



Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

“Melioidosis in Antioquia, Colombia: an emerging or endemic disease? A cases series”[☆]



F.E. Montúfar^{a,b,g,*}, J.E. Ochoa^c, H. Ortega^d, L. Franco^e, M.C. Montúfar^{f,g}, A. Monsalve^{f,g}, C. Jaramillo^{f,g}, M. Zapata^{f,g}

^a Infectious Diseases Section, Pablo Tobón Uribe Hospital, Medellín, Colombia

^b Pulmonology Unit, León XIII Clinic of Antioquia University, Medellín, Colombia

^c Epidemiology Group, National School of Public Health, Antioquia University, Medellín, Colombia

^d Internal Medicine and Pulmonology, Antioquia University, Medellín, Colombia

^e Cardiovascular Clinic, Medellín, Colombia

^f Faculty of Medicine, Pontificia Bolivariana University, Medellín, Colombia

^g Research Group in Respiratory and Infectious Diseases (GIERI), Medellín, Colombia

ARTICLE INFO

Article history:

Received 8 February 2015

Received in revised form 27 May 2015

Accepted 30 May 2015

Corresponding Editor: Eskild Petersen, Aarhus, Denmark

Keywords:

Melioidosis

Sepsis

Pneumonia

Burkholderia pseudomallei

SUMMARY

Background: Melioidosis is endemic in Malaysia, the southwest of Thailand, and northern Australia. The incidence in Thailand is 4.4/1 000 000 inhabitants, where it causes 19% of community-acquired pneumonia (CAP) and 20% of bacteremic pneumonia, and the mortality is 50%. Sporadic cases have been described in Central and South America. The objective of this study was to describe the clinical and epidemiological features and ecological characteristics of melioidosis in Antioquia, Colombia.

Methods: This is a case series description.

Results: Seven cases were identified. *Burkholderia pseudomallei* was isolated from peripheral blood, pleural fluid, and urine and was identified by the automated system VITEK 2 (bioMérieux) and API 20NE biochemical kit. Five of the cases had a bacteremic form with shock and pulmonary compromise and two of these patients died. The non-bacteremic melioidosis cases had genitourinary, abdominal, and osteoarticular compromise. All patients had comorbidities and lived in rural hot and humid areas in the west central region of Colombia (Antioquia). Diabetes mellitus, renal insufficiency, and other chronic diseases are important risk factors for the development of severe forms.

Conclusions: The cases presented here are similar to those occurring in endemic areas regarding comorbidity, risk factors, clinical presentation, and environmental conditions. It is necessary to establish whether melioidosis is an endemic and under-diagnosed disease or an emerging disease in Colombia.

© 2015 The Authors. Published by Elsevier Ltd on behalf of International Society for Infectious Diseases. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

Melioidosis is a disease caused by *Burkholderia pseudomallei*, an intracellular facultative Gram-negative saprophytic bacterium,¹ distributed widely in the environment.² Melioidosis is endemic in Malaysia, southwest Thailand, northern Australia,^{1,3–7} Singapore, Vietnam, Cambodia, and Laos.^{7,8} Australia and northeast Thailand represent hot spots, with annual incidence rates of up to 50 cases

per 100 000 people.^{9–11} The incidence in Thailand is 4.4/1 000 000 inhabitants, where it causes 19% of community-acquired pneumonia (CAP) and 20% of bacteremic pneumonia, and the mortality is 50%.^{3,4,11} Melioidosis is the third most common cause of death from infectious disease in northeast Thailand, exceeded only by HIV infection and tuberculosis.^{10,11} In northern Australia, it is the most common cause of bacteremic CAP.^{4,5}

In Central and South America, sporadic cases have been described in Colombia, Panama, Ecuador, and Brazil.^{12–18} In Colombia, there have been only two published cases of non-bacteremic melioidosis.^{13,14}

In endemic areas, the peak incidence is between 40 and 60 years¹⁹ and epidemics are associated with the winter or rainy season. *B. pseudomallei* is usually found in shallow waters and in damp soil between 25 and 45 cm deep.⁵ It has been proposed that the bacteria surface when humidity is high.^{3–5,7–11}

[☆] Dr Montúfar is a specialist in internal medicine, pulmonology, epidemiology and infectious diseases. He is now coordinator of the stewardship program at Pablo Tobón Uribe Hospital, chief of the pulmonology unit at León XIII Clinic of Antioquia University, and coordinator of the community-acquired pneumonia guidelines in Colombia, published in *Infectio* in 2013.

* Corresponding author. Tel.: +57 4 3385563.

E-mail address: firmontufar@yahoo.com (F.E. Montúfar).

The infection can be acquired by inhalation, percutaneous inoculation, or ingestion.^{1,3,5,7,8,15} Pulmonary involvement is very important, and hematogenous spread leads to the involvement of other organs.^{1,3–6,16} The inhalation of contaminated aerosols is important in endemic areas, and it is considered a risk factor for fatal pulmonary compromise. Less common cases occur by inhalation/ingestion of contaminated water and following almost-drowning episodes.

The incubation period is related to the route of infection, the inoculum size, microorganism virulence, and host factors. In inhalation and almost-drowning cases the infection appears in less than 24 h, and in percutaneous infection cases the incubation period varies from 1 to 21 days, with an average of 9 days.^{4–6,16,20}

The infection can be asymptomatic or present as an acute and severe disease, especially in bacteremic forms with pulmonary involvement in patients with comorbidities such as diabetes mellitus, renal failure, alcoholism, structural pulmonary disease, thalassemia, cancer, immunosuppression, and granulomatous disease.^{1,3–6,8,15,11,21,22} Melioidosis may present relapses after successful treatment and a sub-clinical infection period, of variable length.

