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# COMMENTARY
# *Mycobacterium tuberculosis* and the search for the impossible truth

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The ability of accidentally inoculated *Mycobacterium tuberculosis* to cause skin and soft tissue infections has been known for almost two centuries, yet it was, and remains, a rare form of tuberculosis (TB) [1]. Because *M. tuberculosis* is assumed to have very limited survival outside the host, environmental reservoirs are not felt to have any role in TB transmission [2]. When inoculation TB cases are reported, they tend to be isolated or to include a limited number of cases over a short period of time [3].

In contrast, non-tuberculous mycobacteria (NTM) are ubiquitous in the environment, and are readily identified from water, soil, instruments and other sources [4]. They can be resistant to disinfection, and have been responsible for a range of skin and soft tissue infection outbreaks through a variety of inoculation procedures including tattoos, surgical procedures, injections and acupuncture among others [5]. In one epidemic associated with video-assisted surgical instruments, 1051 possible cases of *Mycobacterium massiliense* wound infection were identified across 38 Brazilian hospitals over an 11-month period [6]. Among mycobacteria, the members of the *M. tuberculosis* complex and NTM are presumed to inhabit two different worlds.

What then is one to make of the recent report by Wang and colleagues in this Journal reporting 13 cases of acupuncture-associated inoculation TB occurring over a 4-month period in patients attending a southeastern China clinic? [7]. The epidemiological evidence supports a point source for the outbreak, and the microbiological evidence supports *M. tuberculosis* as the causative agent. But given conventional wisdom that *M. tuberculosis* should not exist in the environment for any meaningful length of time, one must consider alternative explanations. The first would be that these cases were unrelated; however, the cases all attended the same clinic, developed infections at the site of known injections, had – when tested – the same strain of *M. tuberculosis* and new cases stopped occurring when the clinic switched to disposable needles. The conclusion that these cases were unrelated seems improbable.

Another possibility was that NTM were misidentified as *M. tuberculosis*. All 13 patients were *M. tuberculosis* culture positive, and the 10 patients who underwent interferon-gamma release assay testing using the T-SPOT.TB test were also positive. Five isolates were genotyped at the Disease Control Centre of Zhejiang Province and found to be *M. tuberculosis*, Beijing type. Misdiagnosis of NTM also seems improbable. Another possibility is laboratory cross-contamination. Twelve patients had positive stains for acid-fast bacilli at aspiration or surgical drainage, and granulomatous reactions were found on histopathological examination of biopsies from all patients. The cases also were spread over a 4-month time period, further making laboratory cross-contamination unlikely.

To paraphrase the great fictional detective Sherlock Holmes, once the improbable has been ruled out, one must consider the impossible, i.e. that *M. tuberculosis* can survive in the environment for extended periods of time and remain capable of causing disease. *Mycobacterium bovis*, another member of the *M. tuberculosis* complex, has previously been shown to be able to survive in the environment for extended periods of time, and soil-contaminated *M. bovis* may be responsible for ongoing outbreaks of disease in cattle in the UK, for example [8, 9]. *Mycobacterium canettii*,

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another member of the *M. tuberculosis* complex capable of causing human TB, also has been suggested to have an environmental reservoir [10]. *M. tuberculosis* can be cultured from laboratory-contaminated soil for as long as 1 year after inoculation, and the resulting cultures have been demonstrated to cause granulomas in mice [11]. Mycobacteria including members of the *M. tuberculosis* complex have been shown to be able to survive in free-living amoebae, which may allow for prolonged survival in the environment [12], although the viability of these mycobacteria and their ability to cause disease is unclear [9].

What then are the take-home lessons from the report by Wang and colleagues? First, to consider mycobacteria when confronted with inoculation-associated skin and soft tissue infections that do not respond to conventional antibiotic treatments. Second, pathogen identification of infectious processes remains valuable for recognizing outbreaks and ensuring proper treatment, particularly in challenging cases. Finally, after over 130 years of study, *M. tuberculosis* continues to hold surprises for clinicians and researchers alike. The game is afoot.

## DECLARATION OF INTEREST

None.

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