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Original articles

An outbreak of gastroenteritis linked to a buffet lunch served at a Canberra restaurant

Timothy S Sloan-Gardner, Anna-Jane Glynn-Robinson, April Roberts-Witteveen, Radomir Krsteski, Keith Rogers, Andrew Kaye, Cameron RM Moffatt

Abstract

In 2013, an outbreak of gastrointestinal illness occurred following a buffet lunch at a restaurant in Canberra. An investigation was conducted to identify the cause of illness and to implement appropriate public health measures to prevent further disease. We conducted a retrospective cohort study via telephone interviews, using a structured questionnaire developed from the restaurant buffet menu. A case was defined as someone who ate the buffet lunch at the restaurant on the implicated date and developed any symptoms of gastrointestinal illness (such as diarrhoea, abdominal pain and nausea) following the consumption of food. A total of 74% (225/303) of known attendees were interviewed, of whom 56% (125/225) had become ill. The median incubation period and duration of illness were 13 and 19 hours respectively. The most commonly reported symptoms were diarrhoea (94%, 118/125) and abdominal pain (82%, 103/125). A toxin-mediated gastrointestinal illness was suspected based on the incubation period, duration of illness and the symptoms. The environmental health investigation identified a lack of designated hand washing facilities in the kitchen, an absence of thermometers for measuring food temperatures and several maintenance and minor cleaning issues. A number of food samples were taken for microbiological analysis. Multivariable analysis showed that illness was significantly associated with consuming curried prawns (OR 18.4, 95% CI 8.6–39.3, $P < 0.01$) and Caesar salad (OR 3.6, 95% CI 1.8–7.5, $P < 0.01$). Enterotoxin-producing *Staphylococcus aureus* and *Bacillus cereus* were identified in leftover samples of cooked buffet food, but this food was not epidemiologically implicated. The investigation suggested that a breakdown in cleanliness, temperature control and food handling practices may have resulted in contamination of the buffet food. In order to prevent such outbreaks in the future, caterers and restaurateurs need to ensure they have the appropriate facilities and procedures in place if planning to cater for large groups. *Commun Dis Intell* 2014;38(4):E273–E278.

Keywords: outbreak, gastroenteritis, cohort study, public health, buffet

Introduction

In 2010, 42% (64/154) of the outbreaks investigated by OzFoodNet, Australia's enhanced foodborne disease surveillance network, were associated with restaurants and commercial caterers and affected over 880 people.[1]

Catering for large numbers of patrons can put additional pressure on food preparation systems, particularly if such functions are not a regular occurrence for a particular venue or caterer.[2] A total of 17 outbreaks associated with buffet style meals have been investigated by OzFoodNet since 2000 (OzFoodNet Outbreak Register, August 2013, unpublished data).

Bacterial enterotoxins are known causes of foodborne illness in Australia and worldwide. Symptoms of toxin-mediated gastrointestinal illness include diarrhoea, abdominal pain and vomiting with severity, and incubation period (ranging from 30 minutes to 16 hours) depending on the amount of toxin ingested and individual susceptibility. The illness is self-limiting; cases will usually recover within 48 hours and death is rare.[3–7]

Under the right environmental conditions, such as inadequate cooking, reheating or storage of food, inadequate cooling and temperature abuse, certain bacteria can produce enterotoxins.[4–7] Outbreaks due to bacterial enterotoxins are often underreported due the self-limiting nature of disease and people not seeking medical care or submitting stool samples.[5,8]

In 2013, the ACT Health Protection Service received complaints of gastrointestinal illness from 3 separate groups who attended the same restaurant for a buffet lunch on the same day in Canberra. Following an Acute Response Team meeting, an investigation was launched to identify the cause of illness and implement appropriate public health measures to prevent further cases.

Methods

Epidemiological investigation

Initial interviewing of complainants using a hypothesis generating questionnaire indicated that cases had attended the buffet lunch at a particular restaurant in Canberra on the same day.

We conducted a retrospective cohort study via telephone interview using a structured questionnaire developed from the restaurant buffet menu. The restaurant's booking list and interviews of known attendees were used to identify restaurant patrons on the day of the outbreak. Ethics approval was not sought for this investigation as the data were collected for the purpose of public health surveillance under public health legislation.[9]

A case was defined as a person who ate the buffet lunch at the restaurant on the implicated date and developed any symptoms of gastrointestinal illness (such as diarrhoea, abdominal pain or nausea) following the consumption of food.

Data collection and statistical analysis were conducted using Epi Info version 7.1.1.14 (Centers for Disease Control and Prevention, USA) and Stata version 10 (StataCorp., USA). Gender was compared using a chi-squared test and age was compared using a Wilcoxon rank sum test.

In univariable analysis, we compared food exposures among those who were ill with those who were not and generated crude risk ratios (RR), 95% confidence intervals (CI) and *P* values. We constructed an initial multivariable logistic regression model including food items with P values <0.1 in the univariable analysis, as well as age group, gender and seating location. The final model included statistically significant food items and gender, and generated adjusted odds ratios (OR), 95% CI and *P* values. A likelihood ratio test was conducted on the two models and Hosmer and Lemeshow test was carried out to test model fit.

Environmental health investigation

Environmental health officers (EHO) from the ACT Health Protection Service visited the premises after the outbreak to review the kitchen facilities and preparation procedures. During the initial inspection, samples of leftover foods were taken for laboratory testing.

Laboratory investigation

Food samples were tested by the Microbiology Unit of the ACT Government Analytical Laboratory (ACTGAL), ACT Health Protection Service. All food samples were initially tested for the presence of *Salmonella*, *Listeria monocytogenes*, *Escherichia coli*, coagulase-positive staphylococci (*S. aureus*), *Bacillus cereus* and a standard aerobic plate count was undertaken.

B. cereus and *S. aureus* isolated from food samples were sent to the Microbiological Diagnostic Unit (MDU) Public Health Laboratory, The University of Melbourne for further testing. The presence of *Bacillus* diarrhoeal enterotoxin (BDE), was determined using a 3M Tecra BDE Visual Immunoassay kit (3M Food Safety, Product No: BDEVIA48). The presence of staphylococcal enterotoxin (SET) was determined using a 3M Tecra SET Visual Immunoassay kit (3M Food Safety, Product No: SETVIA48). Analyses for BDE and SET were performed in accordance with the kit manufacturers' instructions, using a microplate reader (ThermoMax, Molecular Devices, USA).

Stool samples from 2 ill attendees were examined for a range of foodborne pathogens by ACT Pathology at the Canberra Hospital. Standard bacterial cultures were set up to test for the presence of *Salmonella*, *Campylobacter* and *Shigella*. Antigen tests were conducted for rotavirus and norovirus, and direct microscopy was performed for parasites.

Results

Epidemiological investigation

We interviewed 74% (225/303) of known attendees, of whom 56% (125/225) became ill (Table 1). None of those ill were hospitalised.

Males were more likely to be ill (crude RR 1.27 CI 1.0–1.6, $P < 0.05$) and there was no statistically significant difference in age ($P > 0.05$) between those ill and not ill.

Food for the buffet lunch was served in 3 different locations and all received the same food from the same kitchen. No significant difference was observed in the seating location between those who were ill and those who were not ($P > 0.5$).

Ninety-four per cent (118/125) of those ill reported experiencing diarrhoea, of which 79% (93/118) experienced 3 or more episodes of diarrhoea in 24 hours, and 82% (103/125) of those ill reported abdominal pain (Table 1). The median incubation period was 13 hours (range 1–33 hours) and the median duration of illness was 19 hours (range 1–55 hours). The epidemic curve was indicative of a point source outbreak, with a short incubation period and tight clustering of cases over time

Table 1: Demographic characteristics and symptoms of those ill and not ill following a buffet lunch, Australian Capital Territory, 2013

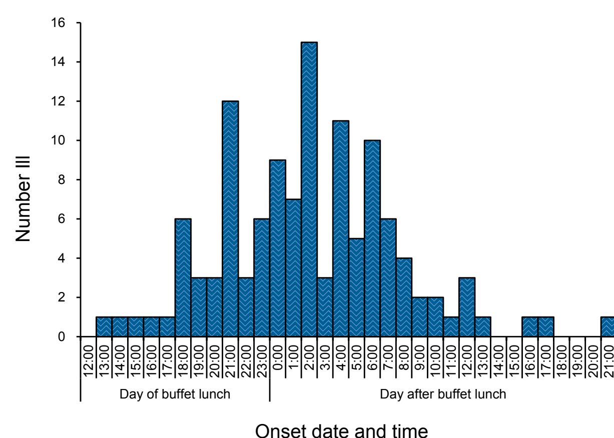
	Ill		Not Ill	
	N	%	N	%
Interviewed	125	56	100	44
Gender				
Male	66	53	39	39
Female	59	47	60	60
Gender unknown			1	1
Age				
Median age (years)	39		29	
0–19	17	14	41	41
20–39	43	34	28	28
40–59	35	28	12	12
60+	21	17	16	16
Age unknown	9	7	3	3
Symptoms				
Diarrhoea	118	94		
Abdominal pain	103	82		
3 or more diarrhoea in 24 hours	93	74		
Fatigue	40	32		
Nausea	38	30		
Headache	19	15		
Chills	15	12		
Fever	11	9		
Vomiting	11	9		
Muscle aches	9	7		
Other symptoms*	6	5		
2 or more vomiting in 24 hours	5	4		
Bloody diarrhoea	5	4		

* Other symptoms included cough, back pain and report of 'being warmer than usual'.

(Figure). A toxin-mediated gastrointestinal illness was suspected based on the incubation period, duration of illness and symptoms.

In the univariable analysis, multiple foods were found to be significantly associated with illness (Table 2). In the multivariable analysis, consuming curried prawns (OR 18.4, CI 8.6–39.3, $P < 0.01$) and Caesar salad (OR 3.6, CI 1.8–7.5, $P < 0.01$) were significantly associated with illness after adjusting for gender. When comparing gender and food consumption, ill males had higher odds (OR 1.9, CI 0.9–3.9, P 0.08) of having consumed the curried prawns and Caesar salad compared with ill females, although this was not statistically significant.

Figure: Epidemiological curve of case onset dates and times (n=120*) following a buffet lunch, Australian Capital Territory, 2013



* Five cases excluded due to missing onset times

Table 2: Univariable analysis of risk factors for foodborne illness following a buffet lunch, Australian Capital Territory, 2013

Food eaten	Exposed			Unexposed			Crude RR	95% CI	*P* value
	Cases	Total	AR %	Cases	Total	AR %			
Curried prawns	92	104	88	31	118	26	3.4	2.5–4.6	<0.01
Caesar salad	95	135	70	27	86	31	2.2	1.6–3.1	<0.01
Sweet and sour pork	103	151	68	20	70	29	2.4	1.6–3.5	<0.01
Beef stroganoff	91	135	67	31	84	37	1.8	1.4–2.5	<0.01
Rice	111	181	61	12	40	30	2.0	1.3–3.3	<0.01
Corn cobs	71	111	64	52	111	47	1.4	1.1–1.7	0.01
Orange and almond cake	55	83	66	68	139	49	1.4	1.1–1.7	0.01
Roast chicken	74	118	63	49	103	48	1.3	1.0–1.7	0.02
Chat potatoes	72	119	61	50	102	49	1.2	1.0–1.6	0.09
Blueberry cheesecake	74	127	58	49	95	52	1.1	0.9–1.4	0.32
Bread rolls	89	165	54	34	57	60	0.9	0.7–1.2	0.46
Condiments	16	31	52	106	190	56	0.9	0.6–1.3	0.67
Sausages	68	124	55	55	98	56	1.0	0.8–1.2	0.85

AR = Attack rate
RR = Risk ratio
CI = Confidence interval

The likelihood ratio test ($P < 0.05$) and the Hosmer and Lemeshow test ($P > 0.05$) indicated that the final model fitted the data well.

Environmental health investigation

The initial environmental health inspection of the premises found the need for kitchen repairs and cleaning of food preparation and non-preparation areas. Additionally, there was no dedicated sink for hand washing in the kitchen area and there was an absence of thermometers for measuring food temperatures. As a result of these findings, improvement notices were issued that required the repairs and cleaning to be carried out, along with staff training in food safety and the development of a food business management plan.

Details of the buffet food preparation and equipment used suggested evidence of temperature abuse through slow or inadequate cooling and prolonged food storage prior to service.

During the inspection, samples of leftover cooked roast chicken, peeled tomatoes in sauce, parboiled chat potatoes, raw bacon, hollandaise sauce, BBQ sauce and cooking cream were taken for laboratory testing.

Laboratory investigation

Initial laboratory testing of foods by ACTGAL detected *S. aureus* and *B. cereus* in samples of leftover cooked roast chicken, parboiled chat potatoes and raw bacon. Samples of the curried prawns and Caesar salad were not available for testing.

Testing at MDU confirmed the presence of both BDE and SET in cultures isolated from the cooked roast chicken and the parboiled chat potatoes. Cultures isolated from the raw bacon were negative for *S. aureus* and *B. cereus* enterotoxins.

The 2 human stool samples were collected 1 and 4 days respectively after the buffet lunch. Both were negative for *Salmonella*, *Campylobacter*, *Shigella*, norovirus and rotavirus.

Discussion

We report a large outbreak of gastrointestinal illness following a buffet lunch at a Canberra restaurant. The environmental health investigation found the need for repairs and cleaning at the restaurant. The results of the epidemiological investigation showed that illness was significantly associated with the consumption of curried prawns and Caesar salad from the buffet. Microbiological

evidence of enterotoxin-producing *B. cereus* and *S. aureus*, 2 pathogens previously implicated in foodborne outbreaks with similar symptom and onset profiles,[10,11] was found in leftover cooked food samples (cooked roast chicken and parboiled chat potatoes) of food served in the buffet. However, we were unable to definitively confirm the aetiological agent for this outbreak.

The results of the outbreak investigation suggest that food served at the buffet was responsible for the outbreak, and a breakdown in cleanliness, temperature control and food handling practices may have been contributing factors. The evidence for multiple food items from the buffet menu being contaminated with *B. cereus* and *S. aureus* suggests there was potential cross-contamination, adding to the evidence for a breakdown in food handling practices, with the resultant implications for human health.

Outbreaks involving buffet style meals have been investigated by OzFoodNet in the past.[12–16] This investigation highlights the care needed when catering for large groups, particularly when such events may not be a regular occurrence for some caterers. Restaurants need to ensure they have adequate facilities and training to cater for the numbers at such functions, and that they are following their food business management plans and food safety procedures in order to limit the potential for such outbreaks to occur.

Limitations

Whilst we were unable to contact and or interview all known attendees of the buffet lunch, approximately three-quarters of the known attendees were interviewed and we have achieved a representative cohort. There is a potential for selection bias due to our broad case definition, however, we are unlikely to have misclassification of those ill due to the rapid onset and severity of the gastrointestinal illness symptoms.

