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The opportunist mycobacteria—a 20-year retrospect

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Summary

A review is presented of the incidence and distribution of infections with opportunist mycobacteria in Wales for the years 1952–71. The most important opportunist pathogen was *Mycobacterium kansasii*.

Although the numbers affected by each species were small, taken together they indicate a genuine increase in incidence over the two decades. As tuberculosis declined by five-sixths over the same period, the relative change has been striking.

The distribution of infections suggest that exposure to dust at work and to heavy air pollution at home predispose to infection by opportunist mycobacteria.

THE Tuberculosis Reference Laboratory is now in its twentieth year of close involvement with the opportunist mycobacteria. This period followed, and was a consequence of, the introduction of chemotherapy for tuberculosis. The new problems of management required a close study of the patient's organism and it then became clear that some infections, clinically and pathologically indistinguishable from tuberculosis, were due to mycobacteria which were not tubercle bacilli. They were first called 'anonymous' mycobacteria but as specific names have now been applied to them, the alternative term of 'opportunist' mycobacteria is more appropriate. The Reference Laboratory has been well-situated to investigate these organisms, as it has access to all the relevant material in Wales where the incidence of opportunist infections is substantial. A few cases may have been missed in the first year or two but the screening procedures applied subsequently are thought to have been completely effective.

Mycobacterium kansasii

The most important opportunist in Britain is *Mycobacterium kansasii*. With few exceptions, the infections caused simulate pulmonary tuberculosis, mostly in middle-aged men. Identification of the organism is not sufficient to establish the presence of an infection; any of the opportunist mycobacteria can appear in specimens by accident and supporting evidence is necessary. However, most isolates of *M. kansasii* in practice prove to be significant. In Wales, kansasii infections are almost confined to miners and people who live in large towns. The rural incidence in England seems to be relatively low as well. Figures 1 and 2 illustrate the contrast between the distribution of tuberculosis and kansasii infection in Wales. The two infections differ also in their trend because whereas the incidence of tuberculosis in Britain is declining, kansasii infections in Wales at least appear to be slowly increasing in number. In Fig. 3 the cases recorded were all pulmonary except for one of cervical adenitis and one joint infection. Over the same period, tuberculosis declined by about five-sixths so that the proportion of cases which present clinically as tuberculosis but are in fact kansasii infection has risen considerably. Overall, the proportion is now 2% or so, but it can be very much higher in urban areas, for example, in the city of Cardiff it is *ca.* 5%. Figure 3 shows also the incidence of patients with single isolates from sputum. Some such cases are non-significant but others represent inadequate follow-up and a few may be examples of short-lived infection.

Figure 4 presents the incidence of *M. kansasii* in Cardiff. The impression given is of a small epidemic imposed on an endemic situation. Figure 5 shows the location of the homes of these patients, excluding men who work in dusty occupations, some of which are believed to favour opportunist infections. The distribution can be seen to be concentrated near the two main channels of communication. There are large residential areas, both working- and middle-class, at some distance from these routes, which have not produced a single case. It appears therefore that people may be predisposed to kansasii infection by air pollution either at their work or, when they live near heavy road or rail traffic, in their homes.

The natural habitat of *M. kansasii* has not yet been demonstrated but it will almost certainly prove to be water. We have never found photochromogens, i.e. mycobacteria like *M. kansasii*, stimulated to form pigment by light, except in water and two

