MELIOIDOSIS IN THE AMERICAS

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Abstract. Melioidosis is a potentially severe bacterial infection caused by Burkholderia pseudomallei. There has been growing awareness of the disease in the Americas, particularly since the Vietnam conflict when it was diagnosed in returning service personnel. Accidental laboratory exposure indicates the difficulty making a culture-based diagnosis when melioidosis has not been considered in the differential diagnosis. Melioidosis is most likely underdiagnosed in tropical Central and South America where conditions are more suited to persistence of B. pseudomallei in the environment. Recent melioidosis case clusters in northeastern Brazil highlight the threat posed to rural populations located far from specialist services. Increased clinical awareness of the disease and improvements in laboratory diagnostic methods are likely to bring wider recognition of melioidosis in the Americas.

INTRODUCTION

Melioidosis is a potentially fatal bacterial infection of the tropical and subtropical zone between 20°S and 20°N.1,2 Some endemic cases occur both north and south of the tropics.3,4 The recent detection of melioidosis in northeastern Brazil highlights the extent of its distribution in the Americas and underlines the need for improved diagnostic methods.5 Melioidosis is a disease of environmental exposure that is normally acquired through occupational or recreational encounters with moist soil or surface water containing Burkholderia pseudomallei, the infective agent. Infection results from inhalation, inoculation, and possibly ingestion of this organism.6 There is debate over the relative importance of these routes of infection. High risk groups include rice farmers, laborers, indigenous groups, and adventure travelers.1 The peak risk period for acute infection is during the wet season, particularly within a week of the onset of heavy rain.7 Melioidosis has an unusually wide range of disease presentation, varying from septicemia with pneumonia and rapid deterioration to multiple organ systems failure through subacute disease with focal suppuration or abscess formation to asymptomatic exposure with no clinical evidence of infection until late-onset acute disease.1,6 The longest disease-free interval between exposure and culture positive melioidosis is 63 years.8 Those at most risk of septicemic or other acute manifestations of melioidosis have underlying medical conditions such as diabetes, chronic renal failure, alcoholic liver disease, or chronic respiratory pathology9 (Table 1).

Although B. pseudomallei is not difficult to culture in sterile fluid samples from patients with acute melioidosis, there are a series of diagnostic pitfalls that cause difficulties for the diagnostician and the clinical pathologist, even in melioidosis-endemic areas where the diagnosis is anticipated (Table 1). These problems include a lack of distinctive features of acute infection, potential involvement of almost any body site by subacute suppurrative disease, unexpected late-onset acute disease months or years after exposure, the finding of more common bacterial pathogens in bacteriologic specimens from non-sterile sites, atypical bacterial colony appearance in primary cultures, misleading bacterial identification results from proprietary laboratory tests, and B. pseudomallei polymerase chain reaction (PCR) inhibitors in tissues affected by suppurative subacute infection. Serologic tests, such as the widely used indirect hemagglutination assay, often give borderline positive or negative results in the early stages of acute septicemic disease.10 Single high titers may be obtained from asymptomatic persons and false-positive reactions may occur. An increasing antibody titer is more specific for recent infection, but is not definitive proof of disease.

A proportion of acute infections will be fatal, despite the best efforts of the attending physician. Those at highest risk of fatal infection are patients with B. pseudomallei meningocencephalitis. Approximately one-fourth of septicemic patients will relapse despite receiving intravenous antibiotics, often at approximately 10–14 days after onset of acute infection (Table 1). The initial treatment regimens currently recommended are ceftazidime plus cotrimoxazole, or meropenem for 2–4 weeks. Concerns about early relapse and late onset disease have led many to follow this first phase of therapy with a second, eradication phase with a combination of oral agents such as cotrimoxazole and doxycycline for at least 12 weeks.11

The bacterial cause of melioidosis is a gram-negative bacillus from the beta-proteobacteria group known as Burkholderia pseudomallei. The species was previously known as Pseudomonas pseudomallei and was grouped with other members of the Pseudomonas group until related bacteria such as P. cepacia were allocated the separate genus of Burkholderia. More commonly encountered Pseudomonads such as P. aeruginosa can be distinguished by their easily recognized phenotypic features such as pigment production, in addition to major genotypic differences. Burkholderia pseudomallei is oxidase positive, resistant to a wide range of antibiotics including gentamicin, polymyxin, and the second-generation cephalosporins, and can survive for long periods in a wide range of environments including distilled water, moist soil, and inside mammalian cells.12–14 It is closely related to the other human pathogens in the genus (B. mallei and B. cenocepacia) and to non-pathogenic neighbors such as B. thailandensis.15
Most cases of melioidosis are caused by *Burkholderia pseudomallei*. Although the disease is not widely recognized as endemic in many tropical locations, distribution is patchy and seasonal.