Measurement bias in our study was minimised using validated and standardised laboratory testing methods. Interviewer and recall bias were minimised by using a structured questionnaire developed around the set buffet lunch menu with prompts for all buffet food items. Potential confounders such as age and sex were controlled for in our regression analysis.

Another limitation of this study was the lack of samples (environmental/food/clinical) for laboratory testing. There were no leftovers of the epidemiologically implicated foods; only 2 stool samples were available for testing; and no environmental swabs were taken. As the stool samples were collected 1 and 4 days after the buffet lunch, it is possible that the enterotoxins may have been cleared by the individuals at the time of collection. Additionally, we were unable to test for the presence of BDE and SET in the stool samples using a validated method. These factors contributed towards not being able to definitively confirm the aetiological agent for this outbreak.

Conclusion

The incubation period, duration of illness and symptom profile were suggestive of a toxin-mediated illness in attendees following a buffet lunch at a Canberra restaurant, however, we were unable to definitively confirm the aetiological agent. The results of the investigation suggest that a breakdown in cleanliness, temperature control and good food handling practices may have resulted in contamination of the buffet food. In order to prevent such outbreaks in the future, caterers need to ensure staff are adequately trained and employing appropriate food preparation and handling practices to reduce potential risks when catering for large groups.

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Surveillance snapshot of *Clostridium difficile* infection in hospitals across Queensland detects binary toxin producing ribotype UK 244

Charlotte A Huber, Lisa Hall, Niki F Foster, Mareeka Gray, Michelle Allen, Leisha J Richardson, Jennifer Robson, Renu Vohra, Sanmarie Schlebusch, Narelle George, Graeme R Nimmo, Thomas V Riley, David L Paterson

Abstract

In North America and Europe, the binary toxin positive *Clostridium difficile* strains of the ribotypes 027 and 078 have been associated with death, toxic megacolon and other adverse outcomes. Following an increase in *C. difficile* infections (CDIs) in Queensland, a prevalence study involving 175 hospitals was undertaken in early 2012, identifying 168 cases of CDI over a 2 month period. Patient demographics and clinical characteristics were recorded, and *C. difficile* isolates were ribotyped and tested for the presence of binary toxin genes. Most patients (106/168, 63.1%) were aged over 60 years. Overall, 98 (58.3%) developed symptoms after hospitalisation; 89 cases (53.0%) developed symptoms more than 48 hours after admission. Furthermore, 27 of the 62 (67.7%) patients who developed symptoms in the community had been hospitalised within the last 3 months. Thirteen of the 168 (7.7%) cases identified had severe disease, resulting in admission to the Intensive Care Unit or death within 30 days of the onset of symptoms. The 3 most common ribotypes isolated were UK 002 (22.9%), UK 014 (13.3%) and the binary toxin-positive ribotype UK 244 (8.4%). The only other binary toxin positive ribotype isolated was UK 078 (n = 1). Of concern was the detection of the binary toxin positive ribotype UK 244, which has recently been described in other parts of Australia and New Zealand. No isolates were of the international epidemic clone of ribotype UK 027, although ribotype UK 244 is genetically related to this clone. Further studies are required to track the epidemiology of ribotype UK 244 in Australia and New Zealand. *Commun Dis Intell* 2014;38(4):E279–E284.

Keywords: *Clostridium difficile;* disease surveillance; hospitals

Introduction

Clostridium difficile commonly causes infectious diarrhoea and is the main aetiological agent of pseudomembranous colitis.[1] *C. difficile* strains of the ribotypes UK 027 and UK 078 have been associated with severe adverse outcomes such as toxic megacolon, colonic perforation, peritonitis, and increased mortality rates in North America and Europe.[2] The hypervirulence of these strains has been attributed to the increased production of toxins A and B, as well as the presence of the binary toxin.[3]

Following the first report of local transmission of *C. difficile* ribotype UK 027 in Australia in 2009,[4] a national laboratory survey was performed, but did not detect any strains of potentially hypervirulent ribotypes in Queensland (unpublished data, personal communication, T Riley). Between October 2011 and early 2012, we observed an increase in *C. difficile* infections (CDI) in Queensland Health facilities using passive surveillance of diagnostic laboratory pathology results.[5] Here we provide a more detailed state-wide snapshot of the epidemiology of hospital-identified CDI cases in Queensland in early 2012.

Methods

Study design and definitions

All Queensland public hospitals (n = 170) and 5 private hospitals in Queensland, were invited and agreed to take part in the cross-sectional prevalence study. Between 10 April and 15 June 2012, patients aged over 2 years with diarrhoea at admission or during hospitalisation and testing positive for *C. difficile* were included in the study. The Australian definitions of hospital identified CDI[6] were used to identify cases, and classify recurrence and severe disease. A summary of these definitions are provided in Table 1. Patient samples collected during this time were cultured when available. *C. difficile* isolates were ribotyped and screened for the presence of the binary toxin in order to investigate the prevalence of epidemic strains.

Surveillance data collection and analysis

Basic demographic and clinical data including data on patient location at onset of symptoms, history of recent hospitalisation and antibiotic use were collected by infection control practitioners on a one page survey. Data were subsequently submit-

ted to the Centre for Healthcare Related Infection Surveillance and Prevention (CHRISP) and entered into a spreadsheet. CHRISP is the state-wide unit responsible for overseeing healthcare associated infection surveillance, and prevention and control policy in Queensland public facilities (www.health.qld.gov.au/chrisp). A follow-up survey was conducted 30 days after symptom onset to determine the prevalence of severe CDI using Australian surveillance guidelines (Table 1). De-identified data were imported into IBM SPSS version 20 for further descriptive analysis, including chi-squared tests for differences in proportions.

Laboratory methods

C. difficile was cultured from stool specimens that tested *C. difficile* toxin positive by either polymerase chain reaction (PCR) or enzyme immunoassay (EIA) at the referring laboratories. At the time of this snapshot a testing algorithm was in place across Queensland to ensure consistency in laboratory methods used. PCR ribotyping was performed as previously described.[7,8] Briefly, genomic DNA was extracted from 24 hour horse blood agar cultures using the UltraClean Microbial DNA Isolation kit (MO BIO Laboratories Carlsbad, CA, United States) then PCR ribotyping was performed, using an ABI 3130 capillary sequencer (Applied Biosystems) with a GeneScan™ 1200 LIZ® Size Standard (Applied Biosystems). The capillary sequencer data were uploaded to the Webribo database (http://webribo.ages.at/). UK ribotypes were determined for a representative of each Webribo ribotype, using the Anaerobe Reference Unit (Cardiff, UK) nomenclature where reference strains were available. This was done by comparing PCR products, concentrated using the Qiagen MinElute PCR purification kit, then separated using the QIAxcel capillary electrophoresis platform (Ambion Inc, Austin, Texas), to the UWA/PathWest reference library as previously described.[10] The library consisted of 50 UK ribotypes including 15 reference strains from the European Centre for Disease Prevention and Control and the most prevalent PCR ribotypes circulating in Australia. If a UK ribotype could not be assigned, local nomenclature (QX type) or webribo (WR type) nomenclature was assigned. Screening for binary toxins was performed as previously described.[10]

Ethics

This study was considered to be a quality assurance audit by the Department.

In Queensland, the use of confidential patient information for audit is legislated under Section 62H of the *Health Services Act 1991*. Approval was obtained from the Chief Health Officer of Queensland Health, and Chief Executive Officers of each private facility.

Ethical approval for this surveillance was not required as: surveillance of CDI in Queensland Health facilities is required in accordance with the Queensland Health Protocol for the Surveillance of Healthcare Associated Infection; private hospitals in Queensland are required to undertake infection control surveillance in accordance with the Infection Control Standard of the *Private Health Facilities Act 1999.*

Results

Patient characteristics

During the audit period, a total of 168 CDI cases were identified. The patients ranged in age from 3 to 100 years, with a median age of 68.5 years. A total of 36 cases were reported from private hospitals. Key descriptive variables such as age and location at onset of symptoms were compared using chi-square tests and did not significantly vary between private and public hospital patients so the data were combined. A summary of patient characteristics is shown in Table 1.

The majority of cases (98/168, 58%) developed symptoms following hospitalisation, however in nine of these patients, symptoms began within 48 hours of admission. Five of the nine had a record of previous hospitalisation in the last month. Of the 62 cases that were community-onset, 27 (43%) had been admitted to a hospital in the previous month and 15 (24%) in the previous 1 to 3 months. Fifteen (9%) of the CDI cases were admitted from a residential or long term care facility (R/LTCF). However, only four of these cases had onset of symptoms within their R/LTCF.

Severe disease

Thirteen (7.7%) CDI cases were classified as severe disease using surveillance definitions. Nine of the 13 had been admitted to hospital in the previous 3 months. No patients with severe CDI had been admitted from an R/LTCF.

The 30-day mortality following diagnosis was 3.6%. Of the 6 patients who died, four had been admitted to hospital within the past month, two had recurrent CDI and two had onset of symptoms in the community. All 6 cases had been prescribed antibiotics in the last month. The mean age of these patients was 75.8 years, (95% CI: 67.1–84.6), which was significantly greater than CDI patients who did not develop severe disease (62.1 years, 95% CI: 57.1–67.0). Due to the pres-

Table 1: *Clostridium difficile* infections patient characteristics

Survey variable	Number of cases (n = 168)	Percentage
Age range		
2–20	10	6.0
21–40	22	13.1
41–60	30	17.9
61–80	59	35.1
80+	47	28.0
Sex		
Male	86	51.2
Female	82	48.8
Patient location at onset of symptoms		
Hospital	98	58.3
Residential/long term care facility	4	2.4
Community	62	36.9
Not reported	4	2.4
Previous hospitalisation		
Within the last month	86	51.2
Within last 1–3 months	33	19.6
More than 3 months ago	16	9.5
No previous hospitalisation	19	11.3
Not reported	14	8.3
Admission from residential/long term care facility		
Within the last month	15	8.9
No previous residential/long term care admission	153	91.1
Is this episode a recurrence (within 8 weeks of onset of previous episode)?		
Yes	20	11.9
No	135	80.4
Not reported	13	7.7
Antibiotic therapy in the last month		
Yes	136	81.0
No	13	7.7
Not reported	19	11.3
Severity of disease		
Intensive care admission for CDI	7	4.2
Colectomy due to CDI	0	0.0
Mortality within 30 days related to infection	6	3.6
No severe disease	91	54.2
Not reported	64	38.1

CDI *Clostridium difficile* infections.

ence of significant co-morbidities it was difficult to ascertain whether the primary cause of death in these patients was CDI.

Ribotyping data

C. difficile isolates were obtained from 83 (81.4%) of 102 specimens submitted for culture. The prevalence of ribotypes detected is shown in Table 2. The most commonly isolated ribotype was UK 002 (22.9%), and UK 014 was the 2nd most prevalent (13.3%). Ribotypes UK 014 and UK 020 are often combined due to difficulty distinguishing between their ribotyping patterns. The UK 014/020 group constituted 19.3% of isolates.

Table 2: Prevalence of ribotypes detected during the study n = 83

Ribotype	N	% of isolates
UK 002	19	22.9
UK 014	11	13.3
UK 244	7	8.4
QX 014 WR AI-37	5	6.0
UK 056	5	6.0
UK 043	4	4.8
UK 020	3	3.6
QX 025	2	2.4
QX 150 WR 632	2	2.4
UK 014/020	2	2.4
UK 017	2	2.4
UK 049	2	2.4
UK 054	2	2.4
UK 070	2	2.4
Unique*	15	18.1

* Includes UK 005, UK 015/191, UK 018, UK 070, UK 076, UK 078, UK 087, UK 126, QX 026 WR 404, QX 029 WR 409, QX 033 WR AI-83, QX 072 WR 629, QX 095 WR AI-34, QX 266 WR 637 and QX 291 WR 641.

There were no isolates of ribotype UK 027, and only 1 isolate was ribotype UK 078. This case (a 46-year-old male) had onset of symptoms more than 48 hours after admission to hospital, and did not develop severe disease.

Ribotype UK244 was the 3rd most common ribotype circulating with 7 cases detected. Further detail on the cases infected with ribotype UK 244 is presented in Table 3.

Discussion

The results of this snapshot give insight into the burden of disease as well as the prevalence of hypervirulent *C. difficile* strains in Queensland. In Queensland all public hospitals (n = 170) are serviced by Pathology Queensland or Mater Pathology laboratories, with consistent laboratory protocols, and data stored in a centralised database. As a result we were able to identify all public hospital CDI cases during this time. In addition, with the support of five of the largest private facilities in the state, and their pathology providers, this study provided a detailed state-wide picture of the prevalence of cases, demographic and clinical risk factors and circulating ribotypes.

The study emphasised the importance of timely surveillance by infection control practitioners (ICPs). We were able to gather very useful information with the support of ICPs, to confirm that CDI is not just a hospital issue in Queensland, with 37% (62/168) of cases developing symptoms in the community.

We believe previous admission to hospital may still play a role in cases with onset of symptoms in the community and residential care facilities. The majority of cases in this study developed symptoms only after hospitalisation (98/168 58%). Of the 9 patients who had their onset within 48 hours of hospital admission, five had had a previous hospital admission in the last month.

Table 3: Characteristics of patients infected with *Clostridium difficile* ribotype 244

Age (years)	Sex	Hospital type	Onset of symptoms	Resident	Severity of disease
54	F	Private	Community	No	No severe disease
85	F	Public	Community	No	ICU admission
42	F	Public	Community	No	No severe disease
25	M	Public	Hospital	No	No severe disease
82	F	Public	Hospital	No	Died
88	F	Public	Hospital	Yes	Unknown
52	M	Public	Hospital	No	No severe disease

ICU Intensive care unit.

Of the 62 cases who developed symptoms in the community, 27 (44%) had been admitted to a hospital in the previous month and 15 (24%) in the previous 1 to 3 months. Frequent movement of patients between hospital and the community may contribute to the challenge of determining the true place of exposure, making traditional classifications of healthcare versus community associated infection misleading.[11]

Thirteen of the 168 (7.7%) CDI cases were classified as severe. The 30-day mortality was 3.6%. However, due to the advanced age of the 6 patients who died, as well as the presence of co-morbidities, it was difficult to ascertain whether the primary cause of death in these patients was CDI.

Only 49% of cases had an isolate ribotyped. We believe this is still representative of circulating ribotypes, as there did not appear to be any particular hospitals or laboratories more likely to have their samples successfully typed. Unfortunately, we were not able to ribotype strains from all cases of severe disease. Clinicians should be reminded to notify ICPs of suspected cases of severe disease in a timely fashion, as they are best placed to liaise with laboratories to ensure typing occurs.