A group of Australian researchers⁵ has classified the infection into bacteremic forms (with the absence or presence of shock) and non-bacteremic forms. Each form may appear with pulmonary, genitourinary, neurological, nodal, soft tissue, and osteoarticular manifestations.^{1,4–7,12,20} The group of Howe et al. has classified the infection into acute (sudden, with septic shock and suppurative localized pneumonia), sub-acute, chronic, and sub-clinical forms.¹⁶

The diagnosis requires a high clinical and epidemiological suspicion, combined with a good microbiological identification system such as microscopy and cultures complemented by biochemical tests or latex agglutination. Serology is neither specific nor sensitive, and at present molecular diagnostics are mainly the domain of reference laboratories.^{15,23–28} Imaging is also valuable to support the diagnosis.^{29,30}

The treatment of melioidosis consists of an initial phase of 14 days of ceftazidime or carbapenems, followed by oral eradication therapy, usually with trimethoprim–sulfamethoxazole with or without tetracyclines for 3 to 6 months.^{24–31}

A series of cases occurring in Antioquia, Colombia, which has geographic regions and weather similar to those of endemic areas, is presented below.

2. Case series

Seven cases were identified in three high-complexity hospitals and reference centers in Medellín, Antioquia, Colombia: Pablo Tobón Uribe Hospital (HPTU), Leon XIII Clinic of Antioquia University, and San Vicente de Paul Hospital (HUSVP); these cases occurred between January 1998 and December 2013. Clinical–epidemiological characteristics are shown in Table 1, laboratory findings are given in Table 2, and radiographic and computed tomography (CT) manifestations are shown in Figure 1. The ecological characteristics and geographic location of the cases are shown in Figure 2 and Table 3.

B. pseudomallei was isolated from peripheral blood, pleural fluid, and urine. Samples were processed in the automated system VITEK 2 (bioMérieux) and with the commercial API 20NE or 20E biochemical kit with a simple screening system. The ID card for Gram-negative bacilli for the VITEK 2 system is a 64-well plastic card containing 41 fluorescent biochemical tests, including 18 enzymatic tests for aminopeptidases and oxidases. The VITEK 2 GN cards were set up as per the manufacturer's instructions using reagents and equipment supplied by bioMérieux. Briefly, individual colonies from a 24-h subculture on MacConkey agar were selected and transferred to a polystyrene test tube containing

3.0 ml of sterile saline (aqueous, 0.45% to 0.05% NaCl, pH 4.5 to 7.0). Tubes were mixed to produce a homogeneous organism suspension and the density was adjusted to be equivalent to a McFarland number of 0.50 to 0.63 using a calibrated VITEK 2 Densicheck. All inoculated cards were placed in the instrument within 30 min of inoculation. Data were analyzed using software version VT2 4.01–7.01.

Four quality control strains (*Escherichia coli* ATCC 25922, *Klebsiella pneumoniae* ATCC 700603, *Pseudomonas aeruginosa* ATCC 27853, *E. coli* ATCC 32218, *Enterobacter hormaechei* ATCC 700323, *Stenotrophomonas maltophilia* ATCC 17666) were loaded with each study batch. All quality control strains had to be identified correctly in order to allow ID of the test strains. In this study, the system produced a result listed as 'very good' (93% to 95% probability) or 'excellent' (96% to 99% probability) for the identification of *B. pseudomallei*.

The main features of identification were the following: Gram-negative rods with bipolar staining, oxidase-positive; rough, wrinkled, and pink colonies on MacConkey agar; oxidative utilization of glucose, lactose, and maltose; lysine decarboxylase-negative; arginine dihydrolase-positive; reduction of nitrates; resistance to gentamicin and polymyxin B and susceptibility to ceftazidime, trimethoprim–sulfamethoxazole, carbapenems, tetracycline, and amoxicillin–clavulanic acid.

Other diagnostic methods, such as the latex agglutination test and molecular biology tests, are not available in Colombia.

In the series presented, five patients had a bacteremic form with shock and pulmonary compromise and two of them died. Two patients had non-bacteremic melioidosis with genitourinary, abdominal, and osteoarticular compromise. All patients had comorbidities and lived in rural hot and humid areas in the west central region of Colombia (Antioquia). Diabetes mellitus, chronic renal failure (CRF), chronic obstructive pulmonary disease (COPD), and other chronic diseases are important risk factors for the development of severe forms of melioidosis.

2.1. Patient 1

Patient 1 was a 10-year-old female school student, living in the rural Puerto Berrío, a hot and humid area. She had been deteriorating progressively over a 4-month period and had symmetric arthritis in the elbows, knees, and ankles as a result of connective tissue disease (CTD). A week before her admission to HUSVP, she presented jaundice, fever, abdominal pain, hematemesis, and exanthema. On admission, she was pale and jaundiced, with hypotension, tachycardia, and tachypnea. Since disseminated vesicles and petechiae were seen, meningococemia was diagnosed, and she was transferred to the intensive care unit (ICU). She presented progressive impairment with respiratory failure, severe hypoxemia (arterial oxygen saturation (SaO₂) of 54%), hemoptysis, and multiorgan dysfunction, and required mechanical ventilation and cardiovascular support. Chest X-rays showed multilobar pneumonia. She died 12 h after her admission. A postmortem diagnosis was established by means of blood cultures.

2.2. Patient 2

Patient 2 was 40-year-old male farmer, living in rural Cañasgordas, a hot and humid area; he had a history of diabetes mellitus. The patient complained of dyspnea and initially attended the local hospital where he received treatment for the presumed diagnosis of asthmatic crisis. He was then transferred to HUSVP due to a lack of response.