This unpredictability continues to cause significant diagnostic difficulty for the attending physician and the clinical laboratory. A bizarre record was kept for the longest interval to delayed onset acute disease. The longest interval, 63 years, was recently reported for a Vietnam veteran.

Exposure to moist soil or surface water

- Rural work outdoors
- Adventure or eco-tourism
- Military service
- During wet season or extreme weather

Peak risk may be two weeks after heavy rainfall. Co-morbidities cause higher risk of septicemic disease, rapid progression, and fatality.

Underlying diabetes, chronic renal failure, alcoholic liver disease or chronic lung disease

Commonest acute presentations are non-specific. Co-morbidities cause higher risk of septicemic disease, rapid progression, and fatality.

Febrile illness

Common intravenous antibiotics (e.g., gentamicin, ceftriaxone) are ineffective and unsuitable for trial of presumptive therapy. Relapse in up to 25%. Commonest acute presentations are non-specific. Common intravenous antibiotics (e.g., gentamicin, ceftriaxone) are ineffective and unsuitable for trial of presumptive therapy. Relapse in up to 25%

Septicemia

Unusual in some locations endemic for melioidosis. Undisclosed abscess may be source of bacteremia. Etiologic diagnosis may be missed if identification of bacteria from non-sterile site depends on substrate-utilization tests.

Pneumonia

Small numbers of *B. pseudomallei* in respiratory secretions outnumbered by commensal bacteria. Growth of *B. pseudomallei* on selective agar media.

Pneumonia with septicemia

*B. pseudomallei* grown from blood culture or respiratory secretions.

Respiratory distress

Primary septic cause may no longer be evident. Bacterial isolation is from non-sterile site in up to 25%.

Multiple organ systems failure

Unusual in some locations endemic for melioidosis. Bacterial isolation is from non-sterile site in up to 25%.

Meningoencephalitis

Unusual in some locations endemic for melioidosis. Bacterial isolation is from non-sterile site in up to 25%.

Focal suppurative abscess, cellulitis or ulcer

- Skin, soft tissues
- Face including orbits
- Osteomyelitis, septic arthritis
- Prostate

Etiologic diagnosis may be missed if identification of bacteria from non-sterile site depends on substrate-utilization tests. Indirect hemagglutination assay rising titer of single high titer in absence of other evidence of melioidosis is only supportive of diagnosis.

Asymptomatic seroconversion

Single high titer does not establish timing of exposure. False-positive and false-negative results occur.

### NORTH AMERICA

**Imported disease in Vietnam veterans.** Most cases of melioidosis in the United States have been in veterans of the Vietnam conflict. It was realized in the late 1960s that melioidosis could be observed as acute febrile illness years in soldiers who returned home from the Indochinese theater of operations when the propensity of this disease to present without warning after a disease-free interval was noted by infectious disease specialists. A bizarre record was kept for the longest interval to delayed onset acute disease. The longest interval reported in a Vietnam veteran is 29 years. The longest interval, 63 years, was recently reported for a veteran of the Pacific war of 1941–1945. Although the disease was not widely recognized until long after the Second World War, there are reports of melioidosis in Far East prisoners of war. This unpredictability continues to cause significant diagnostic difficulty for the attending physician and the clinical laboratory.

The extent of exposure to *B. pseudomallei* in high-risk populations is difficult to gauge from occasional case reports. Sero-epidemiologic studies have not been sufficiently comprehensive nor the methods used sensitive enough to provide an accurate picture of subclinical disease burden, but they do provide evidence for undetected exposure to *B. pseudomallei* in servicemen. The burden of hidden disease in the ageing veteran population is not known. Military field hospitals are said to have seen hundreds of cases of melioidosis in Vietnam. It is interesting to note that clinical melioidosis was only occasionally reported in British troops serving in Borneo during the Malayan emergency despite serologic studies showing evidence of seroconversion. Hypothetical reasons include differences in the virulence of *B. pseudomallei*, the type of vegetation (including the pattern of rice cultivation), and exposure to soil and water experienced by combat troops. It is notable that the Mekong delta carries silt from a river system that drains parts of northeast Thailand now known to be highly endemic for melioidosis.