Of the 102 specimens obtained for culture, 83 were successfully cultured and ribotyped. Of those ribotyped the most frequently isolated ribotype was UK 002 (19/83, 22.9%), which has also been most commonly detected in other regions of the world, such as Southern Scotland,[12] and Hong Kong where it has been associated with increased sporulation.[13] Ribotype UK 014 was the 2nd most prevalent ribotype (13.3%). Ribotypes UK 014 and UK 020 are often combined due to difficulty distinguishing between their ribotyping patterns. The UK 014/020 group constituted 19.3% of isolates. This was concordant with a European study reporting a combined prevalence of 16%.[14]

There were no isolates of ribotype UK 027, which is known to have caused severe disease in North America and Europe.[2] Only 1 isolate was ribotype UK 078, a community-associated strain with increased potential to cause severe disease.[15] However, this case (a 46-year-old male) had onset of symptoms more than 48 hours after admission to hospital, and did not develop severe disease. The link between the presence of hypervirulent strain type and severity of disease remains difficult to elucidate, although evidence for the importance of strain type as an independent risk factor is increasing.[3] In the United States of America, the CDI epidemic saw the emergence of 'hypervirulent' strains in an older and sicker population, which made it challenging to determine whether the rise in severity was due to the pathogen, or due to other host factors such as age and co-morbidities.[16]

There has been Australia-wide interest in the prevalence of ribotype 244 – a recently described strain that appears to be closely related to 027, and which is possibly of similarly high virulence.[17] In Australia, ribotype 244 was first detected by The University of Western Australia in specimens from a large Sydney hospital (personal communication, T Riley, 22 April 2013). Ribotype 244 has since been detected in several parts of Australia, and in New Zealand where it was associated with severe disease and community onset of infection.[18,19]

The risk of ribotype UK 244 in the Queensland population is unknown. Although in other Australian jurisdictions ribotype 244 has previously been reported to be a community ribotype associated with a high probability of severe disease, this was not uniformly the case in this Queensland study. Lim et al have recently published a case-control study of 14 ribotype 244 cases, matched by hospital locality and date of diagnosis to 24 controls; demonstrating a clinically, but not statistically significant increase in severity and 30 day mortality.[19]

Further larger studies, incorporating a more geographically representative range of hospitals, may be required to determine the risk associated with this ribotype in Australia. In addition, regardless of ongoing efforts to monitor hospital infections,[5] it would be useful for a continuous national passive surveillance program to be considered, with periodic ribotyping. This type of surveillance, such as that undertaken for nationally notifiable conditions, would assist decision makers to determine the level of risk to the community, and plan public health interventions in a more timely fashion.

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Histamine fish poisoning in Australia, 2001 to 2013

Katrina E Knope, Timothy S Sloan-Gardner, Russell J Stafford

Abstract

We report on histamine fish poisoning outbreaks in Australia from 2001 to 2013. Histamine fish poisoning results from the ingestion of histamine contained within the flesh of certain fish species that naturally contain histidine, which has been converted to histamine by spoilage bacteria following poor handling or temperature control after harvesting. While symptoms vary, allergic symptoms such as facial flushing, headaches and rashes are frequently reported. Using the OzFoodNet outbreak register, published case reports and surveillance reports, we found data on 57 outbreaks of histamine fish poisoning, which affected 187 people, of whom 14% were hospitalised. There were no deaths reported. Outbreaks were generally small in size, with a median of 2 cases per outbreak (range 1 to 22 people), with 88% of outbreaks comprising less than 5 people. Tuna (in the family Scombridae) was the most frequently reported food vehicle, while 18 outbreaks involved non-scombridae fish. Median incubation periods among the outbreaks were short; being less than 1 hour for 22 outbreaks. The most frequently reported symptoms were diarrhoea and rash. Symptoms of facial/body flushing were reported for at least one case in 19 outbreaks and tingling, burning or swelling of the skin, especially around the lips for at least 1 case in 13 outbreaks. In 3 outbreaks, one or more cases were reported to have had respiratory distress or difficulty breathing. While the condition is often mild, improved recognition and appropriate treatment is important, as it will reduce the possibility of any severe health effects resulting from this condition. Key features of histamine fish poisoning outbreaks are the high attack rate, rapid onset, the typical symptoms and their short duration. *Commun Dis Intell* 2014;38(4):E285–E293.

Keywords: foodborne disease, histamine fish poisoning, OzFoodNet, scombroid, outbreaks

Introduction

Scombroid (or histamine fish) poisoning derives its name from the family of dark fleshed fish, or Scombridae (tuna and mackerel), with which it was first associated.[1] The illness is a chemical intoxication that occurs after the ingestion of bacterially contaminated fish that contain high levels of histamine.[2, 3] Non-scombroid fish with relatively high levels of naturally-occurring histidine in their flesh, including mahi-mahi (dolphinfish), swordfish, salmon, sardines and marlin have since been implicated, thus the disease is now more accurately described as histamine fish poisoning.[3, 4]

Symptom onset is rapid, usually within minutes to a few hours after consumption of the implicated fish.[5] Symptoms may vary for different individuals depending on underlying medical conditions and medications but can include flushing of the face, neck and upper arms, oral numbness and/or burning, metallic taste, headache, itchy rash, hives, nausea, vomiting, diarrhoea and difficulties swallowing. The illness is generally self-limiting and recovery usually occurs within 24 hours. When required, antihistamines are used to treat symptoms.[6] There have been reports of more severe presentations including hypotension, tachycardia, palpitations, respiratory distress and shock,[7,8,9] with a report of histamine fish poisoning leading to asthma exacerbation.[10]

There are 3 elements that are required for histamine fish poisoning to occur. Firstly, the fish must have high levels of free histidine present. Secondly, certain bacteria that produce the enzyme histidine decarboxylase, particularly *Morganella morganii*, *Klebsiella pneumoniae* or other Enterobacteriaceae must be present in the fish.[11] This enzyme is responsible for the conversion of histidine to histamine.[12] Lastly, there must be some form of inappropriate handling or temperate abuse that allows the multiplication of these bacteria and thus the production of histamine. As histamine is heat stable, cooking does not reduce the risk of illness.[12] The Food Standards Code states that the level of histamine in fish and fish products must not exceed 200 mg/kg.[13]

Diagnosis of histamine fish poisoning is usually based on the short onset time, clinical symptoms (including resolution of symptoms following appropriate treatment), and a history of consumption of fish. Occasionally, leftover fish can be collected and tested for high levels of histamine.

In the United States of America (USA), histamine fish poisoning accounted for 7.6% of all foodborne illness outbreaks and 38% of those specifically seafood-related based on USA foodborne illness outbreak data from the Center for Science in the Public Interest from 1990 to 2003.[14] There were 223 outbreaks of histamine poisoning, affecting 865 people

in the US between 2000 and 2007.[15] Combining this with USA poison control centre data from the National Poisoning Data System for 2005 to 2009, and using a model to similar to Scallan et al.,[16] they estimated that there are 35,142 histamine fish poisoning cases annually in the USA.

Histamine poisoning is not notifiable in any state or territory in Australia; hence there is very limited data available on the incidence of this illness. Public health data collected on histamine poisoning is usually derived from outbreak investigations in those jurisdictions in which two or more cases of suspected foodborne illness is notifiable. Based on data circa 2000, OzFoodNet estimates that there are approximately 280 cases of histamine fish poisoning annually in Australia.[17]

Few outbreaks and cases of histamine fish poisoning occurring in Australia prior to 2001 have been reported in the literature. An outbreak related to tailor fish was reported in 1985,[18] an outbreak related to a tuna dish served at a restaurant with two cases was reported in 1993[19] and 2 separate outbreaks involving a total of 7 cases related to West Australian salmon cooked in 2 private homes were reported in 1992.[20] This study represents the first published analysis of national histamine fish poisoning cases. We aimed to describe the epidemiology of histamine fish poisoning cases between 2001 and 2013.

Methods

Study type

We conducted a retrospective descriptive case series analysis of outbreaks and single cases of histamine fish poisoning that occurred in Australia between 2001 and 2013.

Case definition

Outbreaks and single cases where histamine fish poisoning (or scombroid) was listed as the suspected or confirmed aetiology and where onset of the first case (or the single case) occurred during the period 2001 to 2013 were included in the analysis.

Data collection

Data were collected from 3 different sources: published literature, the OzFoodNet outbreak register and OzFoodNet fortnightly enteric surveillance reports. These latter 2 sources are not publically available.

The details of histamine fish poisoning cases or outbreaks identified through the literature or fortnightly enteric surveillance reports but not recorded in the outbreak register were confirmed with OzFoodNet epidemiologists in the state or territory where the outbreak occurred. A preliminary report was obtained for 1 outbreak that had not yet been entered into the outbreak register. A single outbreak that was reported in the literature but not included in the OzFoodNet outbreak register was also included.[21] For the purposes of the analysis, single cases of histamine fish poisoning were treated as outbreaks.

Data were summarised by the number of outbreaks, number affected, median incubation period, the range of reported symptoms and those most commonly reported, whether cases required hospitalisation or other medical treatment, the food vehicles involved and levels of contamination in the foods, the settings where the food was cooked and the factors contributing to the foods involved in the outbreaks becoming contaminated. For the purpose of the analysis, the setting was defined as the place where the food was cooked. Analyses were carried out in Microsoft Excel®.

The year and month of onset was calculated from the date of onset of symptoms for the first case in the outbreak, known as the onset date.

Human research ethics approval

Human research ethics committee approval was not sought or required because the information about outbreaks was collected under state and territory public health legislation, and this analysis is consistent with the purpose for which the data were collected.

Results

Epidemiological features

There were 57 outbreaks of histamine fish poisoning in Australia between 2001 and 2013 (Figure) (Appendix). Nine of these were incidents involving a single person. The OzFoodNet outbreak register contained information on 41 of these outbreaks, while a further 14 were identified through the fortnightly enteric disease surveillance reports, one through an OzFoodNet Epidemiologist sending in a preliminary outbreak summary and one through a published outbreak summary.[21] Clinically compatible illness was reported by 187 people, with 90 people requiring treatment from a medical practitioner, including 27 people (14%) in 13 outbreaks who required hospitalisation. There were no reported deaths.

Outbreaks were generally small in size, with a median of 2 cases per outbreak (range 1 to 22 people), with 88% of outbreaks (50/57)

comprising less than 5 people. Attack rates were high, with 35% of people (105/299) who were known to have consumed the foods becoming ill. Attack rates were between 80% and 100% for the outbreaks for which an attack rate could be calculated (n=18).

All states and territories except Western Australia reported at least one outbreak. Outbreaks occurred in all years except 2002, and there was no clear seasonal trend, although February was the most frequent month of onset (11/57 outbreaks).

Median incubation periods for the outbreaks were short; being less than 1 hour for 39% (22/57) of outbreaks. In five of these, the median incubation period was reported to have been 15 minutes or less. In the remaining 35 outbreaks; 19 had a median incubation period of 1 hour and seven had a median incubation period of between 2 and 4 hours while the median incubation period was unknown or not provided for 9 outbreaks.

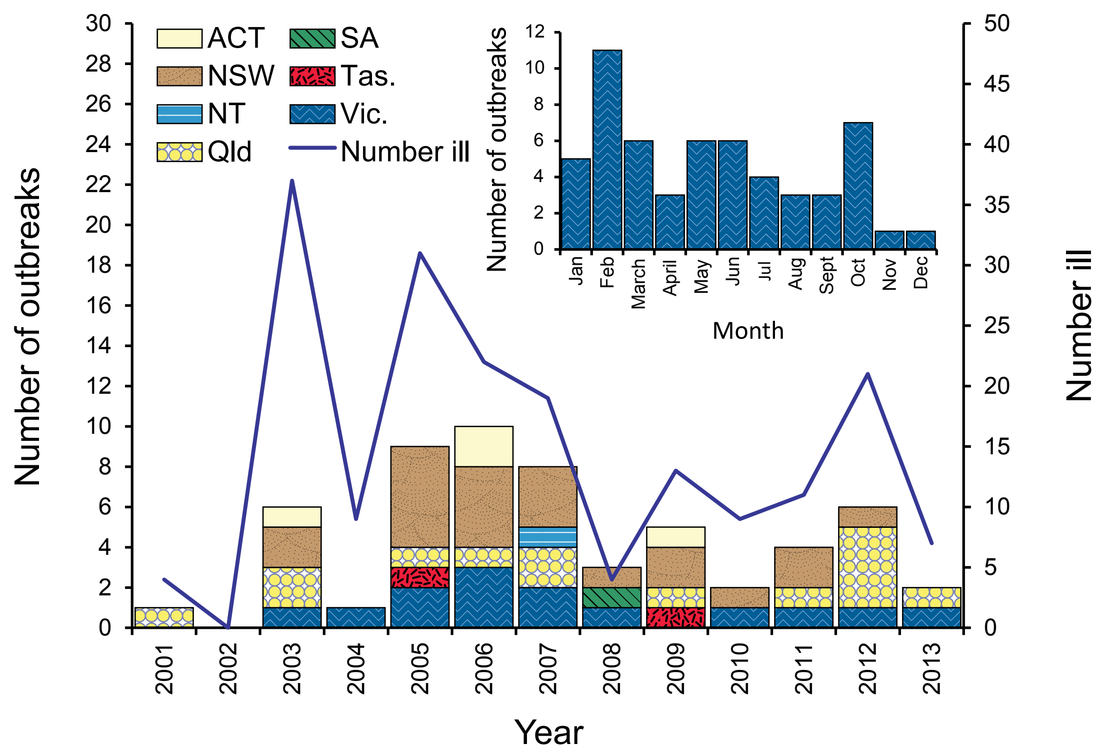
Frequency data for symptoms experienced by cases was not reported for all outbreaks, and the range of symptoms reported varied across outbreaks. For those cases where information of symptoms were available, the most frequently reported symptoms were diarrhoea (78%, 68/87) and rash (77%, 65/84), while nausea, vomiting, fever and abdominal pain were each reported for approximately half of the cases (between 43% and 56%) (Table 1).

Additional information about symptoms were recorded for some outbreaks in a free text comments field. Symptoms reported in this field included facial/body flushing (19 outbreaks), skin-related symptoms (tingling or burning or swelling of skin especially around the lips, but also fingers) (13 outbreaks), headache (10 outbreaks) and cardiac symptoms (racing heart or palpitations or tachycardia or bradycardia) (10 outbreaks). Four cases were reported to have had respiratory distress or difficulty breathing.

Exposure settings

Outbreaks were most commonly associated with foods prepared in restaurants (47%, 27 outbreaks) and private residences (35%, 20 outbreaks). A small number of outbreaks were associated with foods that were commercially manufactured (5%, 3 outbreaks) (Table 2). The 3 commercially manufactured foods were tinned tuna (2 outbreaks) and anchovies (1 outbreak).

Figure: Outbreaks of histamine fish poisoning, Australia, 2001 to 2013, by year and state or territory,* and inset: outbreaks of histamine fish poisoning between 2001 and 2013, by month†



* There were no outbreaks reported from Western Australia.

