

Melioidosis in Travellers

Pitfalls in Diagnosis of *Burkholderia pseudomallei* by Laboratories from Non-endemic Regions

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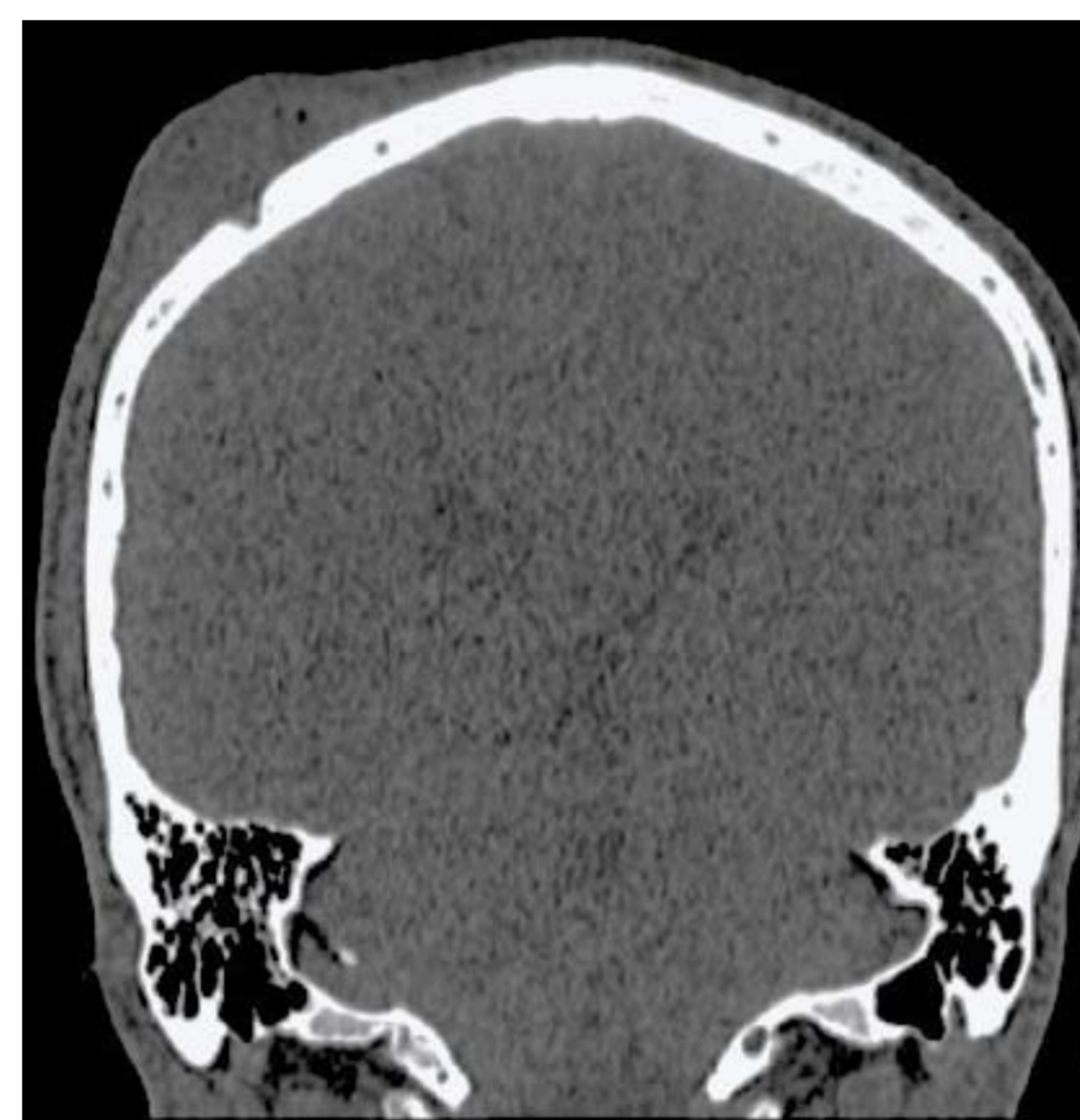
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Introduction

Burkholderia pseudomallei, the etiologic agent of melioidosis, is a saprophytic, gram-negative bacillus widely distributed in tropical soil and water, endemic to tropic regions, mainly in Southeast Asia and northern Australia (cf. Map of Melioidosis Endemicity). It can cause pyogenic or granulomatous lesions. Melioidosis occurs sporadically in travellers returning from disease-endemic areas, and physicians as well as laboratories in regions where this disease is not endemic are not familiar with its broad-ranging manifestations and the identification of *B. pseudomallei*. Laboratories should also be aware of the risks for laboratory personnel handling isolates. Two case reports of travellers with invasive melioidosis presented here illustrate these issues.