On admission, the patient was jaundiced, febrile, had tachycardia, and was experiencing respiratory difficulty, with bilateral

Table 1
Clinical and epidemiological characteristics

Features	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Sex	Female	Male	Female	Male	Male	Male	Male
Age, years	10	40	46	52	65	60	31
Area of origin	Rural	Rural	Rural	Urban	Rural	Rural	Urban
Date attended	May 2003	July 2003	October 2004	April 2005	August 1998	August 1998	November 2012
Occupation	Student	Farmer	House wife	Driver	Farmer	Farmer	Prisoner
Previous disease	CTD	DM	CRF	DM, HTA, UI	COPD	DM	HIV
Duration of symptoms	4 months	2 days	2 months	3 months	4 months	1 month	8 months
Month and year of diagnosis	May 2003	July 2003	October 2004	April 2005	April 2005	April 1998	November 2012
Season	Winter and rainfall season	Summer season with rainfall	Winter and rainfall season	Winter and rainfall season	Winter and rainfall season	Winter and rainfall season	Winter and rainfall season
Main symptoms							
Fever >38 °C	+	+	–	+	+	+	+
Cough	+	+	+	–	–	+	+
Hemoptysis	+	+	–	–	–	–	–
Dyspnea	+	+	+	–	–	–	+
Vomiting	+	–	–	–	+	–	–
Jaundice	+	+	–	–	–	–	–
Epistaxis	+	+	–	–	–	–	–
SST	+	–	–	–	–	+	+
Type of compromise and organs and systems affected							
	Cons Sx Syst Sx Pulmonary GUT SST HC Liver	Syst Sx CV GUT OA Liver	Cons Sx Syst Sx Pulmonary CV Liver Neurological OA Renal	Syst Sx OA Neurological ASV	Cons Sx Syst Sx GUT HC Liver Spleen Prostate GIT	Cons Sx Syst Sx Pulmonary SST OA Spleen	Cons Sx Syst Sx Pulmonary GUT GIT SST Liver Spleen
Physical examination							
Heart rate/min	130	136	100	110	88	100	107
Breathing rate/min	45	32	42	20	16	18	26
Blood pressure, mmHg	99/44	110/70	130/50	140/65	130/70	120/80	128/73
ICU and MV requirement	yes	yes	yes	No	No	No	No
Hospital outcome	Died	Died	Survived	Survived	Survived	Survived	Survived
Australian classification	Bacteremic with shock and pulmonary compromise	Bacteremic with shock and pulmonary compromise	Bacteremic with shock and pulmonary, renal, and OA compromise	Non-bacteremic with GUT and OA compromise	Non-bacteremic with GUT and splenic compromise	Bacteremic with pulmonary, renal, and splenic compromise	Bacteremic with pulmonary, renal, and splenic compromise
Howe classification	Acute, sudden, with shock	Acute, sudden, with shock	Acute with pneumonia	Chronic	Chronic	Acute with pneumonia	Chronic

ASV, abscesses seminal vesicles; Cons Sx, constitutional symptoms (fatigue, weakness and weight loss); COPD, chronic obstructive pulmonary disease; CRF, chronic renal failure; CTD, connective tissue disease; CV, cardiovascular (tachycardia, hypertension and shock); DM, diabetes mellitus; GIT, gastrointestinal tract; GUT, genitourinary tract; HC, hematological compromise; HIV, human immunodeficiency virus; HTA, arterial hypertension; MV, mechanical ventilation ; OA, osteoarticular; SST, skin and soft tissue; Syst Sx, systemic symptoms (fever and chills); ICU, intensive care unit; UI, urinary infection.

Table 2
Laboratory results

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Glucose, mg/dl	82.0	611.0	108	132	106	253	117
Potassium, mg/dl	2.6	3.10	5.6	3.5	4.9	4.8	4.39
Sodium, mg/dl	136.0	147	143	142	128	145	133
Blood urea nitrogen	41.0	118.0	NA	NA	14	12.3	17.17
Creatinine, mg/dl	0.10	7.2	15.4	1.7	1.19	1.09	1.7
Total bilirubin, mg/dl	3.90	3.7	NA	0.32	0.17	0.84	NA
Direct bilirubin, mg/dl	2.50	2.8	NA	0.06	0.06	0.47	NA
AST, U/l	721	274	NA	48	26.4	81	NA
ALT, U/l	130	117	NA	44	40	75	NA
Hb, g%	4.6	11.5	7.7	11.4	9.6	9.5	8.5
Hematocrit	13.5	33.9	23.2	33.3	30	31	NA
WBC $\times 10^9/l$	24	4.8	11.6	13.3	11.7	12.6	11.28
Neutrophils, %	87.8	90.0	80.0	83.5	74	83	85.9
Platelets, $\times 10^9/l$	6	18	91	168	410	158	228
Prothrombin time, s	NDC	10.2	11.8	11.3	13	12.3	10.5
SaO ₂	54%	NA	70%	NA	NA	NA	99%
Culture sample	Blood	Blood	Blood	Urine	Urine	Blood Pleura	Urine Blood
Hospital outcome	Decease	Decease	Alive	Alive	Alive	Alive	Alive

ALT, alanine aminotransferase; AST, aspartate aminotransferase; Hb, hemoglobin; NA, data not available; NDC, no detection of coagulum; SaO₂, arterial oxygen saturation; WBC, white blood cell count.

crackles on auscultation. Leptospirosis was considered and treatment was started with supportive measures and intravenous crystalline penicillin. Because of hemodynamic compromise and respiratory failure, he was transferred to the ICU where mechanical ventilation and cardiovascular support were initiated. Chest X-rays showed mixed infiltrates in both pulmonary fields, with large compromise of the upper right lobe. The patient died. A postmortem diagnosis was established by blood cultures.