† One outbreak in the Australian Capital Territory involving 4 cases is reported by year of publication because no onset dates are available. This outbreak is not included in the inset.

Table 1: Frequency data for symptoms reported for cases in outbreaks of histamine fish poisoning, Australia, 2001 to 2013

Symptom	Number of outbreaks with information	Number of cases with symptom	Number of cases with information available	Proportion of cases reporting symptom %
Diarrhoea	44	68	87	78
Rash	45	65	84	77
Nausea	41	35	62	56
Vomiting	42	14	28	50
Fever	41	23	49	47
Abdominal pain	41	20	47	43

Table 2: Food vehicles involved in outbreaks of histamine fish poisoning, Australia 2001 to 2013, by setting where the food was cooked

Food vehicle	Restaurant	Private residence	Commercially manufactured	Retail	Commercial caterer	School	Unknown	Total
Tuna	12	13	2	2	0	1	2	32
Mahi-mahi	7	1	0	0	0	0	0	8
Yellowtail kingfish/ kingfish	3	0	0	0	0	0	1	4
Fish-unknown species	2	1	0	0	0	0	1	4
Butterfish/ rudderfish	1	0	0	0	1	0	0	2
Seafood marinara	1	0	0	0	0	0	0	1
Seafood extender	0	1	0	0	0	0	0	1
Seafood – unknown	0	1	0	0	0	0	0	1
Sardines	0	1	0	0	0	0	0	1
Mullet	0	1	0	0	0	0	0	1
Marlin	1	0	0	0	0	0	0	1
Anchovies	0	1	0	0	0	0	0	1
Total	27	20	2	2	1	1	4	57

Suspected food vehicles

Tuna (in the family Scombridae) was the most frequently reported food vehicle (57%, 32 outbreaks) (Table 2), while 18 outbreaks involved nonScombridae fish, including mahi-mahi (14%, 8 outbreaks) and yellowtail kingfish, or kingfish (7%, 4 outbreaks). Levels of histamine in the foods associated with illness were reported for 24 outbreaks. Unacceptable levels of histamine (>200 mg/kg) were confirmed in the fish or seafood samples during 16 (28%) outbreak investigations, ranging between 270 mg/kg and 7,000 mg/kg (Appendix). In 6 outbreaks, the food was not considered to have been epidemiologically implicated. For 1 further outbreak, foods were stated to have been positive for histamine, but levels were not stated, and for another outbreak, histamine levels were reported to be high, but levels were not stated. For 4 outbreaks, results for multiple samples were available, and the levels of histamine in the seafood varied widely between samples, for example, ranging between 160 mg/kg and 5,100 mg/kg for samples taken during 1 outbreak investigation.

The source countries for the fish products involved in the outbreaks were rarely reported. In 6 outbreaks, the foods involved were thought to have been imported from overseas. Five of these involved foods imported from Indonesia (4 were tuna and 1 was mahi-mahi) and 1 outbreak involved tinned anchovies imported from Morocco. Two further outbreaks involved canned tuna, but the country of origin of the tuna was not specified.

Possible factors contributing to contamination

Possible factors contributing to the production of toxics levels of histamine in the food were collected systematically for the 41 outbreaks reported in the OzFoodNet outbreak register, while descriptions of possible process failures were also available for eight of these. No information on contributing factors was available for the 16 outbreaks (including the 9 incidents involving a single person) that were identified from sources other than the outbreak register. In two-thirds of the outbreaks (66%, 27/41), investigators reported that inadequate refrigeration, or foods being left at room temperature contributed to toxin production, but this was only confirmed by visual observation for one of the outbreaks.

Discussion

This study represents the first national analysis of histamine fish poisoning cases in Australia. Over the study period, there were 57 outbreaks affecting 187 people, of whom 14% required hospitalisation. The outbreaks reported here are similar to the number reported internationally. In the USA between 2000 and 2007, there were 223 outbreaks of histamine fish poisoning affecting 865 people.[15] In Europe, 34 outbreaks of histamine fish poisoning were reported in 2012, with a total of 241 cases, of which 14 were hospitalised.[22] France and Spain contributed 68% of the cases.[22]

The small size of the outbreaks precluded more detailed analysis of the association between food and illness. However, the descriptive epidemiology of the outbreaks did contribute to identifying linked cases with a common food exposure. The foods involved in the outbreaks reported here were most frequently Scombridae fish (tuna), but the consumption of other fish species (mahi-mahi) were shown to also be important causes of histamine fish poisoning.

Where histamine levels in the foods associated with illness were reported, two-thirds contained a concentration of histamine that exceeded the acceptable level under the Food Standards Code,[13] however, there were 7 outbreaks where the histamine concentrations were below the maximum acceptable levels. Bartholomew et al. noted that some people displayed clinically compatible symptoms of histamine fish poisoning after consuming fish with levels of <200 mg/kg.[23] The toxic dose threshold for histamine in food is unknown, though factors such as the part of the fish eaten and individual susceptibility may increase the toxic effect.[6]

The most frequent setting involved in the outbreaks was restaurants. This is similar to outbreaks reported for Europe in 2012, where 50% of outbreaks were from this setting. In contrast, only 12% of European outbreaks were reported from private homes.[22] The point at which the fish became contaminated, or at which histamine levels in the flesh began to increase cannot be determined from the data presented here, because data are presented by the place where the food was cooked. Once histamine is formed, appropriate handling, and even canning will not reduce the risk of health effects in consumers, as it is heat stable. This is demonstrated through the outbreaks reported here, with 3 outbreaks involving canned fish.

Hospitalisation information for histamine fish poisoning outbreaks is likely to underestimate the proportion of illnesses that might be considered serious. Investigators report that cases frequently present to emergency departments (Jennie Musto personal communication), but emergency department presentations are not counted within the number hospitalised. It is important to note that emergency department presentation is not always an indicator of severity, but may also reflect the time of day (when GP surgeries are closed) or economic reasons.

While the data presented here contained little detail on the possible factors leading to contamination, the most important contributing factor to histamine poisoning is known to be improper refrigeration of the harvested fish, which enables bacterial proliferation.[22] Rapid chilling of fish immediately after they are caught will reduce the risk of histamine formation. It is important that adequate temperature control is maintained from harvesting of fish throughout the wholesale and retail chain to the plate.

A comparison between the number of people affected per year as reported here (14.4 cases per year) and OzFoodNet estimates of annual case numbers (280 cases),[17] suggests that the cases reported in this study represent only 5% of cases occurring in the community each year. The outbreaks reported here were small in size, but it is possible that other cases associated with consumption of the same foods were not reported. A range of factors may contribute to the small size of reported outbreaks, or to outbreaks not being reported. Symptoms of histamine fish poisoning may often be mild, non-specific, and may resolve quickly and without treatment, and therefore the symptoms may be misdiagnosed or missed altogether, and medical attention may not be sought. The lack of a laboratory test to confirm current or recent histamine fish poisoning further reduces case ascertainment. Histamine fish poisoning is not a separately notifiable condition in Australia, and thus cases may only be reported when an outbreak is known to have

occurred. In the USA, where it is estimated that for every histamine fish poisoning case reported within an outbreak there are 317 cases in the community, underreporting of histamine fish poisoning cases still occurs, even in states where reporting of single cases is required.[15]

The increasing importance of international trade in food products can lead to increased risks of foodborne illness. OzFoodNet reports 2–3 outbreaks each year involving foods imported into Australia.[24] Six of the outbreaks in this study involved imported foods, five of them associated with tuna from Indonesia.

Conclusion

This is the first published national analysis of cases of histamine fish poisoning in Australia. Although typically a mild manifestation, histamine fish poisoning can result in more severe outcomes, including hospitalisation. A combination of factors including people not seeking medical care, misdiagnosis, and underreporting results in the true burden of this disease remaining unknown.

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Appendix: Outbreaks of histamine fish poisoning, Australia, 2001 to 2013*

Year	Setting	Number affected	Number required medical treatment	Number hospitalised	Food vehicle	Imported food	Histamine level reported mg/kg
2001	Restaurant	4	Unknown	0	Mahi-mahi fillets		Unknown
2003	Restaurant	6	4	1	Yellowfin tuna		470 and 490
2003	Private residence	2	2	0	Tuna patties		No samples available/taken
2003	Private residence	2	2	2	Sardines		2,961
2003	Restaurant	22	2	0	Butterfish (rudderfish) medallions		270
2003	Restaurant	3	2	0	Mahi-mahi		Unknown
2003	Restaurant	2	2	0	Thai fish cakes		Positive, level not stated
2004	Commercial caterer	9	0	0	Rudderfish		Unknown
2005	Private residence	2	0	0	Fish (unknown species)		60
2005	Private residence	4	4	0	Tuna steak		No samples available/taken
2005	Restaurant	2	1	0	Yellowfin tuna		No samples available/taken
2005	Restaurant	2	2	0	Yellowfin tuna		1,700
2005	Restaurant	2	2	0	Tuna component of nicoise salad		No samples available/taken
2005	Restaurant	1	Unknown	Unknown	Fish-unknown species		No samples available/taken
2005	Unknown	1	Unknown	Unknown	Kingfish		Unknown
2005	Unknown	3	Unknown	Unknown	Tuna		Negative
2005	Unknown	14	Unknown	Unknown	Fish dish		'High levels', but no number stated
2006	Private residence	2	0	0	Bluefin tuna steaks		5,100 or 160 cooked/raw
2006	Private residence	2	1	0	Tuna steak		Unknown
2006	Private residence	1	Unknown	Unknown	Tuna		Unknown
2006	Private residence	2	Unknown	Unknown	Tuna		No samples available/taken
2006	Restaurant	2	2	0	Kingfish		3,450
2006	Restaurant	2	2	1	Tuna steaks		Unknown
2006	Restaurant	1	Unknown	1	Mahi-mahi		Negative
2006	Restaurant	1	Unknown	Unknown	Tuna		<10
2006	Restaurant	3	Unknown	Unknown	Marlin		Unknown
2006	Restaurant	6	0	6	Yellowtail kingfish fillets		362
2007	Commercially manufactured	2	2	0	Suspect tinned tuna		Negative
2007	Private residence	3	2	2	Tuna kebab steaks	Indonesia	Unknown

Appendix continued: Outbreaks of histamine fish poisoning, Australia, 2001 to 2013*

Year	Setting	Number affected	Number required medical treatment	Number hospitalised	Food vehicle	Imported food	Histamine level reported mg/kg
2007	Restaurant	2	1	0	Tuna		No samples available/taken
2007	Restaurant	2	2	0	Mahi-mahi	Indonesia	No samples available/taken
2007	Restaurant	2	2	2	Tuna steak	Indonesia	Unknown
2007	Restaurant	2	2	2	Grilled tuna		Unknown
2007	Retail	2	Unknown	0	Tuna	Indonesia	No sample
2007	Retail	4	Unknown	0	Tuna kebabs		3,600
2008	Commercially manufactured	1	1	1	Tuna from can		Unknown
2008	Private residence	1	Unknown	Unknown	Tuna steaks		Unknown
2008	Private residence	2	Unknown	Unknown	Tuna steaks	Indonesia	2,200 and 5,200
2009	Private residence	2	2	1	Tuna steak		Unknown
2009	Private residence	6	Unknown	0	Tuna		5,000
2009	Restaurant	1	Unknown	Unknown	Seafood marinara		Unknown
2009	Restaurant	2	1	1	Tinned anchovies	Morocco	>360
2009	Unknown	2	Unknown	Unknown	Tuna	Indonesia	Negative
2010	Private residence	4	2	0	Tuna		7,000
2010	Restaurant	5	5	0	Mahi-mahi fillets		Unknown
2011	Private residence	1	Unknown	Unknown	Seafood extender		Negative
2011	Restaurant	3	3	3	Yellowtail kingfish		4,800 and 5,100
2011	Restaurant	3	2	0	Tuna		5500
2011	Restaurant	4	4	4	Tuna		Unknown
2012	Private residence	4	1	0	Seafood - unknown		Unknown
2012	Private residence	4	0	0	Fresh mullet fillets		650
2012	Private residence	3	2	0	Mahi-mahi		>1,600 to 2,050
2012	Private residence	3	3	0	Tuna		No samples available/taken
2012	Restaurant	3	3	0	Mahi-mahi		No samples available/taken
2012	School	4	4	0	Tuna		25
2013	Restaurant	3	2	0	Tuna		Unknown
2013	Restaurant	4	Unknown	Unknown	Mahi-mahi		Unknown

* One outbreak in the Australian Capital Territory involving four cases is reported by year of publication because no onset dates are available.

Short reports

Public health response to a measles outbreak in a large correctional facility, Queensland, 2013

Madhumati Chatterji, Anne M Baldwin, Rajendra Prakash, Susan A Vlack, Stephen B Lambert

Abstract

This report documents the prompt, co-ordinated and effective public health response to a measles outbreak in Queensland in 2013. There were 17 cases in a large, high-security, regional correctional facility, a setting with unique challenges. Recommendations are provided to reduce the likelihood and magnitude of measles outbreaks in correctional facilities. *Commun Dis Intell* 2014;38(4):E294–E297.

Keywords: measles, prisoner, justice, correctional, offender, outbreak, epidemic, Queensland, guidelines, vaccination

Background

The World Health Organization recently declared that Australia has been in a period of sustained measles elimination since at least 2009.[1] However this does not mean an absence of cases; imported cases continue to occur in returned international travellers, and those exposed to them whilst infectious, leading to local outbreaks. By early October 2013, Queensland had experienced more year-to-date notifications (20) than the annual average of the previous 5 years (15), with an ongoing outbreak of 13 cases in South East Queensland.[2] This report documents the public health response to an outbreak of measles in a correctional facility. Measles is a highly contagious disease transmitted by droplet and airborne routes.[3] Correctional facilities present unique challenges for communicable disease control, for reasons including the close living conditions, and number and turnover of prisoners and staff.[4]

Outbreak

On 29 October 2013, the treating physician of a South East Queensland, high-security correctional facility (capacity approximately 1,000 males) notified the local public health unit (PHU) of 4 prisoners with fever and rash suspected to be measles.

Presentations were atypical. One case had a rash starting in the left thoracic area. Another had a protracted flu-like illness with severe cough for 7 days and a rash that started on an elbow before progressing to the rest of the body. The third had diffuse spots with maculopapular rash starting the same day as high fever. The fourth had a flu-like illness for 2 days with a transient ‘spotty’ rash on the chest. The following day, a 5th prisoner was notified with a classical measles rash. Measles virus was detected by polymerase chain reaction (PCR) testing of upper respiratory tract swabs from each case.

