**Commentary**

**Melioidosis, the mimicker of maladies**

The diagnosis of an infectious disease is incomplete without determining its aetiology. Whether it is as simple as pharyngitis, or life-threatening as meningitis, aetiology determines therapy. We all know that physicians often take short cuts, and offer shotgun therapy without detecting or deducing the pathogen involved. For some diseases, the diagnosis is integrally linked with aetiology, such as tuberculosis and typhoid fever. So it is with melioidosis too; laboratory evidence is essential to diagnose and diagnosis is essential to choose the right antimicrobial. Wrong diagnosis is often a fatal mistake – mistake for the doctor, fatal for the sick who trusted the doctor.

Melioidosis is the name applied to any of a spectrum of diseases caused by infection due to *Burkholderia pseudomallei*. It may be recurrent or prolonged fever with or without lymphadenitis, pyogenic abscess(es) of liver, spleen, brain, skin, subcutaneous or any other tissue, osteomyelitis, pneumonia or septicemia with or without multi-organ failure. Clinically these diseases mimic pyogenic bacterial infections, Gram negative septicemia or cryptic tuberculosis. It is so easy to assign incorrect aetiology in any of these conditions and treat accordingly. Patients with localised superficial abscesses may recover with incision and drainage, but later on melioidosis may recur in another form. Some develop recurrent fever and weight loss, simulating tuberculosis, especially when accompanied by lymphadenopathy. Or they may come with, or deteriorate by rapidly developing, florid pneumonia or septicemia with multi-organ failure and die in spite of the usual treatments. Even when investigated, the diagnosis may be missed unless the microbiologist is aware of the presence of this pathogen in all parts of India and for that reason speciates the microbe in hand. Bacteriology may show motile and non-fermenting Gram-negative bacilli, often mistaken for *Pseudomonas* species and either treated as such or ignored considering them as contaminants. Treatment with the combination of broad-spectrum penicillin plus an aminoglycoside is common practice in such cases of suspected or detected Gram-negative sepsis, but it is usually of no help in melioidosis. Histopathology may show granuloma and necrosis mimicking caseation, suggestive of tuberculosis, but without acid-fast bacilli. Antitubercular treatment also fails. Melioidosis has to be treated with ceftazidime, a third generation cephalosporin, followed by trimethoprim-sulfamethoxazole for several weeks to prevent relapse. For some reason, *B. pseudomallei* is inherently resistant to most other antimicrobials.

It was an Indian bacteriologist, CS Krishnaswami, who first detected and described the microorganism in 1912, while working with a physician colleague, A Whitmore, under the British Army in Burma. It was called *Bacillus whitmori*, a name that did not last long. But it remained assigned to the genus *Bacillus* for decades and later shifted to the genus *Pseudomonas*. Until 1992 it was classified as *Pseudomonas pseudomallei*. Currently it is included in a newly named genus of *Burkholderia*, a name given in honour of the American microbiologist who identified a bacterial infection of onions that turned out to be another species included in this genus. The first report of the presence of *B. pseudomallei* in India was not from an Indian laboratory, but from Scotland in 1953, reflecting the decline in our quest for excellence in diagnostic microbiology even in academic institutions. The second report of its presence came from Germany in 1988. In both instances, a traveler got infected here, but the disease manifested later after return to Scotland and Germany respectively, and was aetologically diagnosed in these countries. The credit of the first report from an Indian centre goes to KR Raghavan and colleagues in Mumbai.

*B. pseudomallei* is a soil saprophyte. Infection may be via skin through abrasions or by inhalation. During the American invasion of Viet Nam many soldiers were infected and manifested pulmonary or other forms of melioidosis after return from war duty. Helicopter borne
soldiers were especially prone to lung disease, presumably due to the inhalation of dust raised by landing helicopters, for which reason the disease was nicknamed ‘Viet Nam tuberculosis’. Others fighting in Viet Nam developed various forms of melioidosis, usually years after return to the USA. Therefore it was also nicknamed ‘Viet Nam time bomb’. The Scottish, German and Viet Nam reports illustrate that infection may remain latent for prolonged periods and later manifest with disease, mimicking tuberculosis. Diabetes mellitus, chronic renal failure and cirrhosis of the liver seem to predispose the activation to disease of the otherwise dormant latent infection. Many subjects with melioidosis are otherwise in good health, showing that B. pseudomallei is actually a primary pathogen. It is well recognized in most south east Asian countries and in northern Australia. In northern Thailand, melioidosis is the most common cause of septicaemia. Now we know that its geographic prevalence does not stop at Myanmar but extends to most of India.

The geographic prevalence of melioidosis indicates the widespread occurrence of this saprophyte in soils of almost all states in India. In Vellore region, subclinical infection is not uncommon. A closely related pathogen, namely B. mallei is an obligatory zoonotic parasite causing glanders, but it seems to have virtually disappeared from domesticated animals and humans, decades ago. Other than these two, all other species of the genera of Burkholderia and the closely related Pseudomonas are opportunistic pathogens. So, why is B. pseudomallei a primary pathogen? In this issue of IJMR, there is a report by Jesudason and colleagues, on various toxins of B. pseudomallei. Although exotoxins and endotoxins have been described in these organisms obtained in other geographic locations, it remained to be shown that Indian isolates from various states also possess them. That has now been achieved by the collaborative work between the investigators in Vellore (Christian Medical College) and Kanpur (Indian Institute of Technology).

India’s rural folk live in close proximity to and association with agricultural land. Obviously they are exposed and prone to get infected with B. pseudomallei. One does not require much imagination to expect that melioidosis occurs far more frequently than anyone has suspected so far, and that it ends up in tragic death due to lack of adequate microbiological diagnostic support service in the multitude of our clinics and hospitals. In Singapore melioidosis is a notified and reportable disease. In India it continues to be an under-diagnosed disease. In order to practice evidence-based medicine microbiologists must characterise every isolate of Pseudomonas or Pseudomonas-like organism if obtained from any body tissue, fluid or pus. If it is oxidase positive and gentamicin resistant, the likelihood of it being B. pseudomallei is quite high. It should then be speciated using appropriate biochemical tests and differentiate it from B. cepacia and P. stutzeri, the two organisms with which B. pseudomallei is confused most frequently. Agglutination using specific antiserum helps in rapidly establishing its true identity. Let me hope that our health policy makers and physicians will become aware of this neglected killer disease, killer only if not diagnosed and treated correctly.

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References