2.3. Patient 3

Patient 3 was a previously healthy 46-year-old female housewife, living in the rural area of Zaragoza, also a hot and humid area. She presented a 2-month evolution of general malaise, weight loss, asthenia, fever, non-productive cough, and back pain. She received symptomatic treatment at the local hospital and then later returned due to alterations in consciousness. She was then transferred to HUSVP. On admission she presented alterations in consciousness, mucocutaneous paleness, hypoperfusion, hypotension, tachycardia, respiratory failure with scattered ronchi, and SaO₂ of 70%. Laboratory tests showed anemia and kidney failure. A diagnosis of acute renal failure, acute respiratory failure, and sepsis was made and she was transferred to the ICU. Mechanical ventilation and cardiovascular support were given and hemodialysis was performed. She was started on meropenem. A chest X-ray showed a bilateral alveolar infiltrate mostly in the right lung field. She recovered, but 10 days later the fever reappeared; blood cultures had yielded *B. pseudomallei* and so meropenem was reinstated for 2 weeks and then oral trimethoprim–sulfamethoxazole was given to complete 20 weeks. The patient was followed up and made a complete recovery.

2.4. Patient 4

Patient 4 was a 52-year-old male driver, living in the urban area of Puerto Berrío, who had a history of hypertension, diabetes mellitus, and recurrent urinary tract infection. He was seen at HUSVP because of fever, general uneasiness, chills, myalgia, arthralgia in the right foot and ankles, and fetid urine during the last 3 days. Six hours later, he experienced repeated episodes of anxiety, dizziness, syncope, and alterations in consciousness and was transferred to the ICU. Laboratory findings showed pyuria and hematuria, and urine culture grew 5000 CFU/ml of Gram-negative

bacilli. An abdominal CT showed pyelonephritis and lesions in the seminal vesicle. The patient received empiric therapy with ceftriaxone and doxycycline. He developed arthritis and tenosynovitis in the right ankle. Magnetic resonance imaging demonstrated osteomyelitis and tibiotalar arthritis. A new urine culture yielded *B. pseudomallei*.

The diagnosis was non-bacteremic melioidosis, with urinary and osteoarticular compromise. He received treatment with intravenous ceftazidime and oral trimethoprim–sulfamethoxazole for 2 weeks, with a satisfactory clinical evolution, and made a complete recovery. Oral trimethoprim–sulfamethoxazole was administered to complete 20 weeks.

2.5. Patient 5

Patient 5 was a 65-year-old male farmer, living in the rural area of Liborina, who had a history of smoking and COPD. He was seen at HPTU because of 4 months of fever, general uneasiness, chills, myalgia, nausea and vomiting, and weight loss of 20 kg, and in the most recent 2 weeks he had produced fetid urine and had dysuria and oliguria. Fever, tachycardia, pallor, and abdominal pain were documented on hospital admission. Laboratory findings showed pyuria, hematuria, and bacteria in the urinary sediment. A chest X-ray was normal and an abdominal CT scan showed splenic and prostatic abscesses. Transrectal prostate ultrasonography confirmed multiple abscesses. The patient received empiric treatment with norfloxacin. Urine culture yielded *B. pseudomallei* and blood cultures were negative. The patient underwent a splenectomy. The diagnosis was non-bacteremic melioidosis, with urinary and splenic compromise. He received treatment with endovenous ceftazidime and oral trimethoprim–sulfamethoxazole for 4 weeks and then oral doxycycline plus trimethoprim–sulfamethoxazole for 3 months. The patient had a satisfactory clinical evolution and made a complete recovery.

2.6. Patient 6

Patient 6 was a 60-year-old male farmer, living in the rural area of San Jerónimo, which is hot and dry-humid. He had been diagnosed with diabetes 10 years previously. He presented with a 1-month evolution of general uneasiness, weight loss, asthenia, fever, and a non-productive cough. During the last week, he had experienced chest pain, skin lesions, soft tissue rib cage pain, and