Review of case notes for prisoners with recent rash and fever was undertaken to identify the primary case. Approximately 2 weeks previously, a prisoner was diagnosed with a drug rash from antibiotics administered for a respiratory tract infection. Following look-back, measles virus was detected by PCR in a sample taken from the prisoner. Airborne transmission of the virus is possible and this case had moved widely in the correctional facility, sharing facilities with each of the 5 cases and others during the infectious period. The exposure period, movements and genotype (G3) suggest the prisoner acquired the infection from a community outbreak[2] before entering the correctional facility.

Overall, 17 cases were linked to the outbreak (Table). Cases were laboratory confirmed by PCR, with the exception of 1 confirmed by measles-specific immunoglobulin M in serum. Exposure and infectious periods suggest the correctional facility’s primary case infected 8 cases who in turn infected 7 cases (Figure). Vaccine-strain virus was detected in 1 further case who was vaccinated in the mass vaccination program. One staff case produced documentation of 1 previous dose of measles vaccine. Prisoners’ vaccination histories were not available.

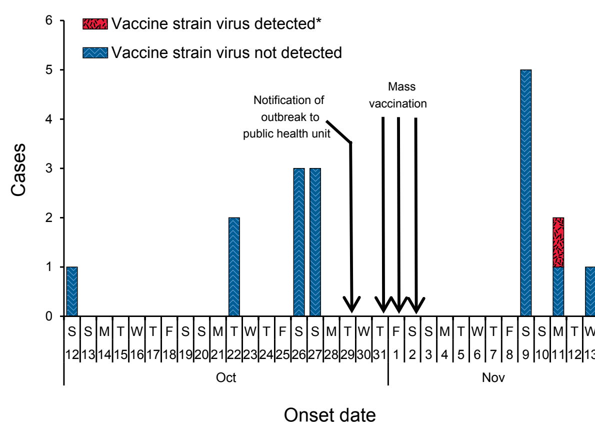
The outbreak was declared over when 36 days (2 maximum expected incubation periods) since the last case’s infectious period had passed without a new, epidemiologically-linked case.

As this response and release of data are provided for under the *Public Health Act 2005*,[5] human research ethics committee approval was not required.

Table: Demographic characteristics of measles cases associated with the correctional facility (n=17)

Age	Range	18–41 years
	Median	28 years
Sex	Female	3 cases
	Male	14 cases
Indigenous status	Indigenous	1 case
	Non-Indigenous	13 cases
	Unknown	3 cases
Group	Prisoner	14 cases
	Correctional centre staff	3 cases

Figure: Symptom onset dates of measles cases associated with the correctional facility, 12 October 2013 to 13 November 2013 (n=17)



* This result does not preclude infection with wild-type virus.

Response

On 29 October 2013, suspected cases of measles were isolated, advice was provided to staff and staff and prisoner movements were restricted. On 30 October following laboratory confirmation, an outbreak control team (OCT) of staff from the state justice department including the correctional facility, state department of health, public health laboratory, local PHU, hospital pharmacy and other hospital and health service (HHS) teams, was assembled.

As prisoners and visitors shared air space via grilles in visitation stalls, prisoner visits were cancelled on 1 November. No admissions of new prisoners were accepted. Prisoners recently transferred out were monitored for symptoms at receiving facilities. Transfers of non-immune prisoners were suspended state-wide.

With around 900 prisoners and 450 staff potentially exposed, individual contact tracing and immune status determination were not considered feasible or sufficiently timely. Consistent with public health recommendations for the management of measles outbreaks in large institutions,[6,7] a mass vaccination approach was adopted.

The department of health procured sufficient vaccine (M-M-R© II, bioCSL/Merck) within 24 hours of planning the activity. The HHS mobilised nurses to vaccinate alongside correctional facility staff, and provided consumables. Pre-vaccination assessment, informed consent, standing orders[8] and adverse event procedures, documents and other resources were developed. The standing orders enabled the measles vaccine administration without a prescription for each prisoner. Key messages regarding measles' infectiousness, complications, prevention and control were disseminated to prisoners, staff, visitors and the general public. State health hotline staff were briefed and the service publicised for enquiries.

On 31 October, approximately 80 staff were vaccinated. Over the next 2 days, approximately 1,150 vaccinations of staff and inmates were administered. In the following week, correctional facility staff conducted mop-up vaccinations, and movement and visitor restrictions were gradually lifted. All were vaccinated except 1 prisoner and 3 staff who refused. These were isolated or excluded from work until the maximum expected incubation period (18 days) had elapsed without symptom onset.

Discussion

Measles in institutional settings can result in explosive outbreaks with large numbers of cases, and difficulties in containing successive waves of infection. The response to this correctional facility measles outbreak was rapid and highly co-ordinated, limiting further cases.

The clinical suspicion of measles in the first 4 identified but atypical cases was crucial to the immediate diagnostic testing and implementation of control activities. It is known that a proportion of all measles cases will not present with classic symptoms—the reason for the clustering of unusual presentations in this outbreak is unknown.

Swift commencement of mass vaccination meant most prisoners and staff received a vaccine within 3 days of the outbreak identification.

The early assembly and central co-ordination of an OCT of key stakeholders and experts meant that

those best placed to provide expertise contributed to decision-making and facilitated speedy deployment of interventions.

No subsequent community cases were epidemiologically linked to this outbreak. Most cases with onset after the mass vaccination were most likely already incubating the disease.

Timely and appropriate communication ensured that the situation and associated risks were well communicated. Surveillance for cases and movement restrictions within the correctional facility allowed rapid responses when new cases were identified. Safety, security and order were maintained.

There were challenges. A higher clinical suspicion of measles in the primary case, given the local outbreak,[2] may have enabled better containment.

Correctional facilities are advised to isolate prisoners with infectious diseases to minimise transmission, where appropriate.[9] Specific guidance for measles outbreak management in correctional facilities is however, absent from national[7] and state[6] health and correctional guidelines,[9] leading to some dependence on expert advice regarding interpretation and implementation of generic guidelines for this setting. As with most measles responses, success came from relying on first principles: timely contact immunisation, case isolation and limiting the movements of exposed individuals.

There are no specific measles immunity data available for Queensland prisoners. However, they are more likely than the general adult population to be born since 1966, thus less likely to have pre-existing natural immunity.[10–12] Additionally, 14% of prison entrants in New South Wales in 2010 who were born since 1969 and tested, were susceptible to measles, compared with 8%–9% of the general population of similar age.[13,14] For a highly contagious virus like measles in a confined institutional setting, this represents a high risk of serial waves of transmission if initial cases are not promptly recognised, and the outbreak response is not swift and comprehensive.

Although measles vaccine is funded in Queensland,[15] it is not routinely offered to prisoners, nor is there screening for measles immunity on prison entry. Immunity and vaccination records were also not readily available during this outbreak, preventing rapid identification of susceptible prisoners.

The setting presented logistical difficulties. Floor plans were unavailable to the OCT for security reasons, preventing the usual outbreak mapping of case movements. It was not feasible for public health staff to directly interview cases. Standard immunisation procedures needed to be modified to maintain correctional facility security and staff safety.

To reduce the likelihood of outbreaks in correctional facilities and improve public health responses, it is recommended that:

1. specific guidance for managing correctional facility measles outbreaks is developed and included in prison and health guidelines;
2. measles vaccination is routinely provided to Queensland's susceptible prisoners; and
3. a high degree of clinical suspicion for measles is maintained, particularly during community outbreaks.

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Toxigenic cutaneous diphtheria in a returned traveller

Nur R Abdul Rahim, Ann P Koehler, Doug D Shaw, Caitlin R Graham

Abstract

Diphtheria is rarely reported in Australia. A case of cutaneous diphtheria was reported to the South Australian Department for Health and Ageing in April 2013 in an Australian-born 18-year-old female following travel in India. The case presented with a skin ulcer on her toe. Toxigenic *Corynebacterium diphtheriae* was isolated from a swab of the lesion. The case was treated with antibiotics. The public health response included infection control advice, assessing the case and household contacts for organism carriage and providing antimicrobial chemoprophylaxis to contacts. Although cutaneous diphtheria is not included as part of the Australian communicable disease surveillance case definition, this may be an oversight as international evidence demonstrates that it is a source of organism transmission and can potentially result in outbreaks among susceptible populations. This formed the rationale for the public health response to this particular case. The protocol for the public health management of diphtheria in South Australia has since been revised to include cutaneous lesions caused by the toxigenic strain of the organism as part of the surveillance case definition. *Commun Dis Intell* 2014;38(4):E298–E300.

Keywords: toxigenic *Corynebacterium diphtheriae,* cutaneous

Introduction

Diphtheria is rare in Australia owing to high immunisation coverage. Cases are largely observed among unimmunised individuals with recent travel to countries where diphtheria remains endemic, or among the contacts of such travellers. Diphtheria endemic countries in the Asia and South Pacific region include Afghanistan, Bangladesh, Cambodia, China, India, Indonesia, Malaysia, Nepal, Pakistan, Papua New Guinea, the Philippines, Thailand and Vietnam.[1] There were 6 cases reported in Australia between the years 2004 and 2013.[2] A death from pharyngeal diphtheria was recorded in 2011 in an unimmunised contact of a traveller who acquired the infection in Papua New Guinea.[3–5] The index case who was the traveller, and 1 other asymptomatic contact in this cluster were previously immunised,[5] demonstrating the protective effect of the vaccine against systemic toxicity. We report the public health response to a case of imported cutaneous diphtheria in South Australia. Informed consent was obtained from the case.

Case presentation

In April 2013, the Communicable Disease Control Branch (CDCB) of SA Health received notification from a laboratory of toxigenic *Corynebacterium diphtheriae* in a clinical specimen collected from an Australian-born 18-year-old female. The specimen was a swab from an ulcerating skin lesion on the first digit of the right foot. In addition to *C. diphtheriae, Streptococcus pyogenes* (Group A) and mixed anaerobes were isolated from the 1st swab of the lesion. Nucleic acid testing confirmed that the *C. diphtheriae* was a toxigenic strain.

The case was a South Australian resident who had travelled to India in January and February 2013. She had previously received 5 doses of diphtheria toxoid-containing vaccine as part of routine childhood immunisation. Approximately 3 weeks after her return, she noted dry skin on her toe, which progressed to become erythematous and tender with purulent discharge 2 days later. She did not report any associated respiratory symptoms. She was initially prescribed dicloxacillin and cephalexin with no clinical improvement. A skin swab was then collected at a 2nd presentation approximately 2 to 3 weeks later, and a course of amoxycillin commenced.

Public health response

An urgent public health investigation was commenced and the case was interviewed on the day of notification. She was requested to submit nasal and throat swabs to assess *C. diphtheriae* carriage status. These were negative for *C. diphtheriae*. The case was referred to an infectious disease physician for further management. Information and education on infection control measures, namely wound contact isolation and hygiene practices associated with wound care were provided. Organism clearance was documented on 2 repeat wound swabs collected at least 24 hours apart with the 1st swab collected 24 hours after completion of the course of antibiotics.

Three household contacts were identified; all reported having received diphtheria toxoid containing vaccines within the last 10 years. It was recommended that they submit nasal and throat

swabs to assess organism carriage status. Two were Australian-based contacts and received antimicrobial chemoprophylaxis with amoxicillin or penicillin prescribed by either a general practitioner or obtained from the emergency department of a public hospital. The 3rd contact was overseas and prescribed antibiotics by a medical practitioner guided by the public health unit at that location. Although the South Australian guidelines recommend isolation of contacts until their carriage status is known, it was not possible to implement isolation in this scenario as 2 contacts were travelling at the time of the investigation. No organism carriage was detected on nasal and throat swabs for the household contacts.

Discussion and public health significance

Cutaneous diphtheria usually presents as indolent, non-healing lesions.[6,7] However a case presenting with a rapidly progressive lower limb ulcer with systemic inflammatory response syndrome was reported in Germany in 2010.[8] Causative organisms include *C. diphtheriae* and *C. ulcerans. C. diphtheriae* is often isolated with other known skin pathogens such as *Staphylococcus aureus* and *Streptococcus pyogenes*; as evident in the case described.[6,7] Treatment requires a course of antimicrobial therapy; however the role of antitoxin in treatment has not been assessed by clinical trials.[8]

Although rarely associated with systemic intoxication, cutaneous lesions form a reservoir for person-to-person transmission with the potential to result in outbreaks in susceptible populations.[6,7,9,10] Organism shedding from skin lesions is more prolonged compared with that from the respiratory tract, and can contaminate the environment through dust and fomites leading to respiratory and cutaneous infections.[6,9] A Canadian review reported non-toxigenic cutaneous diphtheria outbreaks occurring in a susceptible population characterised by homelessness, high prevalence of drug use and multiple comorbidities such as HIV and hepatitis C infections.[7] Experience from the United Kingdom demonstrated the occurrence of laryngeal diphtheria and organism carriage among household and school contacts of a case of cutaneous diphtheria.[9]

Despite such reported experiences, cutaneous diphtheria is not included as part of the national surveillance case definition in Australia and in the United States Centers for Disease Control and Prevention case definition.[11,12] Hence it was unclear at the time of initial notification whether a public health response was warranted. The current Australian definition of a confirmed case requires laboratory definitive evidence and clinical evidence with the clinical evidence defined only as having at least one of pharyngitis and/or laryngitis (with or without a membrane) or toxic (cardiac or neurological) symptoms.[11]

Following discussions with the microbiologist at the regional public health laboratory and a rapid literature review, as well as taking into consideration that the isolate was toxigenic, a decision was made to urgently respond to the notification following the local protocol for the public health management of diphtheria in South Australia. The South Australian case definition for diphtheria was subsequently revised to include cutaneous diphtheria caused by toxigenic strains of the organism to guide public health response for future cases. The omission of skin in the Australian case definition may be an oversight that requires timely review. While antitoxin therapy was not warranted for the case reported here, a revision of the state protocol also provided the opportunity to clarify the role of the CDCB in supporting clinicians to obtain antitoxin when indicated, as this is not routinely stocked in South Australia.

In summary, the occurrence of diphtheria is uncommon in Australia where the most frequently reported exposure factor is travel to diphtheria-endemic countries. Although the risk of systemic toxicity is low in cutaneous diphtheria, the risk of transmission and potential to cause outbreaks among susceptible populations, warrants an urgent public health response and its inclusion in the national case definition to help guide that action.

