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Ralstonia pickettii—innocent bystander or a potential threat?

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ABSTRACT

Ralstonia pickettii can be isolated from water, soil and plants, and can also form part of the commensal flora of the oral cavity and the upper respiratory tract of healthy individuals. *R. pickettii* is an infrequent pathogen, but can cause infections, mainly of the respiratory tract, in immunocompromised and cystic fibrosis patients. It can be isolated from a variety of clinical specimens, including sputum, blood, wound infections, urine, ear and nose swabs, and cerebrospinal fluid. Resistance can occur to ciprofloxacin, trimethoprim–sulphamethoxazole, piperacillin–tazobactam, imipenem–cilastatin and ceftazidime. Early detection of *R. pickettii* allows prompt appropriate antimicrobial therapy with a favourable outcome, but removal of infected indwelling devices is mandatory.

Keywords Antimicrobial susceptibility, cystic fibrosis patients, immunocompromised patients, infections, *Ralstonia pickettii*, resistance

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The human body exists within a ubiquitous microbiological environment in a delicate symbiotic equilibrium that protects against overwhelming growth of the commensal bacterial flora. When this balance is disturbed, some commensal organisms of relatively low virulence, such as *Ralstonia pickettii*, formerly named *Pseudomonas* (*Burkholderia*) *pickettii*, can cause severe disease. First described in 1973, *R. pickettii* is characterised as a Gram-negative aerobic bacillus that is phenotypically homogeneous with other known pseudomonads [1,2]. To date, 11 species of *Ralstonia* have been described, namely *R. pickettii*, *R. solanacearum*, *R. eutropha*, *R. gilardii*, *R. paucula*, *R. basilensis*, *R. oxalatica*, *R. mannitolitytica*, *R. taiwanensis*, *R. campinensis* and *R. metaliidurans* [2]. *R. pickettii* can be isolated from water, soil and plants, and can form part of the commensal flora of the oral cavity and upper respiratory tract [2,3]. In healthy individuals, infections with *Ralstonia* spp. are extremely rare. However, in individuals with declining immunocompetence, *R. pickettii* may progress to become a pathogen that causes infections, mainly of the respiratory tract. *R. pickettii* is also able to invade the bloodstream [2].

Aside from acquired or therapeutic immunosuppression, cystic fibrosis (CF) is the single most important known risk-factor for acquiring an infection with *R. pickettii* [1–3]. In CF patients, *R. pickettii* may be responsible for chronic airway infections and pneumonia [2]. Nosocomial outbreaks of infections with *R. pickettii* have been reported in association with contaminated fluids used for patient care [1,3–6]. *R. pickettii* bacteraemia has been reported in association with central venous line or permanent intravenous system infection, secondary to the use of such fluids [7,8]. In many cases, patients with systemic *R. pickettii* infections are immunocompromised.

Between 2001 and 2004, 38 patients with clinically manifest *R. pickettii* infections were identified at Innsbruck Medical University, Austria (a tertiary referral centre). Twenty-three patients yielded an *R. pickettii* isolate from a single specimen, seven patients yielded *R. pickettii* isolates from two specimens, and six patients yielded *R. pickettii* isolates from three or more specimens (Table 1). In this series, 34% of the cases involved infections of the respiratory tract in patients with CF, mostly as part of mixed

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Table 1. Demographic and clinical data from patients with *Ralstonia pickettii* infection at Innsbruck Medical University, Austria

Patients, *n*	38
Median age, years (range)	35.9 (1.4–81.0)
Gender, male:female	22 : 16
Clinical samples yielding *R. pickettii*, *n*	61[a]
Sputum, *n*	24
Blood cultures, *n*	26
Port-a-cath system, *n*	5
Miscellaneous specimens, *n*	6
Predisposing factors	
Cystic fibrosis, *n*	13
Chronic obstructive pulmonary disease, *n*	2
Malignant disorders, *n*	7
AIDS, *n*	1
Acute renal failure, *n*	1
Diabetes mellitus, renal failure, *n*	1
Poly-trauma, *n*	4
Surgery, *n*	4