**Endemic disease.** There has been a long-running argument over endemic melioidosis in North America fuelled by one case contracted after a farming accident in Oklahoma. The infection had features consistent with subacute melioidosis, but the clinical isolate had some phenotypic features that placed it apart from other clinical *B. pseudomallei* isolates and it was originally thought to be another, unidentified bacterial species. DNA hybridization studies and other molecular...
analyses including multilocus sequence typing subsequently placed this isolate in a separate clade of *B. pseudomallei*.\(^{15}\) The Oklahoma isolate is clearly separate from other members of the species and may represent a distinct bacterial species. In this particular case, there was no evidence of exposure to soil or muddy water outside the United States. There was one other reported instance of melioidosis believed to have been contracted in the United States that involved a young adult who sustained severe facial injuries during a motor vehicle accident.\(^{29}\) Eight weeks after orbital enucleation, he developed *B. pseudomallei* infection in the remaining tissues of the enucleated orbit. There was no history of overseas travel to provide a history of environmental exposure in a recognized endemic location. There have been several cases of melioidosis contracted after direct person-to-person transmission from people who contracted the disease in a recognized endemic zone. One of the best documented cases was a case of probable sexual transmission from a war veteran to his sex partners.\(^{30}\)

**LATIN AMERICA**

The first properly documented case of melioidosis in South America was reported from Ecuador in the 1960s.\(^{31}\) The authors of this report asserted that earlier claims of melioidosis cases from the Western Hemisphere may have been premature.\(^{32–34}\) In two cases, the isolates were not available for independent laboratory confirmation and in the third case the isolate was probably misidentified. The first of these possible cases was diagnosed in the United States in 1945 but the putative exposure could have been outside the United States while the patient was working in the Panama Canal Zone in 1927–1928.\(^{32}\) The report of Beigeleisen and others also mentioned two probable melioidosis cases from Panama.\(^{33}\) There was an unsuccessful attempt to demonstrate the presence of *B. pseudomallei* in rice fields near São Paulo, Brazil.\(^{35}\) There have been other reports of possible melioidosis from Brazil, including isolation of *B. pseudomallei* from burns patients, but these lacked detail on disease presentation, exposure, or corroborating evidence.\(^{36}\) There have been reports of sporadic human melioidosis from other parts of Central America.\(^{37–40}\) More recently, there have been occasional reports of melioidosis diagnosed unexpectedly after presumed exposure in parts of South or Central America not previously known to be endemic for the disease.\(^{41}\) (Champagne J, unpublished data). It is possible that the lack of advanced diagnostic laboratory support in many of these countries, particularly in rural settings where melioidosis is more common, has led to under-diagnosis of the disease.\(^{42}\) Refugee health programs and unusual climate events provide opportunities to test the hypothesis. Refugees from Central America have recently been found to have melioidosis during immigration health screening (Champagne J, unpublished data). Melioidosis has also been reported following flooding.\(^{43}\) It has yet to be seen whether tropical storms cause cases of melioidosis in the region in the same way that cases of the disease were caused after the Indian Ocean tsunami of 2004.\(^{44}\)

The first laboratory-confirmed case of human melioidosis in Brazil was in February 2003.\(^{3,45}\) There was only one survivor from a family group of four children who contracted the disease. A gram-negative bacillus was grown and presumptively identified as *B pseudomallei* five days after death of the third child.\(^{5}\) Although cultures from the one survivor remained negative for *B. pseudomallei*, she did seroconvert by *B. pseudomallei* indirect hemagglutination assay during her convalescence. In 2004, a small cluster of febrile illness occurred in a rural area approximately 165 km from the first case cluster (Figure 1).\(^{45}\) One adult patient with culture-confirmed *B. pseudomallei* septicemia died. In early 2005, a small group of adults developed a febrile illness after an incident in which their car left the road and plunged into a river. One patient progressed to pneumonia with respiratory failure and died. That patient had blood cultures positive for *B. pseudomallei*. Environmental investigations led to the recovery of *B. pseudomallei* from river water and Riverside mud collected during investigation of the second case cluster. A Dutch visitor to the coastal edge of the state developed a febrile illness during his travels in Ceará in 2003 and returned home to The Netherlands where he subsequently died of culture-confirmed melioidosis.\(^{46}\) A recurring theme in melioidosis investigations has been the difficulty of arriving at an etiologic diagnosis when laboratory resources and experience with *B. pseudomallei* are limited. The first Brazil outbreak isolate was confirmed in Rio de Janeiro by phenotypic methods,\(^{5}\) independently confirmed by molecular methods, and subtyped by DNA macrorestriction and Eco RI ribotyping.\(^{45}\) It has been possible to develop a working case definition so that state health authorities can monitor the emergence of melioidosis in Ceará and neighboring parts of Brazil.\(^{11}\) Preliminary seroepidemiologic studies suggest that asymptomatic exposure has occurred more widely than suggested by the children affected by the first case cluster.\(^{45}\) In this rural part of northeastern Brazil, females were more likely to be seropositive. The pattern of seropositivity needs confirmation in larger studies because it is different from that in southeast Asia where melioidosis is common in rice farmers.\(^{47,48}\) Molecular epidemiologic methods (DNA macrorestriction and automated Eco RI ribotyping) demonstrated *B. pseudomallei* strain diversity in northeastern Brazil, and suggest a possible link with melioidosis in northern Australia.\(^{45}\)