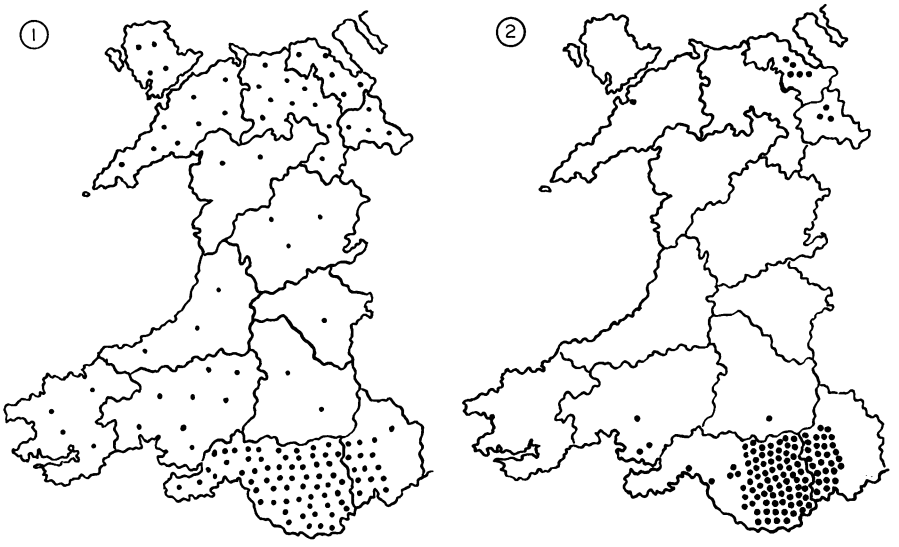

FIG. 1. Distribution of infections with *Mycobacterium tuberculosis* in Wales by counties in 1962. Each spot represents ten cases. FIG. 2. Distribution of infections with *Mycobacterium kansasii* in Wales, 1952–71.

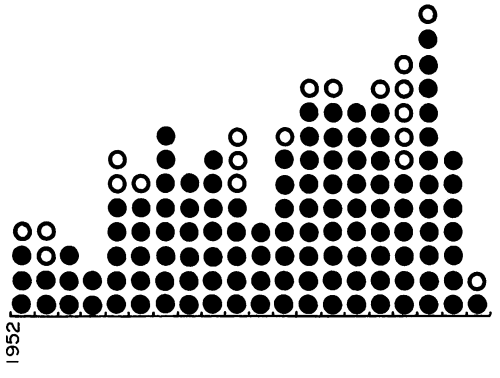

FIG. 3. Incidence of infections with *Mycobacterium kansasii* in Wales 1952–71. Close circles, significant isolates; open circles, significance doubtful.

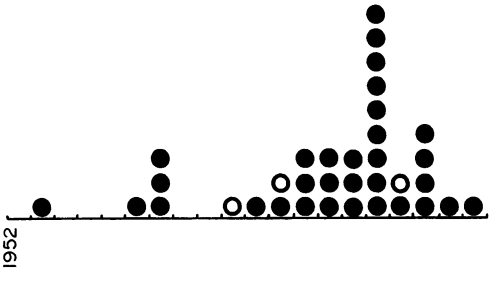

FIG. 4. Incidence of infection with *Mycobacterium kansasii* in Cardiff 1952–71. Closed circles, significant isolates; open circles, significance doubtful.

workers have isolated the organism from piped water or taps. Presumably, infection is by means of aerosols generated in the use of water although ingestion followed by localization in the lung is a possibility.

Kansasii infection rarely spreads to contacts. No case of the infection by a patient of a child or spouse has been met in the present series but it does include a nurse and a small number of miners probably infected by contact. The miners had pneumoconiosis which appears to be responsible for increased susceptibility.

Mycobacterium avium

M. avium is widely distributed as a pathogen of wild and farm birds and not uncommon as an opportunist pathogen for cattle and pigs. Human infections are relatively infrequent and occur more in rural than in urban areas, as might be expected from the organism's normal habitat. Many cases are associated with pneumoconiosis which appears to be a particularly predisposing factor. This perhaps explains the somewhat higher than average incidence of avian infections in Wales, which has a high incidence of pneumoconiosis. Figure 6 records thirty-two cases of infection with *M. avium* of which nineteen were pulmonary and associated with pneumoconiosis. No particular trend or pattern is