Acknowledgements

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Annual report

Australian Meningococcal Surveillance Programme annual report, 2013

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Abstract

In 2013, there were 143 laboratory-confirmed cases of invasive meningococcal disease (IMD) analysed by the Australian National Neisseria Network (NNN). This was the lowest number of laboratory confirmed IMD cases referred to the NNN since the inception of the Australian Meningococcal Surveillance Programme in 1994. Probable and laboratory confirmed IMD is notifiable in Australia. There were 149 IMD cases notified to the National Notifiable Diseases Surveillance System in 2013. Meningococcal serogrouping was determined for 139/143 laboratory confirmed IMD cases; 74.8% (104 cases) were serogroup B infections; 5.8% (8 cases) were serogroup C infections; 8.6% (12 cases) were serogroup W135; and 10.8% (15 cases) were serogroup Y. Primary and secondary disease peaks were observed, respectively, in those aged 4 years or less, and in adolescents (15–19 years). Serogroup B cases predominated in all jurisdictions and age groups, except for those aged 65 years or over where serogroup Y predominated. The overall proportion and number of IMD caused by serogroup B decreased from previous years. The number of cases of IMD caused by serogroup C was low, and has been proportionally stable over recent years. The number of IMD cases caused by W135 and Y serogroups was similar to previous years but the proportion has increased with the overall reduction in numbers of IMD cases. Molecular typing was performed on 92 of the 93 IMD isolates, and 23 of the 50 cases confirmed by nucleic acid amplification testing. In 2013, the most common *porA* genotype circulating in Australia was P1.7-2,4. All IMD isolates tested were susceptible to ceftriaxone; ciprofloxacin and rifampicin. Decreased susceptibility to penicillin was observed in 78.5% of isolates. *Commun Dis Intell* 2014;38(4):E301–E308.

Keywords: antibiotic resistance; disease surveillance; meningococcal disease; *Neisseria meningitidis*

Introduction

The Australian National Neisseria Network (NNN) is a long-standing collaborative network of reference laboratories in each state and territory that undertake laboratory surveillance of the pathogenic *Neisseria* species (*N. meningitidis* and *N. gonorrhoeae*). Since 1994 the NNN has provided a national program for the examination of *N. meningitidis* from laboratory confirmed cases of invasive meningococcal disease (IMD). This program is funded by the Australian Government Department of Health, and is known as the Australian Meningococcal Surveillance Programme (AMSP).[1] The NNN laboratories supply data on the phenotype and the genotype of invasive meningococci and these data supplement the clinical notification data from the National Notifiable Diseases Surveillance System (NNDSS), which includes cases of probable IMD as well as laboratory confirmed IMD. The characteristics of the meningococci responsible for IMD are important for individual patient management; contact management; and to tailor the public health response for outbreaks or case clusters, locally and nationally. The introduction of the publicly funded conjugate serogroup C meningococcal vaccine onto the National Immunisation Program in 2003 has seen a significant and sustained reduction in the number of cases of serogroup C IMD after 2003.[2] However, IMD remains an issue of public health concern in Australia.

Methods

Case confirmation of invasive meningococcal disease

Case confirmation is based on isolation of *N. meningitidis*, or a positive nucleic acid amplification testing (NAAT) from a normally sterile site, defined as laboratory definitive evidence of IMD by the Communicable Diseases Network Australia criteria.[3] Information regarding the site of infection, age and sex of the patients is collated by the NNN for the AMSP.

IMD cases are categorised on the basis of the site from which *N. meningitidis* was isolated or from which meningococcal DNA was detected by the NNN for the AMSP. When *N. meningitidis* is grown from both blood and cerebrospinal fluid (CSF) cultures from the same patient, the case is classified as one of meningitis. Where the diagnosis is made by serology, it is not possible to definitively classify a case as meningitis or septicaemia.

Phenotyping and genotyping of *Neisseria meningitidis*

Phenotyping is limited to the determination of the serogroup by detection of soluble polysaccharide antigens. Genotyping of both isolates and DNA extracts is performed by sequencing of products derived from amplification of the porin genes *porA, porB* and *FetA*.

Antibiotic susceptibility testing

Isolates were tested to determine their minimum inhibitory concentration (MIC) values to antibiotics used for therapeutic and prophylactic purposes: ceftriaxone, ciprofloxacin; rifampicin. This program uses the following parameters to define the various levels of penicillin susceptibility or resistance when determined by a standardised agar plate dilution technique:[4]

Sensitive: MIC ≤ 0.03 mg/L

Less sensitive: MIC 0.06–0.5 mg/L

Resistant: MIC ≥ 1 mg/L

Meningococcal serology

Serological diagnosis of IMD can be made on the demonstration of IgM antibody by enzyme immunoassay to *N. meningitidis* outer membrane protein using the methods and test criteria of the Health Protection Agency UK, and as assessed for Australian conditions.[5–7]

Results

In 2013, there were 143 laboratory-confirmed cases of IMD analysed by the NNN, and 149 cases notified to the NNDSS. Thus laboratory data were available for 96% of notified cases of IMD in Australia in 2013 (Table 1). This is the lowest annual number of IMD cases recorded by the NNDSS and the AMSP since surveillance data collaboration began in Australia. There was a reduction of 31% in the number of IMD cases from 2012 (Figure 1). As in previous years, the peak incidence for IMD continues to be late winter and early spring (1 July to 30 September) (Table 1).

The highest number of laboratory confirmed cases was from New South Wales (43 cases), which was notably lower than the 62 cases in 2012. Other states that recorded a significant reduction in IMD cases were Queensland (32 cases in 2013, compared with 59 in 2012), and Victoria (23 cases in 2013, compared with 33 in 2012). Numbers for the other states were similar to 2012 (Table 2).

Age distribution

Nationally, the peak incidence of IMD was in children less than 5 years of age, which was similar

Figure 1: Number of invasive meningococcal disease cases reported to the National Notifiable Diseases Surveillance System compared with laboratory confirmed data from the Australian Meningococcal Surveillance Programme, Australia, 1991 to 2013

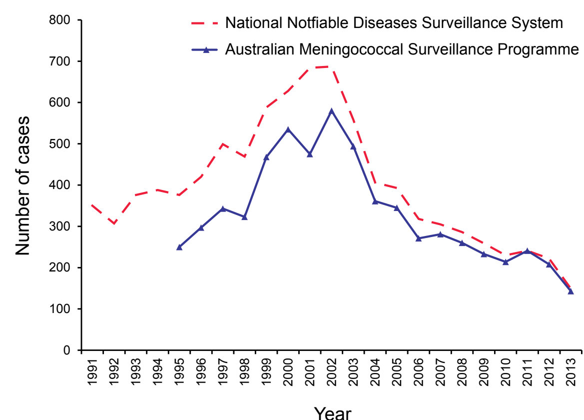


Table 1: Laboratory confirmed cases of invasive meningococcal disease, Australia, 2013, by quarter

Serogroup	1 January to 31 March	1 April to 30 June	1 July to 30 September	1 October to 31 December	Total 2013
B	30	20	32	22	104
C	3	2	2	1	8
Y	1	3	3	8	15
W135	1	2	7	2	12
NG/ND	0	2	2	0	4
Total	35	29	46	33	143

NG Non-groupable.

ND Non-determined (samples were examined by nucleic acid amplification test).

to previous years. Between 2007 and 2012, 28% to 36% of cases were in this age group. In 2013, 47/143 (33%) IMD cases occurred in this age group (Table 3). A secondary disease peak has also been observed in previous years among adolescents aged 15–19 years. Of the total cases of IMD, 26/143 (18%) were in those aged 15–19 years in 2013, which was higher than the proportion reported for 2012 (13.5%); but similar to the proportion reported in the period 2007 to 2011 (17%–20%). The proportion of IMD cases (7.7%, 11 confirmed cases) in those aged 25–44 was lower than in 2012 (13%, 27 confirmed cases). The other age categories represented similar proportions in confirmed IMD cases to previous years.

Anatomical site of samples for laboratory confirmed cases

In 2013, diagnosis was made by a positive culture in 93/143 (65%) cases and 50/143 (35%) cases were confirmed by NAAT testing. There were no IMD cases diagnosed serologically in 2013 (Table 4).

There were 53 diagnoses of meningitis based on cultures or NAAT examination of CSF either alone or with a positive blood sample. There were 86 diagnoses of septicaemia based on cultures or NAAT examination from blood samples alone (Table 4). There were 4 IMD diagnoses by positive joint fluid culture (n = 3) and NAAT (n = 1).

Table 2: Number of laboratory confirmed cases of invasive meningococcal disease, Australia, 2013, by state or territory and serogroup

State or territory	Serogroup						Total
	B	C	Y	W135	NG	ND	
ACT	2	0	1	0	0	0	3
NSW	23	3	9	6	2	0	43
NT	2	0	0	0	0	0	2
Qld	25	2	2	3	0	0	32
SA	19	0	1	1	0	0	21
Tas	2	0	0	0	0	1	3
Vic	19	1	1	1	1	0	23
WA	12	2	1	1	0	0	16
Australia	104	8	15	12	3	1	143
(%)	(72.7)	(5.6)	(10.5)	(8.4)	(2.1)	(0.70)	

NG Non-groupable.

ND Non-determined (samples were examined by nucleic acid amplification test).

Table 3: Laboratory confirmed cases of invasive meningococcal disease, Australia, 2013, by age and serogroup

Serogroup	Age group										Total
	<1	1–4	5–9	10–14	15–19	20–24	25–44	45–64	65+	NS	
B	21	23	5	4	22	10	9	8	2	0	104
C	0	0	0	0	1	2	0	4	1	0	8
Y	0	0	0	0	0	3	1	5	6	0	15
W135	2	0	0	1	3	0	1	1	4	0	12
NG/ND	0	1	1	1	0	0	0	1	0	0	4
Total	23	24	6	6	26	15	11	19	13	0	143
% of B within age group	91.3	95.8	83.3	66.7	84.6	66.7	81.8	42.1	15.3	0	

NS Age not stated.

NG Non-groupable.

ND Non-determined (samples were examined by nucleic acid amplification test).

Table 4: Number of laboratory confirmed cases of invasive meningococcal disease, Australia, 2013, by anatomical source and method of confirmation

Specimen type	Isolate of MC	NAAT positive*	Serology alone	Total
Blood	67	19	0	86
CSF +/– blood	23	30	0	53
Joint fluid	3	1	0	4
Total	93	50	0	143

* Nucleic acid amplification test (NAAT) positive in the absence of a positive culture.

CSF Cerorospinal fluid

Serogroup data

Number of cases of invasive meningococcal disease by serogroup B, C Y W135

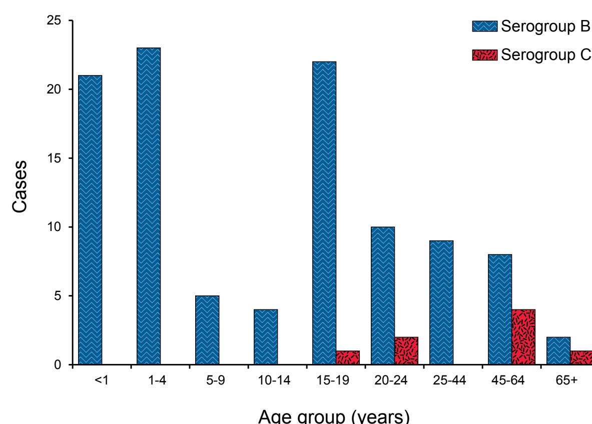
The serogroup was determined for 139 of 143 laboratory confirmed cases of IMD in 2013 (Tables 2 and 3). There has been an overall decrease in the number of cases of IMD in Australia in recent years, which was initially predominantly due to a reduction in the number of cases of IMD caused by serogroup C from 2003 to 2007, followed by a decline in the numbers IMD cases caused by serogroup B from 194 cases in 2009, to 104 cases in 2013. The number of cases of IMD caused by serogroup Y and W135 has remained relatively stable over recent years.

Proportion of serogroup B, C, Y, W135 invasive meningococcal disease

Of the 139 IMD strains for which the serogroup was determined, 74.8% were serogroup B, which is lower than that reported in 2006–2012 (84%–88%). The proportion of cases of IMD caused by serogroup B in those aged less than 20 years, was higher than the previous year (Table 3, Figure 2). However in those aged 20–24 years the proportion of IMD due to serogroup B was lower than in 2007–2010 (66.7%), and 2012 (between 80% and 88%); but higher than in 2011 (61%). In those aged 25 years and over, IMD due to serogroup B accounted for 13.3% of the total number of IMD cases, a marked decrease in proportion of from 25% in 2012. The decrease was most notable in people aged 65 years or over. Serogroup B IMD predominated in all age groups except in those more than 65 years of age.

The proportion of IMD caused by serogroup C was unchanged from 2012 (5.7%). The peak number of serogroup C cases in 2013 occurred in those aged 45–64, which differed from the reported peak of serogroup C in 2011–2012, in those aged

Figure 2: Number of serogroup B and C cases of confirmed invasive meningococcal disease, Australia, 2013, by age



25–44 years age. There was 1 case of IMD caused by serogroup C in those aged less than 20 years in 2013 (2 cases in 2012, no cases in 2011).

Of note, the proportion of IMD caused by serogroup Y (10.8%) was higher than in 2012 (7.7%). Over time the proportion of cases of IMD caused by serogroup Y has been increasing (3.5% in 2009), but the number of cases has remained reasonably stable over recent years. The number and proportion of IMD cases caused by serogroup Y was highest in people aged 45 years or over in 2013; while in people aged 65 years or over, serogroup Y was the most prevalent serogroup causing IMD. Serogroup W135 accounted for 8.6% of IMD cases, which was higher than the 3.4% in 2012.

Genotyping

In 2013, genotyping was performed on 114/143 (80%) IMD cases (Tables 5 and 6). The predominant *porA* genotypes for serogroup B isolates were again P1.7-2,4 (24 cases, compared with 35 in 2012) and P1.22,14 (13 cases, compared with 15 in 2012). P1.7,16-26, previously one of the more common genotypes, showed a decline in case numbers

over recent years (4 cases in 2013, compared with 12 cases in 2012 and 19 in 2011) (Table 5 and Figure 3). The predominant *porA* genotype for serogroup C isolates was again P1.5-1,10-8 (6 cases, compared with 6 in 2012). The AMSP was not aware of any epidemiological link between any of the cases reported where genotyping was available.