**Diagnostic laboratory incidents.** Lack of professional familiarity with endemic melioidosis, combined with the sporadic occurrence of travel-related disease, pose a special problem for diagnostic laboratories in the United States. There are too few culture-positive cases to sustain expertise in hospital laboratories where blood culture and other clinical *B. pseudomallei* isolates are most likely to be recovered. Consequently, the first scientist to encounter a new isolate may not recognize *B. pseudomallei* until the combination of unusual Gram stain features, an antibiotic resistance pattern, and an earthy smell suggest its identity. Recent experience indicates that this kind of exposure can even occur in a well-equipped university center laboratory, and not just in smaller hospital laboratories.\(^{49}\) The most common type of exposure is likely to be touching live cultures with ungloved hands. This is unlikely to pose a significant infection risk unless the laboratory worker has uncovered skin lesions. Aerosol generation is another theoretical risk that can be minimized by handling all such procedures in a biologic safety cabinet. Sniffing presumptive *B. pseudomallei* cultures to detect the characteristic earthy smell is common practice in disease-endemic areas, but there are no reports of melioidosis contracted as a result of this practice. Laboratory-acquired infection with *B. pseudomallei* has been
reported after exposure during a laboratory accident in which direct inoculation of live cultures is believed to have occurred. Contemporary standards of laboratory practice should prevent these types of *B. pseudomallei* exposures. Delayed recognition of *B. pseudomallei* through over-reliance on substrate use tests has been implicated as a potential laboratory safety issue. Rapid diagnostic tests have been developed to resolve this problem but are still not in widespread use outside Australia and southeast Asia.

**Biopreparedness.** Concerns about the deliberate release of biologic weapon agents by terrorist groups have stimulated interest in a small group of uncommon bacterial infections including melioidosis. The inclusion of melioidosis and glanders in Centers for Disease Control and Prevention–listed group B select agents probably relates more to their development and occasional use as biologic weapons by European nations than to any current concern about their utility as agents of bioterrorism. Although *B. pseudomallei* can survive in the inanimate environment for prolonged periods, it is not directly transmissible from human to human and therefore does not pose a serious epidemic threat. Moreover, its tendency to cause overwhelming septicemic disease in adults with underlying medical conditions is consistent with an opportunist pathogen. Uncertainty about the final means of exposure, technical difficulties producing bulk cultures and reducing them to an easily dispersed form, and the limited number of laboratories with *B. pseudomallei* in their culture collections all reduce the suitability of this agent for terrorist