[a]Seventeen mixed infections.

infections. As with other pathogens, colonisation of the respiratory tract of CF patients with *R. pickettii* may be asymptomatic, and therefore a decision of when to start antimicrobial treatment is difficult [2–4]. In non-CF patients, *R. pickettii* respiratory tract infection was a rare event, with only two cases (a patient with chronic obstructive pulmonary disease and a poly-traumatised patient receiving ventilator support). While respiratory tract and other non-systemic infections responded well to systemic antibiotic treatment, intravenous antibiotic therapy showed no success in cases of *R. pickettii* sepsis if a contaminated central venous line or permanent venous system was the source. Blood cultures accounted for 43% and contaminated 'port-a-cath' systems for 8% of the *R. pickettii* isolates in this series. This type of infection remains a significant complication, as such systems are implanted commonly in critically-ill or cancer patients [8]. In all three patients with infected 'port-a-cath' systems, and another three patients with contaminated central venous lines, removal of the indwelling device was necessary to control infection. The spectrum of pathogens associated with line sepsis or contaminated implantable devices is expanding, and non-fermentative bacilli must be considered as important potential pathogens. Compared with sepsis and respiratory tract infection, all other infections with *R. pickettii*, such as urinary tract infections, wound infections, and infections of the ear and nose, were rare (Table 1). To date, such infections have been reported only anecdotally, or not at all. These rare infections all responded to antibiotic treatment.

Isolation and identification of *R. pickettii* can be performed according to standard microbiological methods on MacConkey agar. *R. pickettii* strains are glucose-non-fermentative Gram-negative bacilli, and can be identified readily with commercial identification systems (e.g., API 20NE; bioMérieux, Marcy l'Etoile, France). Alternatively, PCR-based methods may produce more accurate results. Thus, Coenye *et al.* [2] used two combined PCR assays to identify *Ralstonia* spp. in the sputum of CF patients, and concluded that the frequency of these bacteria in this patient population may be underestimated. Routine PCR-based identification of non-fermentative bacilli cannot, to date, be provided by most laboratories, but might be useful for monitoring outbreaks.

Antimicrobial susceptibility testing can be performed with NCCLS disk-diffusion methods on Mueller–Hinton agar. Determination of MICs may be of use in refractory cases. The *Ralstonia* group has been reported to be susceptible to co-trimoxazole, ciprofloxacin and anti-pseudomonal β-lactams, with aminoglycosides having activity against some isolates [3,9]. In the series described above, the *R. pickettii* isolates showed resistance to ciprofloxacin (17%), trimethoprim–sulphamethoxazole (26%), aztreonam (60%), piperacillin–tazobactam (45%), ceftriaxone (40%), ceftazidime (30%), imipenem–cilastatin (38%) and aminoglycosides (> 60%). However, the possibility of discrepancies between in-vitro testing and in-vivo activity should always be considered [1–4,8–10].

Thus, while being low in total numbers, infections with *R. pickettii* may affect immunocompromised patients or patients suffering from CF [2,11,12]. Contaminated medical solutions are one of the most important sources of *R. pickettii* [4,5,13–15]. PCR-based identification and other new systems may be able to improve the efficiency of diagnosis [16–18]. *R. pickettii* produces a wide range of β-lactamases. OXA-60, a chromosomal, inducible, imipenem-hydrolysing class D β-lactamase, has recently been described in detail [19]. As emphasised previously, delayed diagnosis and misinterpretation can be hazardous to patients with infections caused by *R. pickettii* [20]. Early detection of *R. pickettii* allows prompt directed antibacterial treatment, according to the results of susceptibility tests, and is associated with a favourable outcome, but removal of infected indwelling devices is mandatory [18].

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