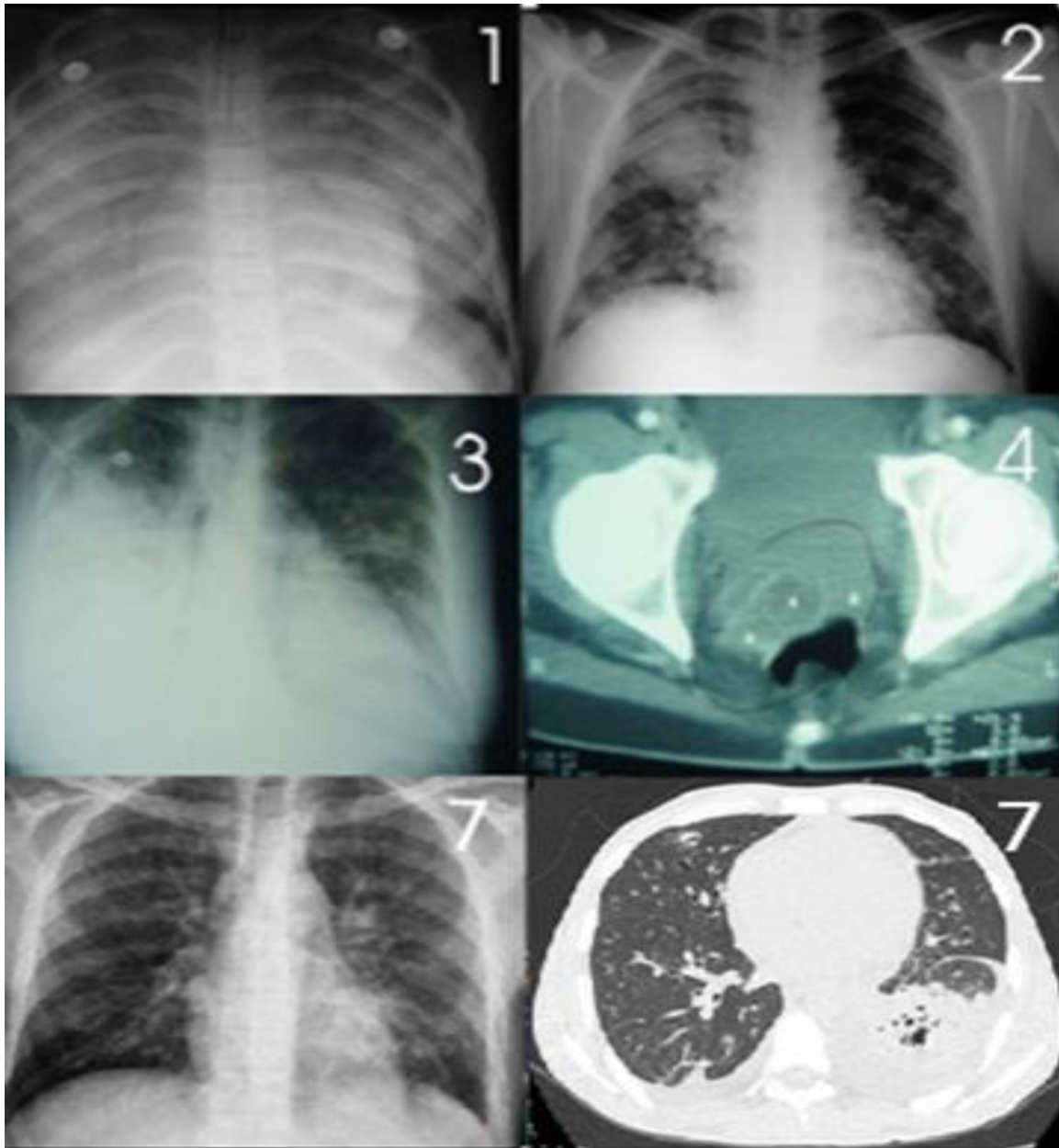


Figure 1. Radiographic and computed tomography (CT) characteristics. (1) Female patient with extended bilateral consolidation (aerial bronchogram; acute respiratory distress syndrome). (2) Male patient with mixed infiltrates in both fields, with a well-defined area of consolidation in the upper right lobe. (3) Female patient with bilateral infiltrates of alveolar occupation in the lower lobes and with larger extension in the right lobe. (4) Male patient with compromise of the urinary tract. The CT shows pyelonephritis and lesions in the seminal vesicles; prostate lesions were not documented. (7) Male patient: X-ray of the thorax shows a diffuse interstitial infiltrate and the thoraco-abdominal CT scan shows necrotizing pneumonia and multiple intra-abdominal collections, such as splenic and hepatic abscesses.

urinary symptoms. On admission to HPTU he had fever, mucocutaneous paleness, tachycardia, skin lesions and soft tissue rib cage lesions, and basal pulmonary rales. Laboratory tests showed anemia and hyperglycemia. A chest X-ray showed a bilateral alveolar infiltrate mostly on the right lung field plus pleural effusion. An abdominal CT scan showed multiple splenic abscesses. The patient received empirical treatment with oxacillin, gentamicin, and ciprofloxacin. After studying the pleural fluid, a diagnosis of empyema was made. The patient presented hemothorax post puncture and required a thoracotomy. The patient underwent splenectomy for splenic abscess. Pleural fluid cultures and blood cultures were positive for *B. pseudomallei*. The diagnosis of bacteremic melioidosis was made. Intravenous imipenem and trimethoprim–sulfamethoxazole were started for

4 weeks, followed by oral trimethoprim–sulfamethoxazole, doxycycline, and chloramphenicol in order to complete 3 months. At the follow-up, the patient had recovered completely.

2.7. Patient 7

Patient 7 was a 31-year-old male prisoner in Bella-Vista Jail, Bello-Antioquia, which has a temperature determined by thermal floors; however, he had been in Puerto Berrío 1 year ago. He had been diagnosed with HIV 27 months previously. He presented an 8-month clinical evolution of self-limited episodes of diarrhea, without mucus or abdominal pain; he also presented violet lesions on the skin. Two months previously, the symptoms had been accompanied by general uneasiness, non-quantified weight loss,