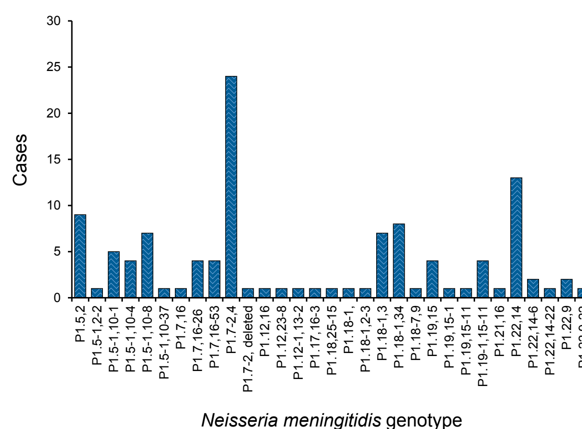
Table 5: Laboratory confirmed cases of invasive meningococcal disease, Australia, 2013, by *porA* gentoype

PorA genotype	B	C	W135	Y	Total
P1.5,2	0	1	6	2	9
P1.5-1,2-2	0	0	0	1	1
P1.5-1,10-1	1	0	0	4	5
P1.5-1,10-4	1	0	0	3	4
P1.5-1,10-8	1	6	0	0	7
P1.5-1,10-37	0	0	0	1	1
P1.7,16	1	0	0	0	1
P1.7,16-26	4	0	0	0	4
P1.7,16-53	4	0	0	0	4
P1.7-2,4	24	0	0	0	24
P1.7-2, deleted	1	0	0	0	1
P1.12,16	1	0	0	0	1
P1.12,23-8	1	0	0	0	1
P1.12-1,13-2	1	0	0	0	1
P1.17,16-3	1	0	0	0	1
P1.18,25-15	0	1	0	0	1
P1.18-1,	1	0	0	0	1
P1.18-1,2-3	0	0	1	0	1
P1.18-1,3	1	0	4	2	7
P1.18-1,34	8	0	0	0	8
P1.18-7,9	1	0	0	0	1
P1.19,15	4	0	0	0	4
P1.19,15-1	1	0	0	0	1
P1.19,15-11	1	0	0	0	1
P1.19-1,15-11	4	0	0	0	4
P1.21,16	0	0	0	1	1
P1.22,14	13	0	0	0	13
P1.22,14-6	2	0	0	0	2
P1.22,14-22	1	0	0	0	1
P1.22,9	2	0	0	0	2
P1.22,9-22	1	0	0	0	1
Total	81	8	11	14	114

Antibiotic susceptibility testing

Testing for antimicrobial susceptibility was able to be performed for 93/143 of the IMD cases (65%) in 2013. All isolates tested were susceptible to ceftriaxone, ciprofloxacin and rifampicin.

Figure 3: Number of *porA* genotypes for serogroup B in cases of invasive meningococcal disease,* Australia, 2013



* Where genotype data were available.

Using defined criteria, 20/93 (21.5%) isolates were fully sensitive to penicillin (MIC 0.03 mg/L or less). There were 73 (78.5%) isolates less sensitive to penicillin (MIC = 0.06–0.5 mg/L). There were no isolates that had an MIC value ≥ 1.0 mg/L (resistant). The proportion of penicillin less sensitive strains was lower than in 2012 (82%) but within the range for those reported in the period 2007 to 2012 (range 72%–85%; mean = 77.4%).

Discussion

In 2013, there were 143 IMD cases laboratory confirmed by the NNN, representing 96% of the number of notifications to the NNDSS.[2] This is both the lowest number of cases reported since laboratory based surveillance for confirmed IMD cases (AMSP) began in 1994, and since notification data collection commenced in 1991. The total number of laboratory confirmed cases of IMD in Australia in 2013 (143) represents less than one-quarter of the laboratory confirmed cases (580) of IMD reported in Australia in 2002, when IMD rates peaked. This is likely to be largely due to the introduction of the serogroup C vaccine to the national immunisation schedule in 2003, which was followed by a steady decline in the total number of cases of IMD in Australia. The primary peak in IMD infection continues to be evident in children aged less than 5 years, as reported in previous years, with a secondary peak in adolescents.

The proportion of IMD cases caused by serogroup B are in the majority, however this was lower in 2013 than that reported from 2006 to 2012. The proportion of IMD caused by serogroup C continues to be small across all age groups. As in previous years, there were only a small number of serogroup C cases in those aged 25 years or over. This

Table 6: Distribution of *porA* genotype laboratory confirmed cases of invasive meningococcal disease, Australia, 2013, by state or territory

Genotype *porA*	ACT	NSW	NT	Qld	SA	Tas.	Vic.	WA
P1.5,2		1C, 4W135, 1Y		1W135	1Y			1W135
P1.5-1,2-2		1Y						
P1.5-1,10-1		3Y		1Y			1B	
P1.5-1,10-4		1B,2Y						1Y
P1.5-1,10-8		2C		1C			1B, 1C	2C
P1.5-1,10-37							1Y	
P1.7,16		1B						
P1.7,16-26	1B			1B	1B		1B	
P1.7,16-53		1B		3B				
P1.7-2,4		4B	1B	7B	10B		2B	
P1.7-2, deleted								1B
P1.12,16								1B
P1.12,23-8				1B				
P1.12-1,13-2							1B	
P1.17,16-3		1B						
P1.18,25-15				1C				
P1.18-1,							1B	
P1.18-1,2-3							1W135	
P1.18-1,3		1Y, 2W135		1Y, 2W135		1B		
P1.18-1,34			1B	5B			2B	
P1.18-7,9							1B	
P1.19,15		1B		1B			1B	1B
P1.19,15-1		1B						
P1.19,15-11				1B				
P1.19-1,15-11		2B		2B				
P1.21,16	1Y							
P1.22,14		4B		4B		1B		4B
P1.22,14-6				2B				
P1.22,14-22		1B						
P1.22,9		1B					1B	
P1.22,9-22							1B	

may reflect the secondary benefit of herd immunity accruing to the wider community following vaccination of those age groups where disease was formerly highly concentrated.[8] Low numbers of infections with serogroups Y and W135 is usual for Australia, and this has remained relatively unchanged over time. However, in the context of decreased overall numbers of IMD cases, there has been a proportional increase in serogroups Y and W135 disease in 2013.

As in previous years, genotypic data found no evidence of a substantial number of cases of IMD caused by *N. meningitidis* that have undergone genetic recombination. There have been concerns that the emergence of new and invasive subtypes following extensive vaccine use would occur given the capacity for genetic recombination within meningococci.[8] Monitoring of meningococcal genotypes will continue as part of the NNN program.

All isolates were susceptible to ceftriaxone, ciprofloxacin and rifampicin. The proportion of IMD isolates with penicillin MIC values in the less sensitive category in 2013 was 78.5%, within the 78%–85% range established from 2007. In the years 2000–2006 the range of penicillin MIC values was 62%–68%. This indicates a shift in penicillin MIC values of IMD isolates from sensitive to less sensitive category over this time frame.

In early 2014, a recombinant multi-component meningococcal B vaccine became available in Australia.[9] This vaccine is not on the immunisa-

tion register but is available for purchase privately. Therefore uptake will be elective and the impact of its introduction is yet to be determined in this country. The AMSP continues to monitor the serogroups and antibiograms of *N. meningitidis* to inform treatment and prevention strategies.

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Australian *Staphylococcus aureus* Sepsis Outcome Programme annual report, 2013

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Abstract

From 1 January to 31 December 2013, around Australia 26 institutions around Australia participated in the Australian Staphylococcal Sepsis Outcome Programme (ASSOP). The aim of ASSOP 2013 was to determine the proportion of *Staphylococcus aureus* bacteraemia (SAB) isolates in Australia that are antimicrobial resistant, (with particular emphasis on susceptibility to methicillin) and to characterise the molecular epidemiology of the isolates. Overall 19.1% of the 2,010 SAB episodes were methicillin resistant, which is significantly higher than that reported in most European countries. Although the SAB 30-day all cause mortality appears to be decreasing in Australia, methicillin-resistant SAB associated mortality remains high (20.1%) and was significantly higher than methicillin-sensitive SAB associated mortality (13%) ($P < 0.0001$). With the exception of the ß-lactams and erythromycin, antimicrobial resistance in methicillin sensitive *S. aureus* remains rare. However, in addition to the ß-lactams, approximately 50% of methicillin-resistant *S. aureus* (MRSA) were resistant to erythromycin and ciprofloxacin and approximately 20% were resistant to co-trimoxazole, tetracycline and gentamicin. Linezolid, daptomycin and teicoplanin resistance was detected in a small number of *S. aureus* isolates. Resistance to vancomycin was not detected. Resistance was largely attributable to 2 healthcare associated MRSA clones; ST22-IV [2B] (EMRSA-15) and ST239-III [3A] (Aus-2/3 EMRSA). ST22-IV [2B] (EMRSA-15) has now become the predominant healthcare associated clone in Australia. Approximately 60% of methicillin-resistant SAB were due to community associated clones. Although polyclonal, almost 50% of community associated clones were characterised as ST93-IV [2B] (Queensland CA-MRSA) and ST1-IV [2B] (WA1). CA-MRSA, in particular the ST45-V [5C2&5] (WA84) clone, has acquired multiple antimicrobial resistance determinants including ciprofloxacin, erythromycin, clindamycin, gentamicin and tetracycline. As CA-MRSA is well established in the Australian community, it is important antimicrobial resistance patterns in community and healthcare associated SAB is monitored as this information will guide therapeutic practices in treating *S. aureus* sepsis. *Commun Dis Intell* 2014;38(4):E309–E319.

Keywords: antimicrobial resistance surveillance; *Staphylococcus aureus,* methicillin sensitive, methicillin resistant, bacteraemia

Introduction

Globally, *Staphylococcus aureus* is one of the most frequent causes of hospital-acquired and community-acquired blood stream infections.[1] Although there are a wide variety of manifestations of serious invasive infection caused by *S. aureus,* the organism can be detected in blood cultures in the majority of cases. Therefore, *S. aureus* bacteraemia (SAB) is considered a very useful marker for serious invasive infection.[2]

Although prolonged antimicrobial therapy and prompt source control are used to treat SAB,[3] mortality ranges from as low as 2.5% to as high as 40%.[4–6] Mortality rates however, are known to vary significantly with patient age, clinical manifestation, co-morbidities and methicillin resistance.[7,8] A recent prospective study of SAB conducted in 27 laboratories in Australia and New Zealand found a 30-day all cause mortality of 20.6%.[9] On univariate analysis, increased mortality was significantly associated with older age, European ethnicity, methicillin resistance, infections not originating from a medical device, sepsis syndrome, pneumonia/empyema and treatment with a glycopeptide or other non-ß-lactam antibiotic.

The Australian Group on Antimicrobial Resistance (AGAR), a network of laboratories located across Australia, commenced surveillance of antimicrobial resistance in *S. aureus* in 1986.[10] The use of an active surveillance strategy with standard methodology for collection and examination of clinically significant isolates has produced longitudinal data accurately reflecting the changing prevalence of antimicrobial resistance in healthcare-acquired and community-acquired *S aureus* infections.[11,12] In 2013, AGAR commenced the Australian Staphylococcal Sepsis Outcome Programme (ASSOP). The primary objective of ASSOP 2013 was to determine the proportion of SAB isolates demonstrating antimicrobial resistance with particular emphasis on:

1. assessing susceptibility to methicillin;
2. molecular epidemiology of methicillin susceptible *S. aureus* (MSSA) and methicillin resistant *S. aureus* (MRSA).

Methods

Participants

Twenty-six laboratories from all 8 Australian states and territories participated in the program.

Collection period

From 1 January to 31 December 2013, the 26 laboratories collected all *S. aureus* isolated from blood cultures. *S. aureus* with the same antimicrobial susceptibility profiles isolated from a patient's blood culture within 14 days of the 1st positive culture were excluded. A new *S. aureus* sepsis episode in the same patient was recorded if it was confirmed by a further culture of blood taken more than 14 days after the initial positive culture. Data were collected on age, sex, date of admission and discharge (if admitted), and mortality at 30 days from date of the 1st positive blood culture. To avoid interpretive bias, no attempt was made to assign attributable mortality. Each episode of bacteraemia was designated healthcare onset if the 1st positive blood culture(s) in an episode were collected more than 48 hours after admission.

Laboratory testing

Participating laboratories performed antimicrobial susceptibility testing using the Vitek2® (bioMérieux, France) or the Phoenix™ (BD, USA) automated microbiology systems according to the manufacturer's instructions. *S. aureus* was identified by morphology and positive results of at least one of the following tests: Vitek MS® (bioMérieux, France), matrix-assisted laser desorption ionization biotyper (Bruker Daltonics, Germany), slide coagulase, tube coagulase, appropriate growth on chromogenic agar and demonstration of deoxyribonuclease production. Additional tests such as fermentation of mannitol, growth on mannitol-salt agar or polymerase chain reaction (PCR) for the presence of the *nuc* gene may have been performed for confirmation.

Minimum inhibitory concentration (MIC) data and isolates were referred to the Australian Collaborating Centre for *Enterococcus* and *Staphylococcus* Species (*ACCESS*) Typing and Research. Clinical and Laboratory Standards Institute (CLSI)[13] and European Committee on Antimicrobial Susceptibility Testing (EUCAST)[14] breakpoints were utilised for interpretation. Isolates with a resistant or an intermediate category were classified as non-susceptible. High level mupirocin resistance was determined using a mupirocin 200 μg disk according to CLSI guidelines on all isolates with a mupirocin MIC > 8 by Vitek2® or > 256 by Phoenix™.[13] Multi-resistance was defined as resistance to three or more of the following non-ß-lactam antimicrobials: vancomycin, teicoplanin, erythromycin, clindamycin, tetracycline, ciprofloxacin, gentamicin, co-trimoxazole, fusidic acid, rifampicin, high level mupirocin, linezolid and daptomycin.

Electrophoresis of chromosomal DNA was performed as previously described, on all MRSA using contour-clamped homogeneous electric field DR III system (Bio-Rad Laboratories Pty Ltd, USA).[15] Chromosomal patterns were examined visually, scanned with Quantity One software (Bio-Rad Laboratories Pty Ltd, USA), and digitally analysed using FPQuest (Applied Maths NV, Belgium). Multilocus sequence typing (MLST) was performed on all unique pulsed-field types as previously described.[16] The sequences were submitted to Multi Locus Sequence Typing via the Internet (http://www.mlst.net) where an allelic profile was generated and a sequence type (ST) assigned.

SCC*mec* typing was performed on all MRSA with a unique pulsed-field pattern, using the Clondiag *S. aureus* Genotyping Array Hybridisation Kit (Alere, USA) as previously described.[17]

Detection of Panton-Valentine leucocidin determinants (PVL) and *mecA* was performed by PCR on all MRSA as previously described.[18, 19]

A chi-square test for comparison of 2 proportions was performed and 95% confidence intervals (95%CI) were determined using MedCalc for Windows, version 12.7 (Medcalc Software, Ostend Belgium).

Approval to conduct the prospective data collection was given by the research ethics committee associated with each participating laboratory.

Results

From 1 January to 31 December 2013, 2,010 unique episodes of *S. aureus* bacteraemia were identified. A significant difference ($P < 0.0001$) was seen in patient sex with 65.4% (1,314) being male (95% CI 63.3%–67.5%). The average age of patients was 58 years ranging from 0–102 years with a median age of 62 years. The place of onset was recorded for 1,960 of the 2,010 episodes, of which 71.6% (1,404) were hospital onset (95% CI 69.6%–73.6%). The all cause mortality at 30-days was 14.4% (95% CI 12.8%–16.2%). Methicillin resistant SAB mortality was 20.1% (95% CI 15.9%–24.7%, 67/334), which was significantly higher than methicillin susceptible SAB mortality (13%, 95% CI 11.3%–14.9%, 179/1378, $P < 0.0001$).

