Escherichia coli bacteraemia in Canberra: incidence and clinical features

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ABSTRACT

Objective: To determine the population incidence and clinical features of *Escherichia coli* bacteraemia in Canberra, Australia.

Design, setting and participants: Canberra (including the nearby local government areas of Queanbeyan and Yarrowlumla) has a geographically isolated population of about 366 000 people. Its six hospitals also provide tertiary medical services for the surrounding region. Confining our analysis (by residential postcodes) to Canberra residents only, we used microbiology laboratory records and population statistics to calculate the population incidence of *E. coli* bacteraemia from January 2000 to December 2004. Clinical data were also collected prospectively on episodes occurring within three of the hospitals.

Main outcome measures: Population incidence of *E. coli* bacteraemia; place of acquisition of infection; focus of infection within body; recovery, new morbidity or death at 7 days.

Results: During the 5-year period, 515 episodes of *E. coli* bacteraemia occurred in Canberra residents, an incidence of 28 per 100 000 population per year. The highest rate was in men aged ⩾ 80 years (463 per 100 000). Overall, *E. coli* bacteraemia occurred in equal numbers in males and females, but incidence was higher in males aged < 1 year and ⩾ 60 years. Most episodes occurred in people aged ⩾ 60 years (316/511 [62%]) and most were community-associated (347/511 [68%]). Half the infections (257/511) had a genitourinary focus and 28% (141/511) a gastrointestinal focus. The 7-day case-fatality rate was 5%. Prostate biopsies and urinary catheters were notable preventable foci of health care-associated bacteraemia. Resistance of isolates to gentamicin (2.1%), ciprofloxacin (1.8%) and cefotaxime (0.4%) was low.

Conclusions: *E. coli* is the most common cause of bacteraemia in Canberra, and incidence increases with age. Most cases have a community onset, but many episodes are related to health care procedures. Ongoing surveillance is important for identifying risk factors that may be modified to reduce disease.

MJA 2008; 188: 209–213

Escherichia coli is one of the commonest causes of bacteraemia around the world, accounting for 15%–40% of all significant bacteraemia isolates,[1-10] with the majority of infections having their onset in the community.[3-5] Before the antibiotic era, *E. coli* was an infrequent bloodstream isolate. Very few cases were reported up until 1929,[11] and reports from Boston in 1935 showed that bacteraemia was much more commonly due to organisms other than *E. coli* (0.7 episodes per 1000 hospital admissions). After the introduction of antibiotics there was a marked increase in the number of cases of *E. coli* bacteraemia.[12-14] Since the 1980s, the reported incidence of *E. coli* bacteraemia has ranged from 1.8 to 5.5 episodes per 1000 hospital admissions.[3,6-8,15] Rising antibiotic resistance now threatens to make treatment of these infections increasingly difficult.

Despite being a common and serious infection, there have been few recent studies describing the clinical features of *E. coli* bacteraemia, and few data are available on its population incidence.

We examined all episodes of *E. coli* bacteraemia in Canberra over a 5-year period. Our aim was to document the causes and outcomes of these infections and to calculate the population incidence of *E. coli* bacteraemia.

METHODS

Setting

Canberra, the capital of Australia, is located within the Australian Capital Territory. In our study, the nearby New South Wales local government areas of Queanbeyan and Yarrowlumla were defined as part of "Canberra". In 2002, Canberra had a geographically well defined population of about 366 000. Because of its geographical isolation, almost all acute medical care for Canberra residents is provided in Canberra, the main exception being for patients requiring solid organ or allogeneic stem cell transplantation.

Canberra is also the tertiary referral centre for a large rural region (58 700 km^2) in the south-east of NSW known as the Australian Capital Region (ACR) (http://www.business.nsw.gov.au/region/profiles/capital+Region.htm). In 2002, the total population of this region, including Canberra, was just over 529 000.

Canberra is serviced by three public hospitals — The Canberra Hospital (TCH) (500 beds), Calvary Public Hospital (175 beds) and Queanbeyan District Hospital (55 beds) — and three private hospitals — Calvary Private Hospital (95 beds), National Capital Private Hospital (80 beds) and Calvary John James Hospital (formerly the John James Memorial Hospital) (150 beds).

Population incidence of *E. coli* bacteraemia

Demographic data on patients with episodes of *E. coli* bacteraemia were obtained from all but one of the microbiology laboratories in Canberra. The excluded laboratory provides a non-acute outpatient service, and therefore would be expected to handle few, if any, episodes of bacteraemia. Microbiology records were also available from the public hospitals within the ACR.

