dissemination from a primary or post-primary lesion at a distant site. The usual group of superficial lymph nodes to be affected in all types of mycobacterial infections are those in the cervical region, accounting for over 90 % of notifications (Report from the Medical Research Council, 1980). However, the incidence of bacteriologically confirmed cases is much lower than the notification rate because positive cultures are only obtained in 30–56 % of all cases (Newcombe, 1971; Campbell & Dyson, 1977), the remainder being diagnosed by histology or on circumstantial evidence. For the last two-and-a-half decades nearly all reports from economically developed countries have described *M. tuberculosis* as being the predominant cause of superficial mycobacterial lymphadenitis at all sites and at

all ages, excepting those isolates from children under ten years of age when atypical mycobacteria preponderate (Enarson, Ashley & Grzybowski, 1979; Lai *et al.* 1984; Marsden & Hyde, 1962). Only 14 % of *M. tuberculosis* isolates, 1·5 % of atypical isolates and 0–1·5 % of *M. bovis* isolates are recovered from glands outside the cervical region (Grange, Collins & Yates, 1982; Report from the PHLS, 1976).

With regard to pathogenesis, most strains of *M. bovis* and atypical mycobacteria are isolated from unilateral lesions of the cervical glands high in the neck (Wolinsky, 1979; Zeller, 1964), reflecting a primary infection of either the tonsil (*M. bovis*) (Bajan *et al.* 1965), or elsewhere in the mouth or on nearby skin (atypical mycobacteria) (Wolinsky, 1979). By contrast, *M. tuberculosis* has been found to be more prevalent in bilateral cervical lesions and glands of the caudal neck (especially supraclavicular) (Newcombe, 1971), in axillary glands and in generalized lymphadenitis tuberculosa (Zeller, 1964). This last form is rare, accounting for only 3 % in two series of superficial tuberculous lymphadenitis (Kent, 1967; Priel & Doler, 1982) and being more frequently seen in non-Europeans in conjunction with hepatosplenomegaly and mediastinal involvement (Citron, 1973). These features suggest that superficial lymphadenitis due to *M. tuberculosis* more commonly represents dissemination from a focus of infection elsewhere (Kent, 1967).

The relative frequency of classical *M. bovis* as a cause of cervical adenitis is completely dependent upon the prevalence of cattle tuberculosis and raw milk consumption, and in England and Wales has fallen from 50–57·5 % in the years 1914–44 (Report to the Medical Research Council, 1949; Crofton, 1954) to 2·8 % in a study in south-east England from 1973 to 1980 (Grange, Collins & Yates, 1982). This has reflected the virtual elimination of infected cattle through the systematic testing and destruction of tuberculin-positive cattle (the Attested Herds Scheme), which was started in 1935. In fact a diminution in the absolute number of young children with cervical gland tuberculosis is the first sign of a reduction in the number of infections resulting from tuberculous cattle (Meissner, 1966). In 1979 only 0·18 % of herds were infected (Collins & Grange, 1983) and this may represent an irreducible minimum due to a small but important secondary reservoir in badgers (Wilesmith, 1983). All six isolates in the present series (4·4 % of the total) were recovered from elderly females, and in five the cervical glands were affected. These women were almost certainly infected early this century when the risk of primary tuberculosis infection from contaminated milk was high and cervical adenitis due to *M. bovis* in children common. All six strains were pyrazinamide-resistant and therefore typical of classical *M. bovis*. The Afro-Asian variant, which shows cultural similarities to *M. bovis* but for which there is no evidence of an association with cattle, is distinguishable by its sensitivity to this drug (Collins, Yates & Grange, 1982). Prior to its elimination, the incidence of cattle tuberculosis and consequently childhood cervical lymphadenitis due to *M. bovis* was particularly high in the north-west of England, accounting for over two-thirds of isolates from cervical lymph nodes between 1943 and 1945 (Report to the Medical Research Council, 1949). One might, therefore, have expected the present study to reveal a higher proportion of reactivated *M. bovis* infections in the elderly than it actually did (11 % of those aged over 50). This suggests that either reactivation is an unusual cause of mycobacterial lymphadenitis in this age group, and the majority of cases represent either a recent primary infection or a re-infection

behaving in a primary fashion, or that *M. bovis* has a lower propensity for reactivation than *M. tuberculosis*.

Accompanying the decline of classical bovine and human tuberculosis in Great Britain, an increasing number of infections due to atypical mycobacteria have been recognized, and these are now the predominant cause of mycobacterial cervical adenitis in children under ten years of age (Grange, Collins & Yates, 1982; Report from the PHLS, 1976). *M. avium-intracellulare* and *M. scrofulaceum* (MAIS complex) account for the majority of infections, which are usually self-limiting (Grange, Collins & Yates, 1982; Marks *et al.* 1977). Six of the ten atypical mycobacteria isolated in the present series were recovered from children under 10 years, and eight involved the cervical glands.

The influence of immigration on the epidemiology of all forms of tuberculosis can be marked both nationally and regionally (Enarson, Ashley & Grzybowski, 1979; Medical Research Council Tuberculosis and Chest Disease Unit, 1982) but is specially noticeable in tuberculous lymphadenitis because of the high frequency of this disease amongst Asians. In surveys of tuberculous lymphadenitis from London and south-east England, where the Asian community is relatively large (Office of Population Censuses and Surveys, 1983), 67·6–79 % of patients were of Asian origin (Grange, Collins & Yates, 1982; Summers & McNicol, 1980). In contrast, from a recent survey in south and west Wales, only one-third of the patients with tuberculous lymphadenitis were non-European, reflecting the smaller immigrant population in the area being surveyed (Monie *et al.* 1982). The influence of the size of the non-european community on the overall results is further exemplified by the present study in Merseyside, where less than one-third of all lymph node isolates came from this group. This small proportion reflects the population of Merseyside metropolitan county, where in 1981 only 1·0 % were New Commonwealth immigrants, compared with the national average of 4·7 % (Office of Population Censuses and Surveys, 1983). However, amongst the non-European patients *M. tuberculosis* lymphadenitis occurred almost exclusively in the third and fourth decades and was the commonest form of extrapulmonary disease, which is in agreement with observations from areas with a large number of isolates from Asians (Grange, Collins & Yates, 1982; Campbell & Dyson, 1977; Summers & McNicol. 1980).

In conclusion, the incidence of bacteriologically confirmed superficial mycobacterial lymphadenitis in the Merseyside region has remained relatively constant over the last 15 years despite a fall in the number of pulmonary and total extrapulmonary isolates. Considering the frequency of *M. bovis* as a cause of childhood cervical adenitis earlier this century it is surprising that this organism only accounted for 11 % of isolates in patients over 50, an age when most disease is considered to represent reactivation. The extent to which the immigrant population size influences the pattern of tuberculous lymphadenitis is demonstrated by the considerable regional variation in Great Britain of the proportions of isolates from non-European patients. The low proportion in the present study reflects the small immigrant population in the area rather than indicating a lower incidence of disease within that community.

We are grateful to our clinical and laboratory colleagues in Merseyside and Dr P. A. Jenkins, Mycobacterium Reference Unit, Public Health Laboratory, Cardiff, for their help.

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