Case 1: Cranial abscess^{1/}

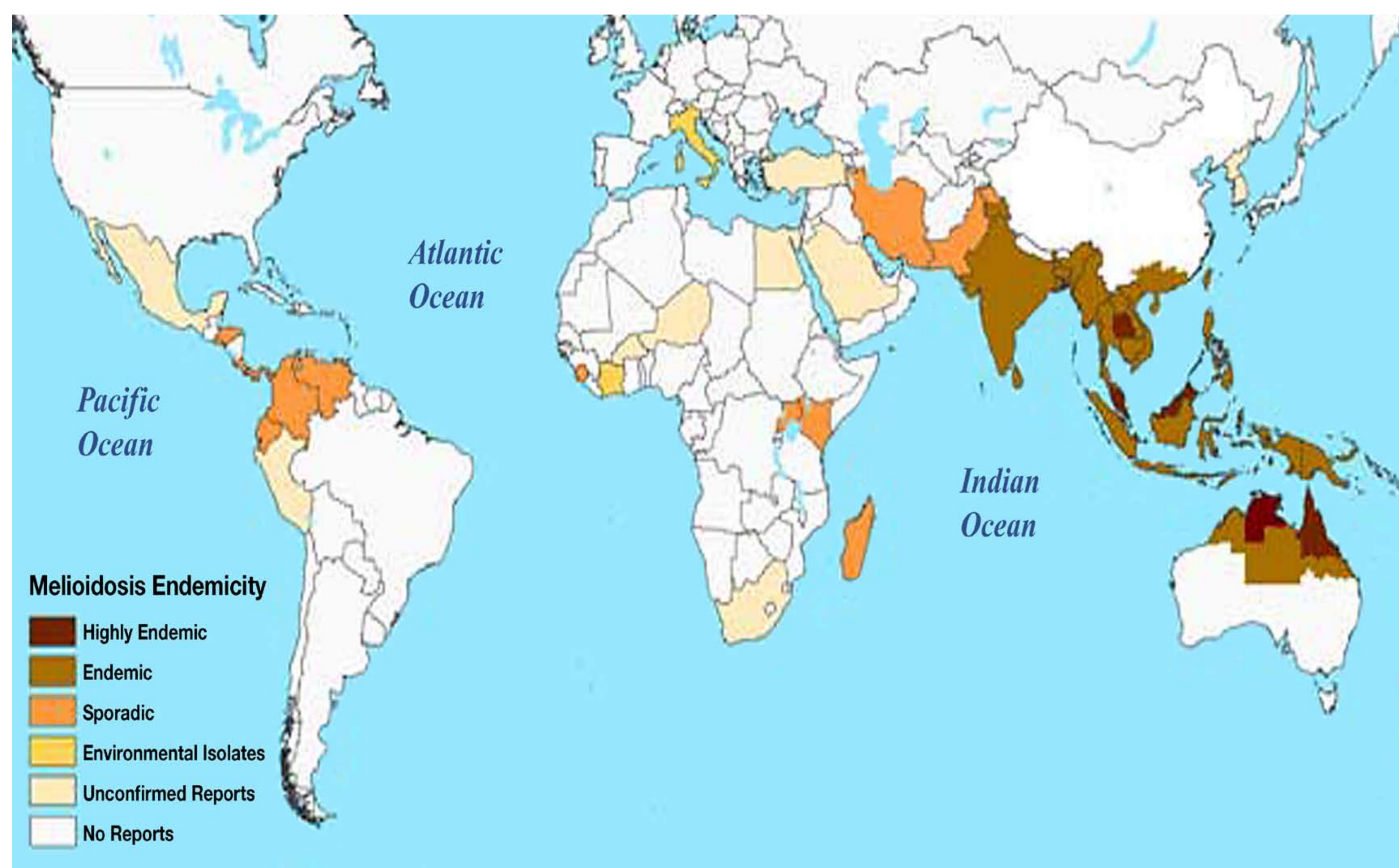
In 2008, a 35-year-old man from Switzerland developed an extradural cranial abscess of the right parietal area and a defect in adjacent bone. In the months before, he traveled to Singapore, Malaysia and Thailand, where he went trekking and river rafting. The patient did not remember receiving a head injury during his trip. Material cultured from the abscess grew a gram-negative rod, identified by Phoenix Automated Microbiology System (Becton Dickinson) as *Burkholderia cepacia*. The diagnosis was regarded as preliminary because identification of *B. cepacia* by common automated identification instruments such as the Phoenix System or VITEK 2 (bioMérieux) requires confirmatory identification. Moreover, an abscess is an uncommon location for *B. cepacia*, the bacterial colonies emitted an unusual odor, and the isolate was unexpectedly sensitive to amoxicillin-clavulanate.