Residential postcodes were used to confine our study of *E. coli* bacteraemia to episodes occurring in Canberra residents only. Age-stratified population data, as at 30 June 2002, were obtained from the Australian Bureau of Statistics for the statistical division of Canberra and local government areas of Queanbeyan and Yarrowlumla.

The *E. coli* bacteraemia hospital study

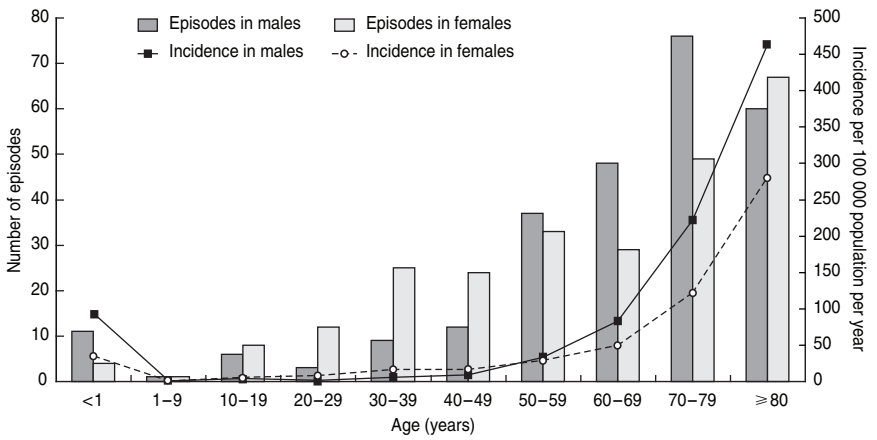
A quality improvement program was established in 1998 to monitor bacteraemia within three Canberra hospitals (TCH, Calvary Public Hospital and Calvary Private Hospital). The program was approved by the ACT Health and Community Care Human Research Ethics Committee.

1 Total episodes of *Escherichia coli* bacteraemia occurring in Canberra, by patients' residential status, 2000–2004

	E. coli bacteraemia hospital study laboratories	Other microbiology laboratories	Total
Total number of episodes	511	74	585
Number of Canberra residents	445	64	509*
Number of non-Canberra residents	66	10	76
ACR residents†	44	5	49
Other NSW residents outside the ACR	9	3	12
Other interstate residents‡	11	2	13
International visitors	2	0	2

ACR = Australian Capital Region. ACT = Australian Capital Territory. NSW = New South Wales.
* Six episodes of *E. coli* bacteraemia in Canberra residents were identified from ACR laboratories outside Canberra. These were included when calculating the population incidence. † Residents of the ACR referral area of south-east NSW. ‡ Residents of Australian states other than the ACT and NSW. ◆

2 Number of episodes and incidence of *Escherichia coli* bacteraemia in Canberra residents, 2000–2004



As part of the program, the clinical records of all patients with positive blood cultures are prospectively reviewed. This process involves multiple chart and patient reviews until Day 7 (or until discharge, if earlier). A multidisciplinary team, including an infectious diseases physician, meets weekly to seek a consensus, for each patient, on the clinical significance of the bacteraemia, place of acquisition, focus of infection and outcome.

Our study examined all episodes of *E. coli* bacteraemia occurring over a 5-year period, from 1 January 2000 to 31 December 2004, at these three hospitals. Susceptibility patterns of isolates during 2003 and 2004 were obtained from the microbiology laboratory computer system. Isolate identification and susceptibility testing were performed using Vitek 1 (bioMérieux, Hazelwood, Mo, USA). Isolates with intermediate resistance were regarded as resistant.

Definitions

E. coli *isolates.* All bloodstream isolates of *E. coli* were considered significant. Repeated isolation within 14 days was regarded as a single episode of bacteraemia.

Place of acquisition. Place of acquisition was classified as either community-associated or health care-associated (inpatient or non-inpatient), according to national definitions.[16] Health care-associated infections were those acquired during hospitalisation or as a direct complication of an indwelling device, medical procedure or instrumentation, or associated with drug-induced neutropenia. Inpatient health care-associated infections were episodes that occurred more than 48 hours after hospital admission and within 48 hours of discharge. All other health care-associated infections were classified as non-inpatient health care-associated infections. All other episodes were classified as community-associated.

Focus of infection. Focus of infection was classified according to the body system affected and/or primary site of sepsis, as adapted from national definitions.[16] The focus was classified as "haematological" if associated with neutropenia without evidence of an alternative focus. Bacteraemia in the neonate, acquired from the mother during delivery, was classified as a "maternal" focus.