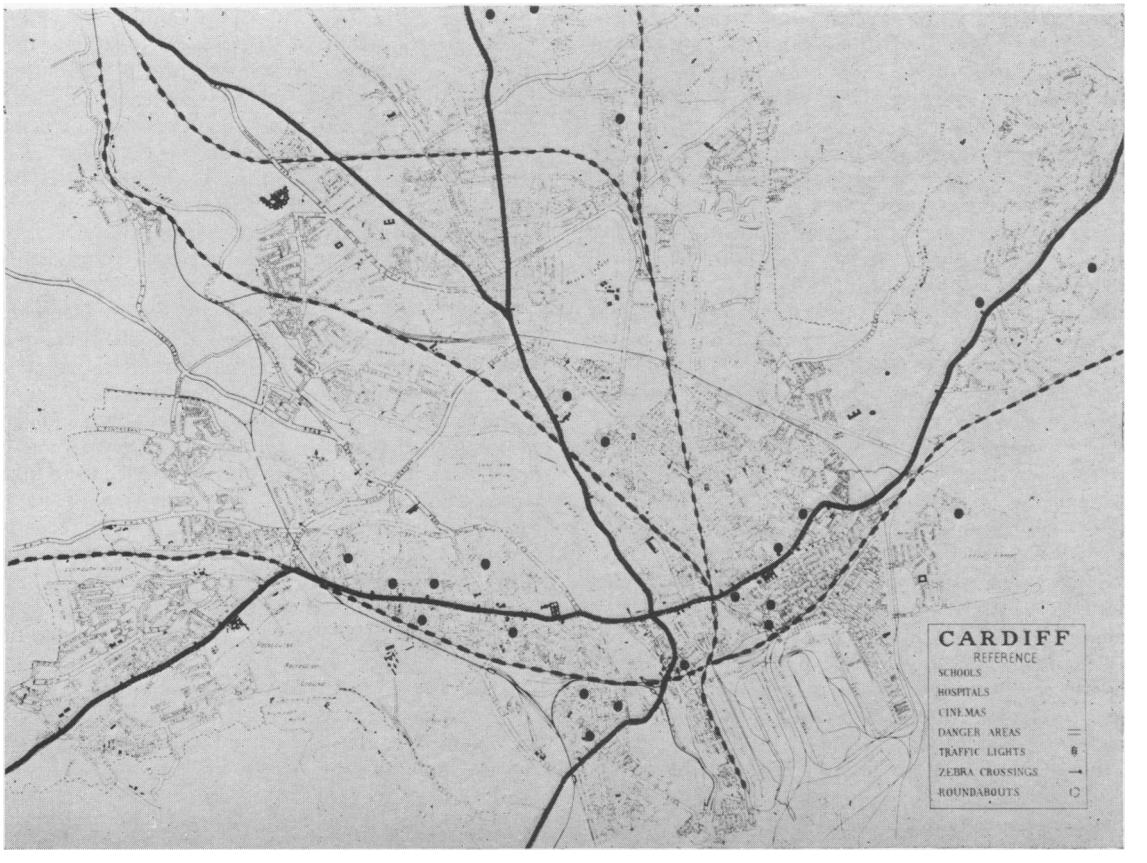

FIG. 5. Distribution of infections with *Mycobacterium kansasii* in Cardiff, excluding those subjects with a history of industrial dust exposure.

evident in the occurrence of these infections. There were seven other lung infections, one in a young Cardiff butcher and presumably occupational. The rest represent isolates from cervical adenitis, an abscess, a wrist ganglion, an appendix, pericardial fluid and two from endometrium. In the last four cases, the significance of finding *M. avium* is uncertain. These infections show little or no response to chemotherapy. Systemic infection is fatal and pulmonary cases have a bad prognosis, although deterioration may be slow. However, infections of lymph nodes and superficial tissues recover spontaneously or with the help of surgery.

Mycobacterium intracellulare

This organism has also been called the Battey bacillus after a Sanatorium where its role as a pathogen was established. The species differs from *M. avium* in minor biochemical properties and in that its members are not natural pathogens for birds;

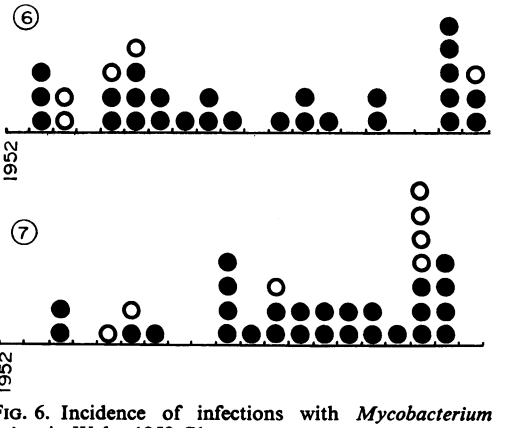

FIG. 6. Incidence of infections with *Mycobacterium avium* in Wales 1952–71.
FIG. 7. Incidence of infections with *Mycobacterium intracellulare* in Wales 1952–71. Closed circles, significant isolates; open circles, significance doubtful.

nor are they usually virulent for fowls experimentally. The species appears to live normally in soil and is therefore ubiquitous. One consequence is that the special rural incidence of *M. avium* is absent and another is that the organism not infrequently appears in specimens as a contaminant. Special care is therefore needed in assessing the significance of an isolate. In some countries, the environment of certain areas is densely populated with *M. intracellulare* and in these the incidence is high both of clinical infection and non-significant isolates.

In general, *M. intracellulare* is much more frequent as an opportunist pathogen for man than *M. avium* is, but the reverse is true for animals. In Britain it most commonly causes cervical adenitis in children but in most other countries, lung infections in adults.