Computed cranial tomography image of the patient showing a swelling at the right parietal area and a small defect of the bone.

The organism was eventually identified as *B. pseudomallei* sequence type 306, by sequence analysis of a 500-bp fragment of the 16S rRNA gene and Multilocus sequence typing. The patient was treated with imipenem, cotrimoxazole and leucovorine for 2 weeks and later with cotrimoxazole and leucovorine for 6 months. He recovered with a small indentation without signs of inflammation at the site of the abscess.

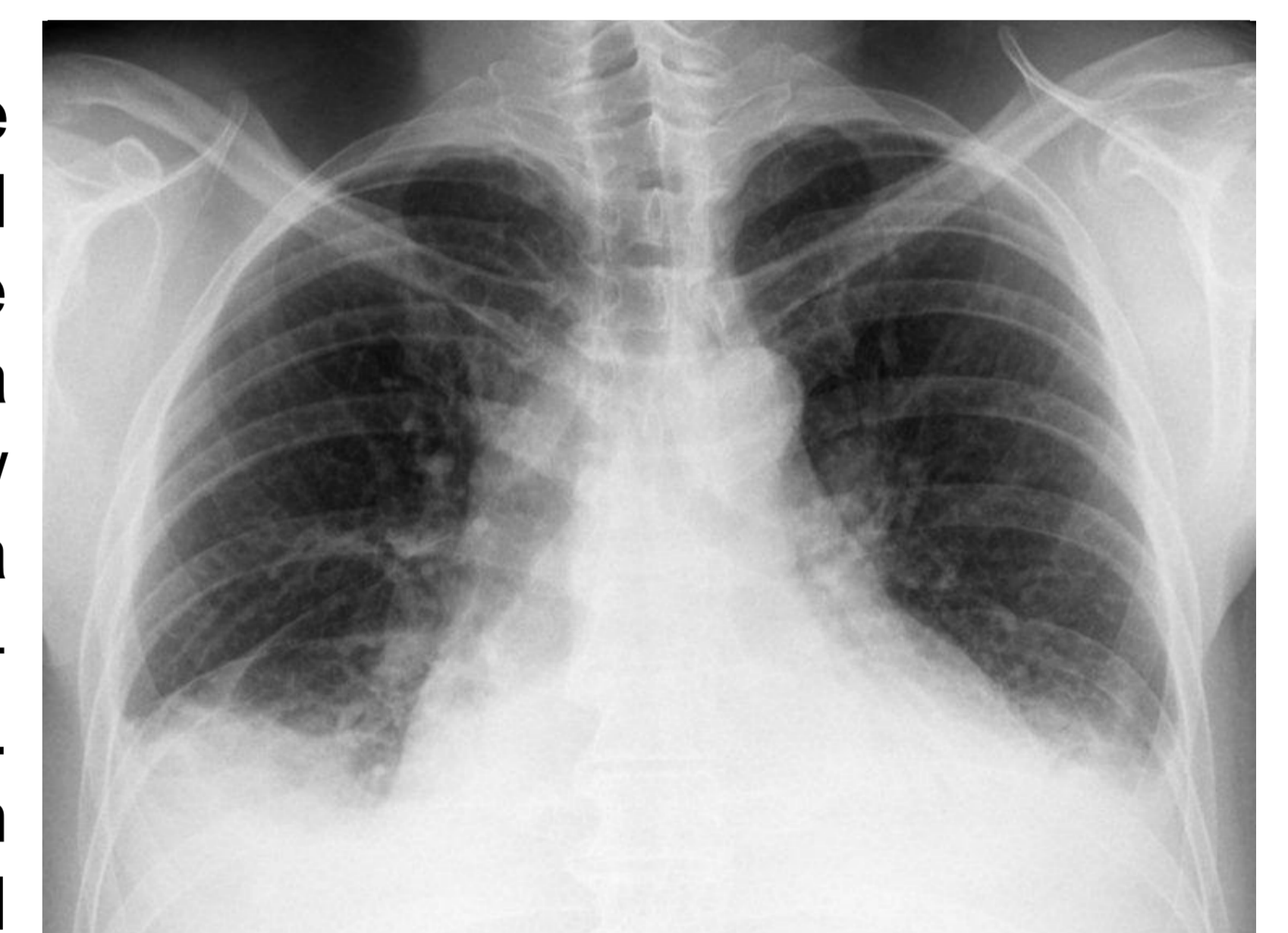
Without knowing the isolate's identity, laboratory personnel handled cultures of *B. pseudomallei* outside a BSL-3 facility for identification and drug resistance testing, smelled culture plates, but none became ill or showed signs of melioidosis.