Outcome. Death at 7 days or earlier was attributed to sepsis, to other causes, or to a combination of sepsis and other causes. Patients who were alive at 7 days were classified as being nearly/fully recovered from sepsis, having ongoing sepsis, or suffering a significant new morbidity as a result of the sepsis.

Statistical analysis

Significance tests for differences in proportions were calculated using two-sided χ^2 tests.

RESULTS

Population incidence of *E. coli* bacteraemia

Over the 5-year study period, 585 episodes of *E. coli* bacteraemia occurred in Canberra (Box 1), of which 76 episodes were excluded from our analysis as they were in non-Canberra residents (most of whom lived in the surrounding ACR). Six additional episodes of *E. coli* bacteraemia occurred in Canberra residents while attending hospitals within the ACR. Thus, 515 episodes of *E. coli* bacteraemia were identified in Canberra residents (mean age, 63 years; median age, 68 years). Population incidences, by age and sex, are shown in Box 2. The overall incidence was 28 episodes per 100 000 population per year, with the highest incidence being 463 per 100 000 in men aged 80 years and over.

The *E. coli* bacteraemia hospital study

E. coli was the most common significant isolate in bacteraemia episodes occurring in the three study hospitals. The 511 episodes of *E. coli* bacteraemia in the three study hospitals accounted for 87% of all episodes that occurred in Canberra. The incidence of *E. coli* bacteraemia averaged 1.4 episodes per 1000 admissions. Most episodes occurred in older adults (62% in people aged ≥ 60 years and 47% in people ≥ 70 years).

3 Place of acquisition of *Escherichia coli* bacteraemia, 2000–2004*

		Health care-associated	
	Community-associated	Non-inpatient	Inpatient
Males† (*n* = 255)	153 (60%)	46 (18%)	55 (22%)
Females (*n* = 256)	194 (76%)	20 (8%)	42 (16%)
Total† (*n* = 511)	347 (68%)	66 (13%)	97 (19%)

* Based on episodes recorded in the hospital study (The Canberra Hospital, Calvary Public Hospital and Calvary Private Hospital). † For one male, the place of acquisition was not recorded. ◆

Sixty-eight per cent of episodes were community-associated, 19% were inpatient health care-associated and 13% were non-inpatient health care-associated. Females were more likely to have community-associated bacteraemia, while males had higher rates of health care-associated bacteraemia (Box 3).

Genitourinary and gastrointestinal tract foci accounted for three-quarters of the episodes (Box 4) and were mostly community-associated. The majority of patients with genitourinary infections were female (60%), while gastrointestinal infections predominated in males (62%).

Twenty-three per cent of episodes with a genitourinary focus were health-care associated. In males, prostate biopsies (13 cases) and urinary catheter insertion (13 cases) were the main precipitating events, while in females, urinary catheter insertion (13 cases) and urogenital procedures (10 cases) were the main associations.

By Day 7, 82% of people were at or near full recovery from sepsis and 13% showed evidence of ongoing sepsis or significant new morbidity as a result of the sepsis. There were 26 deaths (5% of all hospital study patients with *E. coli* bacteraemia), of which five were considered directly due to the sepsis, 20 due to a combination of sepsis and other causes, and one due to another cause. The median age of patients who died was 72 years.

Deaths within 7 days were less common in patients with community-associated infections (4% of cases) and when the focus of infection was the genitourinary tract (2%), but higher in maternally acquired neonate infections (40%), inpatient health care-associated infections (8%) and infections associated with an intravascular device (11%), the respiratory tract (11%) or an unknown focus (21%).

Antibiotic resistance was most common to ampicillin (47%), amoxycillin-clavulanate (23%), cotrimoxazole (20%), cephalothin (19%) and ticarcillin-clavulanate (14%). In contrast, few isolates were resistant to gentamicin (2.1%), ciprofloxacin (1.8%) and cefotaxime (0.4%). Resistance was significantly higher in health care-associated isolates than in community-associated isolates (Box 5).

DISCUSSION

Few studies have examined the population incidence of *E. coli* bacteraemia. In a Copenhagen study,[15] the highest incidence was 464 episodes per 100 000 population per year in men aged 80–90 years. The percentage of health care-associated episodes in that study (55%) was much higher than the percentage in our study (32%), suggesting that not all community-associated episodes were captured in the Danish study.

In a recent, large, retrospective cohort study of people aged ⩾ 65 years in the state of Washington, USA, the rate of community-onset *E. coli* bacteraemia was 150 per 100 000 person-years.[17] In men aged over 85 years, the rate was 462 per 100 000 person-years. As the study excluded health care-associated infections, the overall true incidence of *E. coli* bacteraemia may have been 30%–50% higher.