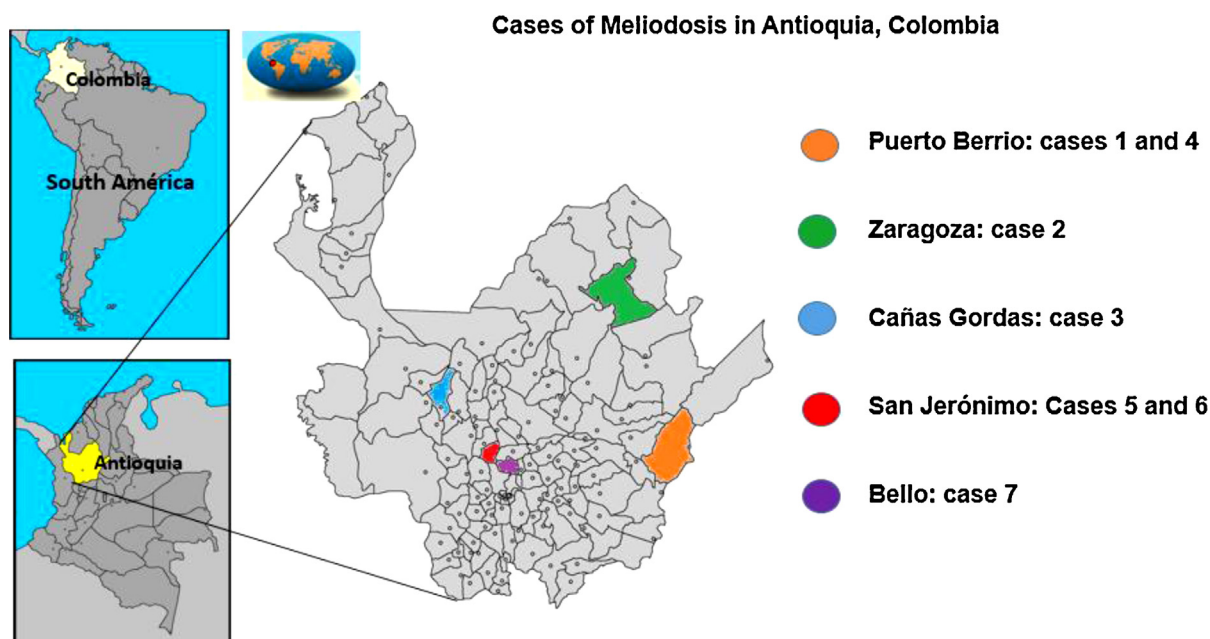


Figure 2. Geographic location of the cases. Colombia is located in the northwest of South America, between 12°26'46" north latitude (Punta Gallinas – Guajira Peninsula) and 4°12'30" south latitude (Amazon River), over the equinoctial line in the Torrid Zone. Colombia is bordered by the Caribbean Sea to the north and the Pacific Ocean to the west. It borders Panama to the northwest, Venezuela and Brazil to the east, and Ecuador and Peru to the south. As a tropical country, Colombia has only two seasons: winter and summer. Intense rainfall can occur in both of these seasons. The Department of Antioquia is situated in Colombia between 8°55'22" north latitude (Punta Arboletes) and the 5°25'30" south latitude (Cerro Caramanta). The climate of Antioquia is diverse, and is hot at sea level in Urabá up to the moor at a maximum altitude of 4080 m above sea level in Páramo de Sabana or Frontino. Antioquia has extended wild and mountainous zones.

asthenia, episodes of fever, nocturnal diaphoresis, dyspnea, and an intensified productive cough. On admission to the Leon XIII Clinic of Antioquia University, a chest X-ray showed a diffuse interstitial infiltrate and consolidation compatible with pneumonia. The patient received therapy with piperacillin–tazobactam, trimethoprim–sulfamethoxazole, and clarithromycin. An incidental finding revealed a urine culture positive for *B. pseudomallei*, therefore it was decided to change the therapy to ceftazidime. Two blood cultures were positive for *B. pseudomallei*. A thoraco-abdominal CT scan showed necrotizing pneumonia and multiple intra-abdominal collections, such as splenic and hepatic abscesses, all of them caused by the same microorganism. Ceftazidime was prescribed for 2 weeks, followed by oral trimethoprim–sulfamethoxazole plus doxycycline, with a good outcome. In the first approach, no opportunistic infections were documented. Subsequently the patient developed a febrile syndrome and new investigations for opportunistic infections were performed. An immune reconstitution syndrome (IRIS) was established as the cause of the febrile

episode. Prednisolone and trimethoprim–sulfamethoxazole plus doxycycline were initiated and the patient was discharged to home. Fifteen days later the patient returned to the hospital because of herpes-like perianal ulcers, which were treated with aciclovir. The patient was tested again for tuberculosis and this infection was documented by a positive bronchoalveolar lavage for *Mycobacterium spp.* The patient was sent home with a tuberculosis scheme plus treatment for melioidosis. The patient made satisfactory clinical progress.

3. Discussion

Few cases of melioidosis have been reported in Latin America.¹² Two cases presenting in the USA were thought to have been acquired in Honduras.^{18,32} Two cases have also been reported from Puerto Rico: severe melioidosis in a patient with chronic granulomatous disease and a case of the disorder described in a patient with diabetes.¹⁸ Some cases have been reported from

Table 3
Ecological characteristics and geographic location

Municipality (Case(s))	Latitude	Average temperature, °C	Month and year of diagnosis	Season ^a	Altitude, ^b m
Puerto Berrio (Cases 1 and 4)	6°29'26"N	29	May 2003 April 2005	Winter and rainfall season	125
Zaragoza (Case 2)	7°29'23"N	36	July 2003	Summer season with rainfall	50
Cañasgordas (Case 3)	6°44'59"N	21	October 2004	Winter and rainfall season	1320
San Jerónimo (Cases 5 and 6)	6°26'30"N	25	April 2005 April 1998	Winter and rainfall season	750
Bello (Case 7)	6°19'55"N	26.7	November 2012	Winter and rainfall season	1250

^a As a tropical country, Colombia has only two seasons: winter and summer. Intense rainfall can occur in both seasons. By location, Colombia is at the equatorial and inter-tropical convergence point and is influenced by the winds from the northern and southern Caribbean, the Pacific, and the great Amazon plain. The altitude of Antioquia allows vapors and moisture from the two oceans to concentrate, forming cloud masses that keep the average annual rainfall at around 2500 mm.³⁷

^b Meters above sea level.

Ecuador, Guadeloupe, and Aruba. Although there have not been many cases in the Americas per se, there has been an increase in the number of cases in Brazil. Brilhante et al. described 13 cases of melioidosis in Ceará, Brazil.³³ Only one case has been reported in Argentina.³⁴ A few cases have been reported in Colombia, including two cases of non-bacteremic melioidosis.^{12–14}

B. pseudomallei has become the most frequent etiology of CAP in endemic regions such as northern Australia. Likewise pneumonia with or without bacteremia is the most common clinical presentation of the disease and represents more than half of the cases.^{8,15,35} Bacteremic spread can result in clinical manifestations involving virtually any site. Overall, around half of patients are bacteremic and up to a quarter can present with septic shock.¹¹ The remaining patients present non-bacteremic clinical forms. Pneumonia is the most common clinical presentation of melioidosis in all studies.^{11,15,35,36} Bone and joint infections are uncommon and may be difficult to differentiate from other causes of infection; surgical drainage is often required, together with long courses of intravenous antibiotics.^{8,15,25,35} In the Darwin Prospective Study, 540 cases of culture-confirmed melioidosis were followed prospectively in northern Australia over 20 years; 28% of patients without bacteremia presented with skin ulcers or abscesses.¹⁰ Genitourinary melioidosis presents with fever in association with suprapubic pain, dysuria, difficulty passing urine, or acute urinary retention requiring catheterization. A tender, boggy prostate may be found on rectal examination. Abscesses in the internal organs are well recognized, especially in the spleen, kidney, prostate, and liver. Fevers, chills, and rigors with and without hypotension are common, but localizing symptoms are often absent.⁵