The incidence of intracellular infections in Wales more than doubled in the second decade of the present survey as compared with the first decade (Fig. 7). The number of cases was small but taking them together with our kansasii cases, which have also increased in number, there seems to have been a genuine increase in opportunist infections. It is tempting to relate this increase to the decline of tuberculosis which must have left many people having a low immunity to mycobacteria open to opportunist infection. However, in Western Australia where intracellular infection is exceptionally common, its incidence has not changed during the local recession of tuberculosis. So far as lung infections are concerned, the difference in trend may be due to the effect of air pollution in Wales.

Mycobacterium scrofulaceum

M. scrofulaceum is closely related to *M. intracellulare*. It appears to be less virulent on the whole, however, because although it causes cervical adenitis in children and occasionally superficial lesions, lung infections are very rare and limited to people subject to obvious predisposing conditions. Although we have only isolated this species once from natural soil, this seems its likely habitat. A pot of soil artificially inoculated retained a flourishing population of the organism when cultured more than 2 years later. Non-significant isolates are not unexpected therefore—there were six in our series compared with four significant. Contaminating strains are sometimes recovered from urine. Opportunist mycobacteria of any kind in urine have not proved significant in our own experience but have been reported to be excreted in rare cases of systemic infection or epididymitis. Otherwise, isolates from urine should be dismissed except as a signal for cleaner collection of specimens.

Mycobacterium xenopi

M. xenopi has some resemblance to the three species last discussed but has a number of highly distinctive characters of its own. For example, it is the only opportunist mycobacterium to be clearly thermophilic. In Britain, it is found chiefly in London and on the South Coast but also presents in coastal and estuary areas which are not too far North. The distribution is shown in Fig. 8 which records the first 104 cases identified in the Reference Laboratory. Isolates are frequent on the opposite Channel coast but have so far been recognized only sporadically elsewhere in Europe.

In certain of our coastal towns, the environment appears to be heavily contaminated, resulting in a high incidence of non-significant isolates, but also some genuine infections. *M. xenopi* has been found in the water supply of a hospital—the hot system was more affected than the cold. But its true habitat is not known. Its distribution and preference for a high temperature suggest that *M. xenopi* may be a pathogen or commensal of sea-birds. Very recently we have begun to receive a few isolates from the Midlands and it may not be a co-incidence that sea-birds are said to have ventured further inland than usual in the last few years. However, we have no concrete evidence for the theory, as yet.

If the heavily infested areas are excluded, about half of the isolates of *M. xenopi* met are significant. In Wales, the proportion has been eight significant to six non-significant. All the cases found in Britain have been adults with lung infection. There has been no apparent relation to industry or air pollution, perhaps because of the special distribution of the

FIG. 8. Distribution of 104 isolates of *Mycobacterium xenopi* obtained in England and Wales.

organism. The organism is sensitive to several drugs *in vitro* but its response *in vivo* is uncertain. Resection of lung has been useful in some cases.

Mycobacterium fortuitum

Rapidly-growing mycobacteria are isolated from sputum with unusual frequency in Wales. The best-known species is *M. fortuitum* but *M. peregrinum* is even more common and there are a number of other entities which lack names. They are mostly found in the sputum of miners, sometimes repeatedly over long periods. No obvious clinical illness can be attributed to the presence of these mycobacteria, so one must assume a carrier state, presumably due to an impairment of normal clearing mechanisms in men heavily exposed to coal dust. A study of Welsh miners has also shown that they develop allergy to opportunist antigens with undue frequency and it is possible therefore that a form of long-term damage, perhaps even progressive massive fibrosis, could be initiated by opportunist colonization. The special prevalence of the fast-growing mycobacteria in Welsh as opposed to English miners has not yet been explained because *M. fortuitum* at least is ubiquitous. It is possible that this phenomenon and the high local incidence of pneumoconiosis are both due to some special property of Welsh coal such as a high toxicity or a particular tendency to produce particles in the respirable range.

Mycobacterium marinum

The organism known as *M. marinum* and formerly as *M. balnei* is responsible for swimming-bath granuloma. Cardiff has the unfortunate distinction of having provided the only major outbreak in Britain of this infection. The organism is able to live freely in water or on surfaces bathed by water but is also well-known as a pathogen for fish, amphibia and reptiles. It is also now recognized as the occasional cause of skin lesions in people with home aquaria but in a few cases there is no history incriminating water. *M. marinum* is a psychrophile and therefore never causes internal disease. For the same reason, attempts to culture it will usually fail unless a temperature below 37°C is used.

The opportunist mycobacteria present a number of interesting problems, especially as regards their habitat and epidemiology. Whatever happens to tuberculosis they will always be with us and they are likely to assume more importance than they have at present. It is therefore advisable for us to learn more about these creatures in order to be well prepared.