In a rural hospital in Kenya,[18] the incidence of *E. coli* bacteraemia in children under 1 year old was high, at 204 per 100 000 children per year, but considered to be an underestimate because of the relatively high number of children who died before hospitalisation.

Since 2001, the European Antimicrobial Resistance Surveillance System has reported data on episodes of invasive *E. coli* isolates (from the bloodstream and cerebrospinal fluid).[1] However, population and hospital coverage within countries is variable, with resultant large differences in calculated incidence rates between countries. In countries that appear to have good population coverage, we calculate that the incidences of invasive *E. coli* infections per 100 000 population in 2004 were as follows: Austria, 32; Ireland, 32; Finland, 39; Sweden, 39; and Iceland, 40.

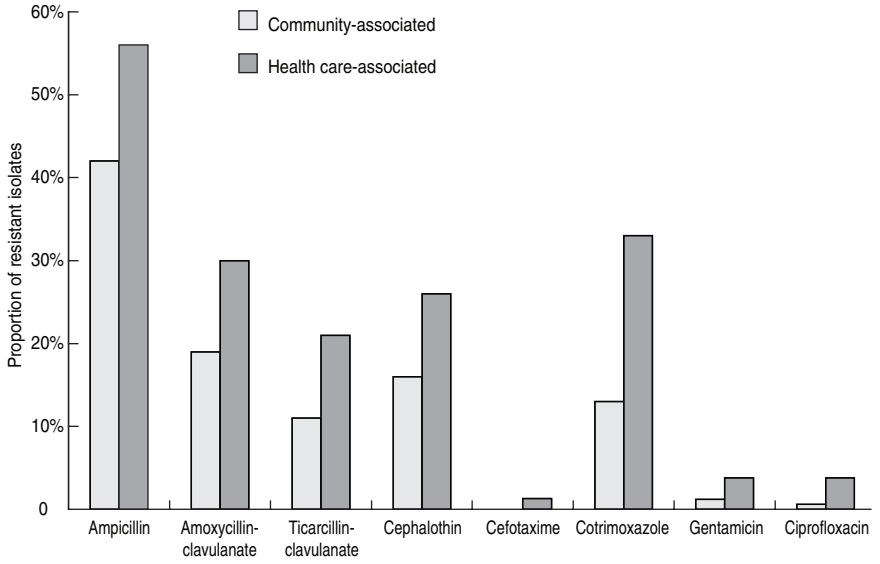
The incidence in our study was the same as that in the Copenhagen study (28 episodes per 100 000 population per year).[15] Our results are likely to slightly underestimate the incidence, as we were unable to capture Canberra residents who became bacteraemic outside Canberra. Over the study period, an average of 4480 Canberra residents per year were admitted to Australian hospitals outside Canberra.[19-23] Based on our incidence of 1.4 episodes per 1000 admissions, an additional 32 episodes of *E. coli* bacteraemia may have occurred in Canberra residents treated elsewhere over the 5-year study period, bringing the total number of episodes to 547 and the population incidence to 30 episodes per 100 000 population per year. However, "leakage" of cases or under-diagnosis was more likely to have occurred in other studies with less well

4 Focus of infection* of *Escherichia coli* bacteraemia, 2000–2004†

	Males	Females	Total
Genitourinary	102 (40.0%)	155 (60.5%)	257 (50.3%)
Gastrointestinal	88 (34.5%)	53 (20.7%)	141 (27.6%)
Haematological	19 (7.5%)	10 (3.9%)	29 (5.7%)
Respiratory	8 (3.1%)	10 (3.9%)	18 (3.5%)
Skin and soft tissue	7 (2.7%)	4 (1.6%)	11 (2.1%)
Intravenous device	5 (2.0%)	4 (1.6%)	9 (1.8%)
Maternal	3 (1.2%)	2 (0.8%)	5 (1.0%)
Musculoskeletal	2 (0.8%)	0	2 (0.4%)
Neurological	1 (0.4%)	0	1 (0.2%)
Unknown	20 (7.8%)	18 (7.0%)	38 (7.4%)

* Major system affected and/or primary site of sepsis. † Based on episodes recorded in the hospital study (The Canberra Hospital, Calvary Public Hospital and Calvary Private Hospital). ◆

5 Antibiotic resistance of *Escherichia coli* bacteraemia isolates, 2003–2004*



* Based on episodes recorded in the hospital study (The Canberra Hospital, Calvary Public Hospital and Calvary Private Hospital), 2003–2004. ◆

defined or inclusive populations[1,15,17,18] than in our study, which involved an entire geographically isolated region.