**FIGURE 1.** Distribution of melioidosis in the Americas. Numbers indicates references cited in this paper.
<table>
<thead>
<tr>
<th>Year</th>
<th>Presenting complaint</th>
<th>Complications</th>
<th>Outcome</th>
<th>Culture results</th>
<th>Diagnosis</th>
<th>Identity confirmed</th>
<th>Travel</th>
<th>Exposure</th>
<th>Occupation</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1947</td>
<td>Buttock abscess</td>
<td>Sinus</td>
<td>Discharge</td>
<td><em>M. pseudomallei</em></td>
<td>USA</td>
<td>None</td>
<td>Panama</td>
<td>Fall on buttock</td>
<td>Machinist</td>
<td>32</td>
</tr>
<tr>
<td>1948</td>
<td>Retropertioneal abscess</td>
<td>Septicemia</td>
<td>Died</td>
<td><em>M. pseudomallei</em></td>
<td>USA</td>
<td>None</td>
<td>Panama</td>
<td></td>
<td>Marine Corps</td>
<td>33</td>
</tr>
<tr>
<td>1951</td>
<td>Ingual abscess</td>
<td>Sinus</td>
<td>Discharge</td>
<td><em>M. pseudomallei</em></td>
<td>USA</td>
<td>None</td>
<td>Unknown</td>
<td></td>
<td>Stockyard</td>
<td>34</td>
</tr>
<tr>
<td>1960</td>
<td>Optic and peripheral neuritis</td>
<td>CHL toxicity</td>
<td>Discharge</td>
<td><em>P. pseudomallei</em></td>
<td>USA</td>
<td>Yes</td>
<td>Unknown</td>
<td>Panama</td>
<td>Soldier</td>
<td>64</td>
</tr>
<tr>
<td>1964</td>
<td>Necrotic foot ulcer</td>
<td>Delirium</td>
<td>Died</td>
<td><em>P. pseudomallei</em></td>
<td>USA</td>
<td>Yes</td>
<td>Unknown</td>
<td>Ecuador, rice field</td>
<td>Farmer</td>
<td>31</td>
</tr>
<tr>
<td>1965–1969</td>
<td>72 cases, various</td>
<td>Unknown</td>
<td>14 died</td>
<td><em>P. pseudomallei</em></td>
<td>USA</td>
<td>62 in Vietnam</td>
<td>Unknown</td>
<td></td>
<td>Servicemen</td>
<td>65</td>
</tr>
<tr>
<td>1967</td>
<td>9 cases, pneumonitis</td>
<td></td>
<td>Survived</td>
<td><em>P. pseudomallei</em></td>
<td>USA</td>
<td>Unknown</td>
<td>Vietnam</td>
<td>Unknown, no combat wounds</td>
<td>Soldiers</td>
<td>66</td>
</tr>
<tr>
<td>1967</td>
<td>Pelvic abscess</td>
<td>Tibial tenderness</td>
<td>Survived</td>
<td><em>P. pseudomallei</em></td>
<td>USA</td>
<td>Yes, CDC</td>
<td>Vietnam, Asia</td>
<td>Motor vehicle</td>
<td>Marine veteran</td>
<td>17</td>
</tr>
<tr>
<td>1967</td>
<td>Calf abscess</td>
<td>Lung nodules</td>
<td>Discharge</td>
<td><em>P. pseudomallei</em></td>
<td>USA</td>
<td>Yes, CDC</td>
<td>Mexico</td>
<td>Soil contaminated</td>
<td>Waste disposal</td>
<td>29</td>
</tr>
<tr>
<td>1980</td>
<td>Eye socket after enucleation</td>
<td>Not recorded</td>
<td></td>
<td><em>P. pseudomallei</em></td>
<td>USA</td>
<td>Yes, CDC</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Laboratory worker</td>
<td>50</td>
</tr>
<tr>
<td>1986</td>
<td>Septicemia meningitis</td>
<td>Pneumonia</td>
<td>Died</td>
<td><em>P. pseudomallei</em></td>
<td>USA</td>
<td>None</td>
<td>Vietnam</td>
<td>Shrapnel wound</td>
<td>Marine veteran</td>
<td>68</td>
</tr>
<tr>
<td>1991</td>
<td>Burn wounds</td>
<td>Septicemia</td>
<td>Not recorded</td>
<td><em>P. pseudomallei</em></td>
<td>USA</td>
<td>Yes, CDC</td>
<td>Puerto Rico</td>
<td>Unknown</td>
<td>37</td>
<td></td>
</tr>
<tr>
<td>1995</td>
<td>Fever, cough, neck pain</td>
<td>Hilar lymph nodes</td>
<td>Died during therapy</td>
<td><em>B. pseudomallei</em></td>
<td>USA</td>
<td>Yes, CDC</td>
<td>Martinique</td>
<td>Unknown</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td>2001</td>
<td>Fever</td>
<td>Pleurral effusion</td>
<td>Survived</td>
<td><em>B. pseudomallei</em></td>
<td>USA</td>
<td>Guadeloupe</td>
<td>El Salvador</td>
<td>Unknown</td>
<td>Child</td>
<td>39</td>
</tr>
<tr>
<td>2002</td>
<td>Fever, hoarseness</td>
<td>Arterial aneurysm</td>
<td>Survived</td>
<td><em>B. pseudomallei</em></td>
<td>USA</td>
<td>Unknown</td>
<td>Borneo</td>
<td>Unknown</td>
<td>Management consultant</td>
<td>71</td>
</tr>
<tr>
<td>2003</td>
<td>Renal abscess pneumonia</td>
<td>Survived</td>
<td>B. pseudomallei</td>
<td>Portugal</td>
<td>Unknown</td>
<td>Resident in Venezuela</td>
<td>Recent heavy rainfall</td>
<td>Child of goat farmer</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>2004</td>
<td>Septicemia</td>
<td>Died</td>
<td>B. pseudomallei</td>
<td>Yes, Australia</td>
<td>Australia</td>
<td>Outbreak; children of goat farmer; others: sitting in river water, immersion in river</td>
<td>45</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2005</td>
<td>Respiratory distress septicaemia</td>
<td>Blood culture of <em>B. pseudomallei</em></td>
<td>5 deaths, 1 survivor</td>
<td>Brazil</td>
<td>Yes</td>
<td>Outbreak, recent heavy rainfall</td>
<td>45</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2005</td>
<td>Pneumonia</td>
<td>Died</td>
<td>B. pseudomallei</td>
<td>The Netherlands</td>
<td>USA</td>
<td>Yes</td>
<td>Brazil</td>
<td>Culture exposure</td>
<td>Laboratory staff, tourist</td>
<td>46</td>
</tr>
<tr>
<td>2005</td>
<td>Exposure, plus index case</td>
<td>No disease, survived</td>
<td>B. pseudomallei</td>
<td>USA</td>
<td>NA</td>
<td>Clinical laboratory Australia</td>
<td>Unknown</td>
<td>49</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* M. = Malleomyces; CHL = chloramphenicol; CDC = Centers for Disease Control and Prevention; SLE = systemic lupus erythematosus; CGD = chronic granulomatous disease; NA = not applicable.
use. Nevertheless, recent advances in laboratory biopreparedness have improved knowledge of the pathobiology of melioidosis pathogenesis. Work on the role of \textit{B. pseudomallei} capsular polysaccharide, the genetic determinants of secreted exoproducts, the genetic relatedness of \textit{B. pseudomallei} and \textit{B. mallei}, and laboratory models of melioidosis\textsuperscript{54–58} are important steps towards vaccine development. However, useful progress has been made on application of PCR protocols to \textit{B. pseudomallei} identification. Several PCR protocols have been validated for identification of \textit{B. pseudomallei} based on specific gene targets. These include a portion of the sequence between the 16S and 23S encoding sequences,\textsuperscript{50} genes encoding a type-three secretion system,\textsuperscript{60} a synonymous single nucleotide polymorphism,\textsuperscript{61} and a specific fatty acid tandem mass spectrometry.\textsuperscript{62} We recently proposed a laboratory discovery pathway that integrates preliminary diagnostic laboratory steps with PCR-based methods.\textsuperscript{63} A selection of specific genetic targets have been combined in a molecular typing system known as multilocus locus typing to give a reproducible measure of genetic relatedness between \textit{B. pseudomallei} strains.\textsuperscript{15} These molecular diagnostic and typing methods are available only in larger reference and research laboratories. Commercially available diagnostics suitable for use outside melioidosis-endemic regions are likely to take even longer to become available.