In this report, the cases of seven patients with melioidosis are described; five were men, the average age of all patients was 43.4 years and five of them lived in rural areas of Antioquia. These patients presented different comorbidities: diabetes mellitus ($n = 3$), COPD ($n = 1$), CRF ($n = 1$), CTD ($n = 1$), and HIV ($n = 1$). Five patients had bacteremic melioidosis, three of whom had the bacteremic form with shock and pulmonary compromise; two patients had the non-bacteremic form with genitourinary, abdominal, and osteoarticular compromise. Two patients died. The sociodemographic and epidemiological features were similar to those of cases reported in Brazil, where this pathology has been considered an emerging disease since 2003, with 13 cases reported up to 2011.³³

All of the patients in the present series had co-morbidities. Diabetes mellitus, CRF, COPD, HIV, and other chronic diseases are important risk factors for the development of severe forms of melioidosis, as was identified in this study. All of the case patients lived in rural hot and humid areas in the west central region of Colombia (Antioquia). In six cases, the disease occurred in the winter season in conditions of intense rainfall; one case occurred during the summer season but during a period of rainfall.³⁷

There are some reported risk factors for melioidosis. Between 37% and 60% of patients with the disease have been found to be diabetic, mainly type 2. All series reported from Australia, Thailand, Malaysia, and Singapore have demonstrated a male preponderance. It has been established that renal impairment or renal failure is also associated with an increased risk of melioidosis.⁴

The present series showed the occurrence of the bacteremic form of melioidosis with pulmonary, urinary, and splenic involvement in a patient with an HIV infection. This situation has not been described previously, and highlights the fact that this type of immunosuppression can also promote the presentation of widespread and severe forms.

Melioidosis in Antioquia, Colombia is similar to descriptions of the disease from endemic areas regarding comorbidities, risk factors, clinical presentation, and environmental conditions.

The detection of these cases in areas where the disease is possible indicates the need to establish whether melioidosis is an endemic and under-diagnosed disease or an emerging disease in Colombia. A prospective study is required, with the implementation of other diagnostic methods such as serological tests, the latex agglutination test, or molecular biology tests in our institutions, to determine their true prevalence and incidence of this disease.

Acknowledgements

We are grateful to our colleagues at Pablo Tobón Uribe Hospital (HPTU), Leon XIII Clinic of Antioquia University, and San Vicente de Paúl Hospital (HUSVP) in Medellín, Colombia. Special thanks to the members of the research group in respiratory and infectious diseases who participated in some stages of the study.

Ethical approval: The development of this research met medical and ethical principles (respect for persons, beneficence, and justice), always protecting the privacy of the subjects involved. Its development was subject to the approval of the research ethics committee and Article 11 of Resolution 008430 (1993) of the Ministry of Health; as such, signed consent was not required.

Conflict of interest: The authors declare that they have no conflicts of interest and received no money from any institution. The research group offered all the logistical support needed to carry out data collection, statistical analysis, and preparation of the research paper.

References

- White NJ. Melioidosis. *Lancet* 2003;**361**:1715–22.
- Dance DA. Ecology of *Burkholderia pseudomallei* and the interactions between environmental *Burkholderia* spp. and human-animal hosts. *Acta Trop* 2000;**74**:159.
- Chaowagul W, White NJ, Dance DA, Wattanagoon Y, Naigowit P, Davis TME, et al. Melioidosis: a major cause of community-acquired septicemia in north-eastern Thailand. *J Infect Dis* 1989;**159**:890–9.
- Suputtamongkol Y, Chaowagul P, Lertpatanauwun N, Intaranongpai S, Ruchutrakool T, Budhsarawong D, et al. Risk factors for melioidosis and bacteremic melioidosis. *Clin Infect Dis* 1999;**29**:408–13.
- Currie BJ, Fisher DA, Howard DM, Burrow JN, Lo D, Selva-nayagam S, et al. Endemic melioidosis in tropical northern Australia: a 10-year prospective study and review of the literature. *Clin Infect Dis* 2000;**31**:981–6.
- Gilligan PH, Lum G, Vandamme PA, Whittier S. *Burkholderia*, *Stenotrophomonas*, *Ralstonia*, *Brevundimonas*, *Comamonas*, *Delftia*, *Pandoraea*, and *Acidovorax*. In: Murray P, Baron EJ, Jorgensen JH, Pfaller MA, Tenover FC, Tenover FC, editors. *Manual of clinical microbiology*. 8th ed., Washington DC: American Society of Microbiology; 2003. p. 729–74.
- Dance DA. Melioidosis: the tip of the iceberg? *Clin Microbiol Rev* 1991;**4**:52–60.
- Cheng AC, Currie BJ. Melioidosis: epidemiology, pathophysiology, and management. *Clin Microbiol Rev* 2005;**18**:383–416 [Erratum, *Clin Microbiol Rev* 2007;**20**:533].
- Limmathurotsakul D, Wongratanacheewin S, Teerawattanasook N, Wongsuvan G, Chaisuksant S, Chetchoisak P, et al. Increasing incidence of human melioidosis in Northeast Thailand. *Am J Trop Med Hyg* 2010;**82**:1113–7.
- Currie BJ, Ward L, Cheng AC. The epidemiology and clinical spectrum of melioidosis: 540 cases from the 20 year Darwin prospective study. *PLoS Negl Trop Dis* 2010;**4**:e900.
- Simpson AJ, Newton P, Chierakul W, Chaowagul W, White NJ. Diabetes mellitus, insulin and melioidosis in Thailand. *Clin Infect Dis* 2003;**36**:71–2.
- Inglis TJ, Rolim DB, Sousa AdeQ. Melioidosis in the Americas. *Am J Trop Med Hyg* 2006;**75**:947–54.
- Severiche D. Neumonía adquirida en la comunidad por *Pseudomonas pseudomallei*. *Rev Colomb Neumol* 1998;**10**:188–92.
- Gonzalez G, Mantilla WA, Rada R. Neumonía y osteomielitis por *Burkholderia pseudomallei*, reporte de un caso clínico. *Rev Med* 2009;**17**:146–9.
- Inglis TJ, Rolim DB, Rodríguez JL. Clinical guideline for diagnosis and management of melioidosis. *Rev Inst Med Trop Sao Paulo* 2006;**48**:1–4.
- Howe C, Sampath A, Spotnitz M. The *Pseudomallei* group: a review. *J Infect Dis* 1971;**124**:598–606.
- Rolim DB, Vilar DC, Sousa AQ, Miralles IS, de Oliveira DC, Harnett G, et al. Melioidosis, northeastern Brazil. *Emerg Infect Dis* 2005;**11**:1458–60.
- Dorman SE, Gill VJ, Gallin JI, Holland SM. *Burkholderia pseudomallei* infection in a Puerto Rican patient with chronic granulomatous disease: case report and review of occurrences in the Americas. *Clin Infect Dis* 1998;**26**:889–94.
- Pagnarith Y, Kumar V, Thaipadungpanit J, Wuthiekanun V, Amornchai P, Sin L, et al. Emergence of pediatric melioidosis in Siem Reap, Cambodia. *Am J Trop Med Hyg* 2010;**82**:1106–12.

