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Population-based laboratory surveillance for tribe Proteeae isolates in a large Canadian health region

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ABSTRACT

The tribe Proteeae comprises the genera *Proteus*, *Morganella* and *Providencia*. Few studies have specifically investigated the epidemiology of infections caused by the Proteeae, and none has been conducted in a large non-selected population. The present study was a population-based laboratory surveillance in the Calgary Health Region (population 1.2 million), Canada during 2000–2005 that aimed to define the incidence, demographical risk-factors for acquisition and antimicrobial susceptibilities of Proteeae isolates. In total, 5047 patients were identified from whom Proteeae isolates were obtained (an annual incidence of 75.9/100 000), with females and the elderly being at highest risk. Incidence rates were 64.8, 7.7 and 3.4/100 000/year for the genera *Proteus*, *Morganella* and *Providencia*, respectively. Overall, 85% of infections were community-onset, and the overall rate of bacteraemic disease was 2.0/100 000. Compared with other species, *Proteus mirabilis* occurred at a much higher frequency, especially among females, and was less likely to be isolated from hospital-onset infections or to be part of a polymicrobial infection. Among isolates from community-onset infections, *Providencia* spp. were less likely to be from outpatients and more likely to be from nursing home residents. There were low overall rates of resistance to ciprofloxacin (4%) and gentamicin (5%), with *Prot. mirabilis* generally being the most susceptible. Members of the Proteeae were isolated frequently in both the community and hospital settings, but were infrequent causes of invasive disease. The occurrence, demographical risk-factors and microbiology of Proteeae isolates varied according to the individual species.

Keywords Incidence, laboratory surveillance, Proteeae, *Proteus mirabilis*, risk-factors, susceptibility

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INTRODUCTION

The tribe Proteeae consists of three genera: *Proteus*, *Morganella* and *Providencia* [1]. These organisms cause a range of human infections of different severities, and have been associated with outbreaks of infection in hospitals and nursing homes [2–5]. While antimicrobial resistance surveys have revealed that members of the Proteeae are relatively frequent among clinical isolates, and a number of series have investigated specific subsets of infections caused by these organisms [6–10], few studies have focused on the Proteeae as a whole [11]. Kim *et al.* [11] described 132 episodes of bacteraemia involving Proteeae in a tertiary-care centre in Korea, with *Morganella morganii* being the most frequent isolate (61 cases), followed by *Proteus mirabilis* (41) and *Proteus vulgaris* (20). However, this study was performed at a single hospital and was focused solely on isolates from bacteraemia. The occurrence and determinants of all tribe Proteeae infections in a non-selected population remain to be defined. Population-based studies, in which all incident cases of a disease occurring in a defined

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geographical region are studied, minimise selection bias associated with hospital- or clinic-based studies [12,13]. The present study describes a population-based laboratory surveillance for all Proteeae isolates in a large Canadian health region, with the aim of defining their incidence, associated demographical risk-factors and microbiological features.

MATERIALS AND METHODS

Study population

The Calgary Health Region (CHR) provides all publicly funded healthcare services to the 1.2 million residents of the cities of Calgary and Airdre, as well as numerous adjacent surrounding communities, together covering an area in Canada of 37 000 km^2. Acute care is provided principally by one paediatric and three major adult hospitals, with *c.* 2000 acute-care beds and 100 000 discharges yearly. With the exception of a few small rural hospitals, all routine microbiological tests for community and hospital sites in the CHR are performed by Calgary Laboratory Services. The study included all patients from whom Proteeae isolates were obtained from specimens submitted at hospital and community-based collection sites within the CHR to Calgary Laboratory Services between 1 January 2000 and 31 December 2005. Patients were assumed to be CHR residents and were included in the analysis if they were outpatients with Alberta Personal Healthcare numbers from whom specimens were submitted to CHR-based collection sites, or if they were admitted to a CHR acute-care facility. Since laboratory data without personal identifiers were studied and individual clinical records were not reviewed, specific institutional ethics review was not required.

Population-based surveillance

Active, population-based surveillance of all Proteeae isolates from patients in the CHR during the study was performed at Calgary Laboratory Services. Hospitals, nursing homes, physicians' offices and community collection sites were included in the surveillance. Following identification of Proteeae isolates, basic laboratory and demographical data were obtained from the regional laboratory information system (PathNet Classic v.306; Cerner, Kansas City, MO, USA). Community-onset isolates were defined as isolates submitted from community-based collection sites or nursing homes, or obtained within 2 days of admission to an acute-care facility; hospital-onset isolates were those isolated >2 days after hospital admission. In order to minimise the bias associated with repeated culturing of specimens from the same episode of clinical disease, only one culture/patient/species/year was included in the assessment of incident cases.

Clinical laboratory testing

Proteeae isolates were obtained using standard techniques; identification and susceptibilities to antimicrobial agents were determined using the Vitek-Legacy system (Vitek AMS; bioMérieux Vitek Systems Inc., Hazelwood, MO, USA) with customised antimicrobial susceptibility testing cards, and were interpreted according to CLSI criteria [14]. At Calgary Laboratory Services, identification is performed routinely to the species level on all clinically relevant isolates, but individual speciation and antimicrobial susceptibility testing is occasionally not performed on some non-invasive isolates. In the present study, intermediately-susceptible results were grouped with and reported as resistant; when susceptibility test results were not available, rates were reported using the number actually tested as the denominator. Bacteraemia was defined by the isolation of Proteeae strains from at least one set of blood cultures. Polymicrobial episodes were those in which non-Proteeae strains were co-isolated from a single clinical specimen.

Statistical analysis

All analyses were performed using Stata v.9.0 (Stata Corp., College Station, TX, USA). Differences in proportions among categorical data were assessed using Fisher's exact test. Medians with inter-quartile range (IQR) were used to describe asymmetrically distributed continuous variables. Incidence rates were calculated using regional demographical data as the denominator. Category-specific risks were calculated and reported as risk ratios (RRs) with exact 95% CIs, as described previously [15].

RESULTS

During the 6-year surveillance period, 6527 Proteeae isolates were obtained from 6466 clinical specimens from 4495 CHR residents. The overall annual population incidence of Proteeae isolation was 5047 episodes, or 75.9/100 000 population; the rates for *Proteus*, *Morganella* and *Providencia* were 64.8, 7.7 and 3.4/100 000, respectively. Bacteraemia occurred in 134 patients (110 community-onset; 82%), giving an incidence rate of 2.0/100 000/year. The majority (4290 of 5047; 85%) of incident Proteeae isolates were community-onset, with 803 (19%) from emergency departments or inpatients within 2 days of admission, 970 (23%) from nursing homes, and 2517 (59%) from outpatients. Hospital-onset isolates were identified a median of 12 (IQR 6–29) days after admission to an acute-care hospital.

The median age of patients with Proteeae isolates was 69.6 (IQR 41.6–81.8) years, and 3460 (69%) were female. There was a significant relationship between age, gender and the incidence of isolation, with the rates increasing dramatically above the age of 60 years (Fig. 1). Overall, females had twice the risk of isolation of Proteeae relative to males (103.8 vs. 47.8/100 000; RR 2.17; 95% CI 2.04–2.30; p <0.0001), and this excess risk was observed across all age groups, with the exception of those aged <10 years