Earlier studies of *E. coli* bacteraemia showed a predominance of hospital-associated infections (55%–72%).[6,11,14] But most recent studies have shown that community-associated infections are more common, with hospital-associated infections now accounting for only 14%–30% of episodes.[3-5] In our study, 40% of infections in males and 24% of infections in females were health care-associated and therefore potentially preventable. A third of these arose from the genitourinary tract, predominantly resulting from prostate biopsies or urinary catheterisation. Changes in practice relating to prostate biopsies, prompt definitive prostate surgery for obstruction in older men, and timely removal of urinary catheters could help reduce such episodes.

Before the advent of antibiotics, the case-fatality rate among people with *E. coli* bacteraemia ranged from 15% to 40%.[11,12] Despite the introduction of antibiotics, the case-fatality rate from the 1950s to the early 1990s showed no significant improvement.[4,6-8,13-15] More recently, reported 7-day case-fatality rates have ranged from 5.9% to 9% — however, rates continue to rise to 16% at 1 month.[9,10,17] Our 7-day case-fatality rate was 5%. Extended follow-up (from September 2000 to August 2001) of a subset of 46 patients aged over 16 years showed that case-fatality rates increased to 18% at 1 month and 31% at 6 months.

The relatively low antibiotic resistance rates in *E. coli* blood isolates examined in our study were similar to rates reported in other recent Australian data.[24] Resistance rates were significantly higher in health care-associated infections, presumably reflecting more frequent exposure of patients to antibiotics in health care environments. Resistance rates, particularly to aminoglycosides and fluoroquinolones, were much lower in our study than rates reported in many other countries (Box 6).

E. coli is currently the most common cause of bacteraemia in Canberra, and the incidence rises dramatically with age. Although antibiotic resistance in Canberra is relatively low, increasing rates of resistance worldwide make treatment difficult. Almost a third of episodes are associated with exposure to the health care system, and are therefore potentially preventable. Continued surveillance is necessary to monitor trends and identify factors that can be modified to reduce the number of infections.

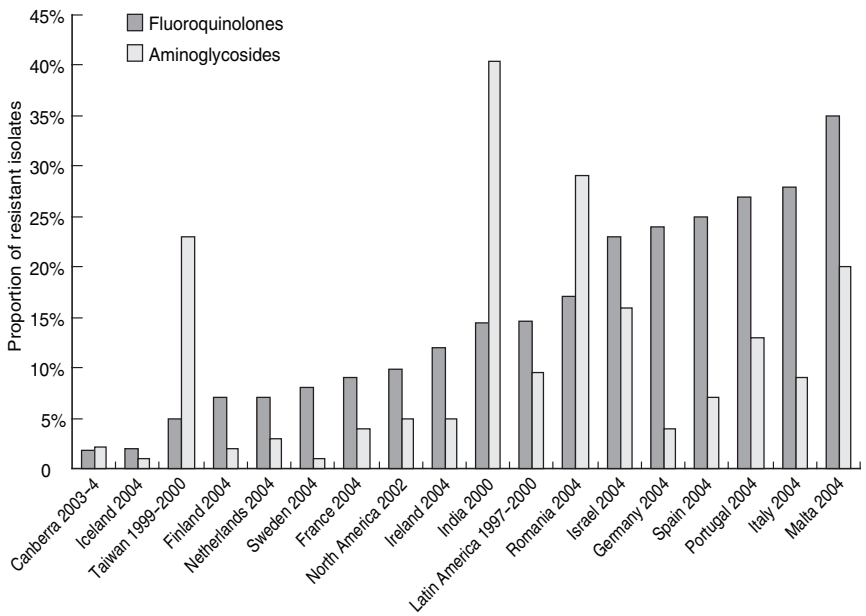
ACKNOWLEDGEMENTS

We would like to thank Angelique Clyde-Smith of ACT Pathology; Reimke Kampen, Dianne Dreimanis, Wendy Beckingham, Greg Morley and Philippa Keating from the Bloodstream Infection Surveillance Project; and Paul Whiting and Aline Nguyen from Capital Pathology for assistance in data collection. We also thank Anne Gardner for contributing the 1- and 6-month mortality data.

COMPETING INTERESTS

None identified.

6 International resistance rates of *Escherichia coli* bacteraemia isolates to aminoglycosides and fluoroquinolones*[1,2,25-27]



* The European Antimicrobial Resistance Surveillance System[1] also includes isolates from cerebrospinal fluid. ◆

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(Received 7 May 2007, accepted 10 Sep 2007) ❑