Map of Melioidosis Endemicity: modified from Cheng AC, Currie, BJ. Melioidosis: epidemiology, pathophysiology, and management. Clin Micro-biol Rev. 2005;18:383-416.

Case 2: Pneumonia and pericardial effusion

In 2009, a 44 year-old man from Switzerland developed fever and productive cough, after returning from north-eastern Thailand, where he had stayed from December 2008 to February 2009. His general practitioner treated the fever with paracetamol. Subsequently, the patient developed dyspnea with a pulmonary infiltrate and was treated with amoxicillin-clavulanate for seven days. After initial improvement, he became febrile again and dyspnoic, and chest x-ray showed bilateral pleural effusions. At hospital admission, the patient was febrile (38.2°C), with sinus tachycardia (130 bpm) and slight icterus of skin and conjunctiva. Laboratory test results showed anaemia, neutrophil leucocytosis, abnormal liver function tests, elevated C-reactive protein (141 mg/l) and BNP B-type natriuretic peptide (208 ng/l). All test results normalized until hospital discharge, with the exception of C-reactive protein (25 mg/l). Computed tomography of the chest showed bilateral pleural effusions, atelectasis of the inferior lobes, nodular densities in the upper lobes, mediastinal lymphadenopathy and pericardial effusion. Echocardiography showed a dynamically relevant pericardial effusion, with slight diastolic impression of the right ventricle, that improved after puncture of 700 ml clear yellowish fluid. Pleural and pericardial effusion tested negative for bacteria, including mycobacteria and yeasts. Sputum samples grew normal upper respiratory tract flora and blood culture sets taken on 4 consecutive days turned out negative. A 10 ml-aliquot of pericardial effusion and of a second punctate of pleural effusion were additionally inoculated into blood culture sets. Solely the



chest x-ray with "tent shape" of the heart on day 20 of illness

aerobic bottle containing the pericardial effusion grew Gram-negative rods. They were identified as *Burkholderia cepacia* in the BD Phoenix Automated Microbiology System, but regarded as preliminary, for the same reasons as stated in Case 1. The following investigations were done in a Biosafety Level 3 facility, in order to prevent infection of the laboratory personnel. The isolate was identified as *B. pseudomallei* sequence type 207 by API 20NE and by molecular methods. Under treatment with ceftazidime i.v. for two weeks, followed by orally given doxycycline, cotrimoxazole and leucovorine for three months, the patient gradually recovered, although with long persistence of tachycardia. On day 40 of illness, CRP was still elevated and moderate pericardial effusion was visible on echocardiography, with complete recovery after four months.

Without considering travel history, the pneumonia was inadequately treated with orally given amoxicillin-clavulanate, thereby potentially reducing bacterial load in sputum samples and blood cultures, and thus unabling detection of *B. pseudomallei*. Eventually, pericardial effusion grew the causative *B. pseudomallei*, thus permitting the correct therapy of this life-threatening infection.

Conclusions

- (i) Physicians considering melioidosis in travellers returning from endemic regions should ensure appropriate sampling prior to commencement of antibiotic therapy, in order to obtain viable bacteria and thus enabling timely identification and correct therapy of *B. pseudomallei*.
- (ii) Microbiology laboratories in non-endemic regions need to be informed of the possibility of melioidosis, as those not familiar with it can misidentify *B. pseudomallei* and laboratory personnel may become infected when handling cultures outside a BSL-3 facility.
- (iii) Laboratories should be aware of misdiagnosis of isolates by automated microbiology systems that do not contain the adequate profile for identification.
- (iv) *Burkholderia spp.* should be confirmed by molecular methods or by the API 20NE system in suspected cases of *B. pseudomallei* infection.

^{1/} Weissert C, Dollenmaier D, Rafeiner P, Riehm J, Schultze D. *Burkholderia pseudomallei* Misidentified by Automated System. Emerg. Infect. Dis. Vol. 15 (11) 2009

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