



Short report

# Characterizing the burden of invasive *Pseudomonas* infection on neonatal units in the UK between 2005 and 2011

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## SUMMARY

Concern about *Pseudomonas* infection in neonatal units has focused on outbreaks. This study analysed cases of invasive *Pseudomonas* infection in 18 UK neonatal units participating in the NeonIN Neonatal Infection Surveillance Network from January 2005 to December 2011. Forty-two cases were reported. The majority (35/42, 93%) of cases were late-onset (median 14 days, range 2–262 days), the highest incidence was seen in extremely-low-birthweight infants and all cases were sporadic. One-third of cases were known to be colonized prior to invasive disease. Attributable mortality was 18%. Opportunities for preventing invasive disease due to this important pathogen should be prioritized.

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## Introduction

*Pseudomonas aeruginosa* is associated with environmental reservoirs (sinks and mechanical ventilator equipment) as well as carriage by healthcare workers, and is an important cause of healthcare-associated infection, particularly in neonatal units (NNUs).<sup>1,2</sup> Principal risk factors for invasive *Pseudomonas*

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infection include very low birth weight (VLBW; <1500 g), extreme prematurity (<29 weeks), exposure to antibiotics, and mechanical ventilation.<sup>3</sup> *P. aeruginosa* is responsible for a wide range of clinical syndromes including meningitis, sepsis, pneumonia and skin infections. In VLBW neonates, infection with *P. aeruginosa* is associated with a higher mortality rate than infection with other Gram-negative bacilli.<sup>4,5</sup>

To date, published studies have largely focused on descriptions of outbreaks in NNUs. A recent systematic review included 15 published studies of nosocomial outbreaks of *P. aeruginosa* colonization or infection in NNUs.<sup>6</sup> Eleven of these studies identified the outbreak strain in the environment, five reported antibiotic-resistant strains, and three reported multi-drug-resistant strains. The latest and most widely publicised outbreak occurred in NNUs in Northern Ireland between December 2011 and January 2012. The subsequent UK Government inquiry review published 32 recommendations in its final report.<sup>7</sup> A recurring theme and final recommendation was that 'surveillance arrangements should be established for *Pseudomonas aeruginosa* for augmented care settings including neonatal care'. At present, this is not routine practice in UK NNUs.

The aims of this study were to define and describe the clinical burden of invasive neonatal *Pseudomonas* infection on NNUs within a UK neonatal infection surveillance network.

## Methods

### Case definition

Invasive episodes were defined where *Pseudomonas* spp. were isolated from blood or cerebrospinal fluid (CSF) of infants in the seven years between January 2005 and December 2011, and where the clinician gave appropriate antibiotic treatment for at least five days or until death. Repeat positive cultures collected within a period of seven days were considered to be part of the same episode. Early-onset infection was defined as disease within the first 48 h of life.

### Design, setting and study population

In the Neonatal Infection Surveillance Network (<http://www.neonin.org.uk/>), participating NNUs record data on culture-proven infections prospectively on a web-based database. At the time of this study, there were 18 participating NNUs across the UK (15 NNUs provide care for extremely preterm infants of any gestation, and three NNUs provide care exclusively for infants  $\geq 26$  weeks gestation). Any patients treated in any of the participating NNUs were eligible for inclusion in this study. Anonymized demographic and clinical data were matched to microbiology records and cross-checked routinely for accuracy and completeness.

### Data extraction

A study-specific proforma was completed on all eligible infants to obtain clinical and demographic information. Corresponding microbiology and resistance data were also collected from the routine microbiology laboratory service at each NNU.

## Statistical analyses

Data were entered into an Excel (Microsoft Corp, Redmond, WA, USA) database and exported into Stata Version 9 (Stata-Corp, College Station, TX, USA) for analysis. *t*-tests were used for continuous data, and Chi-squared tests or Fisher's exact tests were used for dichotomous variables. Denominator data (number of live births and number of NNU admissions) by birthweight categories (<1000 g, 1000–1499 g, 1500–249 g, >2500 g) were available for all units over the study period.

## Ethics

This study received ethical approval from the London–Surrey Borders Research Ethics Committee (Ref. 05/Q0806/34) as a multi-centre project. Each participating NNU received local ethical approval.

## Results

In total, 42 infants with invasive *Pseudomonas* infection were recorded over the seven-year study period. Two isolates were *Pseudomonas stutzeri* and all other isolates were *P. aeruginosa*. Clinical data were available for 39 infants. In 37 of the 39 infants, *Pseudomonas* spp. were isolated from blood, and in the remaining two infants, *Pseudomonas* spp. were isolated from CSF. Twenty of the 39 infants had a lumbar puncture during the episode (13 after the commencement of antibiotics), and two of these 20 (10%) infants had culture-proven meningitis.

### Incidence

The number of participating NNUs increased over the study period: five NNUs participated in 2005, seven in 2006, nine in 2007, 12 in 2008, 13 in 2009, 14 in 2010 and 19 in 2012. One NNU has since closed, so clinical data were unavailable on the three infants with *Pseudomonas* infection from that NNU. Cases of invasive *Pseudomonas* infection were reported from 12 NNUs, and no cases were identified from the remaining six NNUs. The overall incidence of *Pseudomonas* infection was 0.1 per 1000 live births and 1.1 per 1000 neonatal admissions. The incidence varied markedly across NNUs, ranging from 0 to 2.41 per 1000 neonatal admissions. The highest incidence of invasive *Pseudomonas* infection (12.8 per 1000 live births) was seen in extremely-low-birthweight infants (ELBW, <1000 g); this was significantly higher than the incidence in infants with birth weight >1000 g ( $P < 0.001$ ).

### Case characteristics

In total, 47 *Pseudomonas* culture-positive episodes were recorded in 39 infants. The median gestational age was 26 weeks (range 22–40 weeks) and median birth weight was 840 g (range 490–3712 g). The median postnatal age at onset was 14 days (range 1–262 days); the vast majority (36/39, 93%) were late-onset cases (>48 h of age).

Table I presents details of the factors associated with invasive *Pseudomonas* infection. The salient clinical and laboratory features noted during the first week of the infectious episode are shown in Table II.

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