20. Mary IP, Lars G, Chau PY, Raffin T. Melioidosis pulmonary. *Chest* 1995;**108**:4420–4.
21. Phetsouvanh R, Phongmany S, Newton P, Mayxay M, Ramsay A, Wuthiekanun A, et al. Melioidosis and Pandora's Box in the Lao People's Democratic Republic. *Clin Infect Dis* 2001;**32**:653–4.
22. Wiersinga WJ, Currie BJ, Peacock SJ. Melioidosis. *N Engl J Med* 2012;**367**:1035–44. <http://dx.doi.org/10.1056/NEJMra1204699>.
23. Hong Low JG, Lin Quek AM, Kong Sin Y, Peng Ang BS. Mycotic aneurysm due to *Burkholderia pseudomallei* infection: case reports and literature review. *Clin Infect Dis* 2005;**40**:193–8.
24. Currie BJ, Fisher DA, Anstey NM, Jacups SP. Melioidosis: acute and chronic disease, relapse and re-activation. *Trans R Soc Trop Med Hyg* 2000;**94**:301.
25. Peacock SJ, Schweizer HP, Dance DA, Smith TL, Gee JE, Wuthiekanun V, et al. Management of accidental laboratory exposure to *Burkholderia pseudomallei* and *B. mallei*. *Emerg Infect Dis* 2008;**14**. Available from <http://wwwnc.cdc.gov/eid/article/14/7/07-1501>.
26. Ashdown LR. An improved screening technique for isolation of *Pseudomonas pseudomallei* from clinical specimens. *Pathology* 1979;**11**:293–7.
27. Cheng AC, O'Brien M, Freeman K, Lum G, Currie BJ. Indirect hemagglutination assay in patients with melioidosis in northern Australia. *Am J Trop Med Hyg* 2006;**74**:330–4.
28. Steinmetz I, Reganzerowski A, Brenneke B, Haussler S, Simpson A, White NJ. Rapid identification of *Burkholderia pseudomallei* by latex agglutination based on an exopolysaccharide-specific monoclonal antibody. *J Clin Microbiol* 1999;**37**:225–8.
29. Tan AP, Pui MH, Tan LK. Imaging patterns in melioidosis. *Australas Radiol* 1995;**39**:260–4.
30. Currie BJ, Fisher DA, Howard DM, Burrow JN, Selvanayagam S, Snelling PL, et al. The epidemiology of melioidosis in Australia and Papua New Guinea. *Acta Trop* 2000;**74**:121–7.
31. Chetchotisakd P, Chierakul W, Chaowagul W, Anunnatsiri S, Phimda K, Mootsikapun P, et al. Trimethoprim-sulfamethoxazole versus trimethoprim-sulfamethoxazole plus doxycycline as oral eradication treatment for melioidosis (MERTH): a multicentre, double-blind, non-inferiority, randomised controlled trial. *Lancet* 2013. [http://dx.doi.org/10.1016/S0140-6736\(13\)61951-0](http://dx.doi.org/10.1016/S0140-6736(13)61951-0) [Epub ahead of print, Nov 22].
32. Centers for Disease Control, Prevention (CDC). Imported melioidosis—South Florida, 2005. *MMWR Morb Mortal Wkly Rep* 2006;**55**:873–6.
33. Brilhante RS, Bandeira TJ, Cordeiro RA, Grangeiro TB, Lima RA, Ribeiro JF, et al. Clinical-epidemiological features of 13 cases of melioidosis in Brazil. *J Clin Microbiol* 2012;**50**:3349–52.
34. Almuzara M, Barberis C, Bravo M, Pisarevsky A, Petrucci E, Carlos V, et al. Un caso de melioidosis en la Argentina. *Medicina (Buenos Aires)* 2011;71.
35. Limmathurotsakul D, Peacock SJ. Melioidosis: a clinical overview. *Br Med Bull* 2011;**9**:125–39.
36. Gibney KB, Cheng AC, Currie BJ. Cutaneous melioidosis in the tropic top end of Australia: a prospective study and review of the literature. *Clin Infect Dis* 2008;**47**:603–9.
37. Porras H. Boletín Temático. Anuario Estadístico de Antioquia 2011: "Medio Ambiente", Antioquia: Aguas sustentando la vida. Available at: http://www.antioquia.gov.co/PDF2/boletin_2011_medio_ambiente.pdf. (accessed may 19 2015).