**LESSONS FROM THE AMERICAS**

The changing epidemiology of melioidosis in the Americas provides useful insight into this emerging infectious disease (Table 2). In North America, melioidosis is generally a travel-related disease affecting people who visit disease-endemic locations for pleasure, business, or military reasons.\textsuperscript{16–19,22,23,30,64–66} Sporadic cases of melioidosis in adventure travelers and military veterans will continue to puzzle physicians for the foreseeable future, and the history of potential exposure will often be established after laboratory diagnosis.\textsuperscript{20,21,46} In Latin America, melioidosis is a disease of mainly rural and remote communities and probably goes undetected most of the time.\textsuperscript{5,32,33,45,66,67} Molecular typing of clinical isolates from recent cases in northeastern Brazil does not support recent incursion and rapid spread of one strain.\textsuperscript{45} The impression that the disease may be spreading in Latin America can be explained by gradual improvement in diagnostic laboratory methods combined with increasing awareness of the disease. If melioidosis has been present in northeastern Brazil for some time, subacute disease and some septicemic cases may have been missed and smoldering subacute infections occur more widely in the region. A better grasp of the epidemiology of melioidosis in the Americas will shed more light on its regional origins, the critical exposure required to establish infection, and how \textit{B. pseudomallei} adapts to such a variety of environmental habitats. The current research focus on biosecurity will accelerate improvements in diagnosis, therapy, and prevention of this naturally occurring emergent disease.

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