Methicillin susceptible *Staphylococcus aureus* antimicrobial susceptibility

Overall 80.9% (1,626) of the 2,010 isolates were methicillin sensitive of which 79.6% (1,294) were penicillin resistant (MIC > 0.12 mg/L). However, as ß-lactamase was detected in 69 phenotypically penicillin susceptible isolates, 83.8% of MSSA were considered penicillin resistant. Apart from erythromycin non-susceptibility (11.0%) resistance to the non-ß-lactam antimicrobials among MSSA was rare, ranging from 0% to 3.9% (Table 1). A single isolate was linezolid resistant (MIC > 8 mg/L), 5 isolates were non-susceptible to daptomycin (MIC 2–4 mg/L), and using the EUCAST resistant breakpoint of > 2 mg/L 1 isolate was teicoplanin resistant (MIC = 4 mg/L). Vancomycin non-susceptibility was not detected. Twenty (1.2%) of the 1,626 isolates had high level mupirocin resistance of which 16 isolates were referred from Queensland. Inducible resistance to clindamycin was determined by the Vitek2® susceptibility system. Of the 1,478 isolates tested, 8.6% (127) were erythromycin non-susceptible/clindamycin intermediate/susceptible (CLSI and EUCAST breakpoints) of which 89.8% (114) were classified as having inducible clindamycin resistance. Multi-resistance was uncommon in MSSA (1.7%, 28/1626).

There were no significant differences in interpretation for any drug when CLSI or EUCAST non susceptibility breakpoints were utilised ($P > 0.05$).

Methicillin-resistant *Staphylococcus aureus* antimicrobial susceptibility

The proportion of *S. aureus* that were MRSA was 19.1% (95%CI 17.5%–21.0%). Of the 384 MRSA identified, 97.9% were either cefoxitin screen positive by Vitek2® (363/384) or had a cefoxitin MIC > 8 by Phoenix™ (13/384). Eight isolates that were either cefoxitin screen negative (4/8), or had a cefoxitin MIC ≤ 2 mg/L (4/8), were oxacillin resistant (MIC > 2 mg/L) and *mecA* positive by PCR. Although two of the 384 isolates were phenotypically penicillin susceptible, both isolates were ß-lactamase positive. Among the MRSA isolates, non-susceptibility to non-ß-lactam antimicrobials was common except for rifampicin (MIC 2–≥ 32 mg/L), fusidic acid (MIC 2 – ≥ 32 mg/L), nitrofurantion (MIC ≥ 64 mg/L)

Table 1: Number and proportion of methicillin sensitive *Staphylococcus aureus* isolates non-susceptible to penicillin and the non-ß-lactam antimicrobials, Australia, 2013

Antimicrobial	Tested	Breakpoint (mg/L)	Non-susceptible n	Non-susceptible %
Penicillin	1,626	> 0.12*	1,342	82.5
Vancomycin	1,626	> 2*	0	0.0
Teicoplanin	1,626	> 8†	0	0.0
		> 2‡	1	< 0.1
Rifampicin	1,587	> 1†	0	0.0
Fusidic acid	1,480	> 1‡	61	3.9
Gentamicin	1,626	> 4†	15	0.9
	1,480	> 1‡	16	1.1
Erythromycin	1,626	> 2†	178	11.0
		> 1‡	179	11.0
Clindamycin	1,626	> 0.5†	39	2.4
	1,480	> 0.25‡	36	2.4
Tetracycline	1,553	> 4†	31	2.0
		> 1‡	35	2.3
Co-trimoxazole	1,626	> 2/38*	33	2.0
Ciprofloxacin	1,626	> 1*	46	2.8
Nitrofurantoin	1,550	> 32†	30	1.9
Linezolid	1,626	> 4*	1	< 0.1
Daptomycin	1,552	> 1*	4	0.3

* Clinical and Laboratory Standards Institute (CLSI) and European Committee on Antimicrobial Susceptibility Testing (EUCAST) non-susceptible breakpoint.

† CLSI non-susceptible breakpoint.

‡ EUCAST non-susceptible breakpoint.

and daptomycin (MIC 2–4 mg/L) where resistance was below 3% nationally (Table 2). Resistance was not detected for vancomycin, teicoplanin or linezolid. Of the 384 MRSA isolates, 1.8% (7/384) had high level mupirocin resistance. Of the 327 isolates tested by Vitek2®, 27.8% (91) were erythromycin non-susceptible/clindamycin intermediate/susceptible (CLSI and EUCAST breakpoints) of which 89.0% (81) were classified as having inducible clindamycin resistance. Multi-resistance was common in MRSA (25.8%, 99/384).

There were no significant differences in interpretation for any drug when CLSI or EUCAST non-susceptibility breakpoints were utilised ($P > 0.05$).

Methicillin-resistant *Staphylococcus aureus* molecular epidemiology

Of the 384 MRSA identified, 368 were referred to *ACCESS* Typing and Research for strain characterisation. Based on molecular typing, 41.0% (151) and 59.0% (217) of isolates were classified as healthcare-associated MRSA (HA-MRSA) and community-associated MRSA (CA-MRSA) clones respectively (Table 3).

Healthcare-associated methicillin-resistant Staphylococcus aureus

For the 151 HA-MRSA strains, 50.3% (76) were epidemiologically classified as hospital onset (blood culture collected more than 48 hours after admission) and 47.7% (72) were classified as community onset. The date of hospital admission was not available for 3 patients. Three HA-MRSA clones were identified: 88 isolates of ST22-IV [2B] (EMRSA-15) (23.9% of MRSA and 4.4% of *S. aureus*); 59 isolates of ST239-III [3A] (16.0% and 2.9%) and 4 isolates of ST5-II [2A] (USA100/New York Japan MRSA).

ST22-IV [2B] (EMRSA-15) was the dominant HA-MRSA clone in Australia accounting for 58.3% of HA-MRSA, ranging from 42.9% in the Australian Capital Territory to 100% in Tasmania (Table 4). ST22-IV [2B] was typically PVL negative and using CLSI breakpoints, while 100% and 67% were ciprofloxacin and erythromycin resistant respectively.

Table 2: Number and proportion of methicillin-resistant *Staphylococcus aureus* isolates non-susceptible to penicillin and the non-ß-lactam antimicrobials, Australia, 2013

Antimicrobial	Tested	Breakpoint (mg/L)	Non-susceptible	
			n	%
Penicillin	384	> 0.12*	381	99.2
Vancomycin	384	> 2*	0	0.0
Teicoplanin	384	> 8†	0	0.0
		> 2‡	0	0.0
Rifampicin	381	> 1†	7	1.8
Fusidic acid	327	> 1‡	9	2.3
Gentamicin	384	> 4†	68	17.7
	327	> 1‡	52	16.0
Erythromycin	384	> 2†	192	49.9
		> 1‡	192	49.9
Clindamycin	384	> 0.5†	84	21.9
	327	> 0.25‡	67	20.5
Tetracycline	363	> 4†	63	17.4
		> 1‡	79	21.8
Co-trimoxazole	384	> 2/38*	71	18.5
Ciprofloxacin	384	> 1*	195	50.8
Nitrofurantoin	378	> 32†	11	2.9
Linezolid	384	> 4*	0	0.0
Daptomycin	362	> 1*	4	1.1

* Clinical and Laboratory Standards Institute (CLSI) and European Committee on Antimicrobial Susceptibility Testing (EUCAST) non-susceptible breakpoint.

† CLSI non-susceptible breakpoint.

‡ EUCAST non-susceptible breakpoint.

Table 3: Proportion of healthcare-associated and community-associated methicillin-resistant *Staphylococcus aureus*, Australia, 2013, by clone, healthcare and community onset, and Panton-Valentine leucocidin carriage

Strain	Total		Onset: Healthcare		Onset: Community		Unknown		PVL positive	
	n	%*	n	%†	n	%†	n	%†	n	%†
Healthcare-associated MRSA										
ST22-IV [2B] (EMRSA-15)	88	23.9	38	43.2	49	55.7	1	1.1	0	0.0
ST239-III [3A] (Aus-2/3)	59	16.0	35	59.3	22	37.3	2	3.4	0	0.0
ST5-II [2A] (USA100)	4	1.1	3	75.0	1	25.0	0	0.0	0	0.0
Sub-total	151	41.0	76	50.3	72	47.7	3	2.0	0	0.0
Community-associated MRSA										
ST93-IV [2B] (Queensland)	50	13.6	10	20.0	40	80.0	0	0.0	48	96.0
ST1-IV [2B] (WA1)	45	12.2	17	37.8	28	62.2	0	0.0	4	8.9
ST5-IV [2B] (WA3)	25	6.8	9	36.0	16	64.0	0	0.0	0	0.0
ST78-IV [2B] (WA2)	20	5.4	6	30.0	14	70.0	0	0.0	0	0.0
ST30-IV [2B] (SWP)	18	4.9	7	38.9	11	61.1	0	0.0	14	77.8
ST45-V [5C2&5] (WA84)	17	4.6	4	23.5	13	76.5	0	0.0	0	0.0
ST8-IV [2B] (USA300)	7	1.9	2	28.6	3	42.9	2	28.6	6	85.7
ST73-IV [2B] (WA65)	6	1.6	1	16.7	5	83.3	0	0.0	0	0.0
ST835-IV [2B] (WA48)	4	1.1	1	25.0	3	75.0	0	0.0	0	0.0
ST72-IV [2B] (Korean)	3	0.8	1	33.3	2	66.7	0	0.0	0	0.0
ST953-IV [2B] (WA54)	3	0.8	0	0.0	3	100.0	0	0.0	0	0.0
ST5-IV [2B] (WA121)	2	0.5	0	0.0	2	100.0	0	0.0	2	100.0
ST923-IV [2B] (WA62)	2	0.5	0	0.0	2	100.0	0	0.0	2	100.0
ST5-IV [2B] (WA71)	2	0.5	2	100.0	0	0.0	0	0.0	1	50.0
ST45-V [5C2] (WA4)	1	0.3	1	100.0	0	0.0	0	0.0	0	0.0
ST45-IV [2B] (WA23)	1	0.3	0	0.0	1	100.0	0	0.0	0	0.0
ST6-IV [2B] (WA66)	1	0.3	0	0.0	1	100.0	0	0.0	0	0.0
ST5-V [5C2] (WA90)	1	0.3	0	0.0	1	100.0	0	0.0	0	0.0
ST5-IV [2B] (WA96)	1	0.3	0	0.0	1	100.0	0	0.0	0	0.0
ST8-IV [2B] (WA101)	1	0.3	0	0.0	1	100.0	0	0.0	0	0.0
STnovel-IV [2B] (WA114)	1	0.3	0	0.0	1	100.0	0	0.0	0	0.0
ST5-V [5C2] (WA109)	1	0.3	0	0.0	1	100.0	0	0.0	0	0.0
ST612-IV [2B] (WA20)	1	0.3	0	0.0	1	100.0	0	0.0	0	0.0
ST1-V [5C2]	1	0.3	0	0.0	1	100.0	0	0.0	0	0.0
ST45-V [5C2]	1	0.3	0	0.0	1	100.0	0	0.0	0	0.0
ST59-V [5C2]	1	0.3	0	0.0	1	100.0	0	0.0	0	0.0
ST5-V [5C2]	1	0.3	1	100.0	0	0.0	0	0.0	0	0.0
Sub-total	217	59.0	62	28.6	153	70.5	2	0.9	77	35.5
Total	368	100.0	138	37.5	225	61.1	5	1.4	77	20.9

PVL Panton-Valentine leucocidin.

MRSA Methicillin-resistant *Staphylococcus aureus*.

* Percentage of all MRSA.

† Percentage of the strain.

ST239-III [3A] (Aus-2/3 EMRSA) accounted for 39.1% of HA-MRSA ranging from 0% in Tasmania to 100% in the Northern Territory (Table 4). PVL negative ST239-III [3A] (Aus-2/3 EMRSA) were typically resistant to erythromycin (100%), co-trimoxazole (100%), ciprofloxacin (97%), gentamicin (97%), tetracycline (84%) and clindamycin (81%).

Community-associated-methicillin-resistant Staphylococcus aureus

For the 217 CA-MRSA strains, 28.6% (62) of episodes were epidemiologically classified as hospital onset and 70.5% (153) were classified as community onset. The date of hospital admission was not available for 2 patients. Twenty-seven different CA-MRSA clones were identified by pulsed-field gel electrophoresis corresponding to 19 MLST/SCC*mec* clones (Table 3). Overall, 80.7% of CA-MRSA were classified into 6 clones, each having more than 10 isolates (Table 5).

ST93-IV [2B] (Queensland CA-MRSA) accounted for 23.0% of CA-MRSA, ranging from 15.4% in Western Australia to 100% in Tasmania (Table 5). PVL positive ST93-IV [2B] (Queensland CA-MRSA) was typically resistant to the ß-lactams only (77.1%, 37/48) or additionally resistant to erythromycin (10.4%, 5/48). Four isolates were resistant to erythromycin and clindamycin. A single isolate was non-susceptible to ciprofloxacin with an MIC of 2 mg/L. One isolate exhibited high-level mupirocin resistance.

ST1-IV [2B] (WA1) accounted for 20.7% of CA-MRSA, ranging from 0% in the Australian Capital Territory and Tasmania to 26.9% in Western Australia (Table 5). Typically PVL negative, 66.7% of isolates were resistant to the ß-lactams only (30/45) or additionally resistant to erythromycin (8.9%, 4/45) or fusidic acid (6.7%, 3/45) or both (2.2%, 1/45). Four isolates were non–susceptible to ciprofloxacin and additionally resistant to erythromycin and clindamycin (1); erythromycin, gentamicin, daptomycin and tetracycline (1); erythromycin, fusidic acid, and co-trimoxazole (1); or erythromycin, clindamycin and nitrofurantoin (1). Single isolates were non-susceptible to nitrofurantoin; or resistant to gentamicin; gentamicin, erythromycin and high-level mupirocin; erythromycin or fusidic acid; and tetracycline.

ST5-IV [2B] (WA3) accounted for 11.5% of CA-MRSA ranging from 0% in the Australian Capital Territory and Tasmania to 17.9% in South Australia (Table 5). PVL negative ST5-IV [2B] (WA3) was typically resistant to the ß-lactams only (44%, 11/25) or additionally resistant to erythromycin (20%, 5/25). Three isolates were non-susceptible to ciprofloxacin including one isolate additionally resistant to erythromycin and clindamycin. Two isolates exhibited high-level mupirocin resistance. Two isolates were resistant to erythromycin and clindamycin. Single isolates were resistant to erythromycin and co-trimoxazole, or rifampicin.

ST78-IV [2B] (WA2), PVL negative, accounted for 9.2% of CA-MRSA and was isolated predominately in Western Australia (Table 5). Isolates were resistant to the ß-lactams only (50%, 10/20) or additionally resistant to erythromycin (45%, 9/20). One isolate was additionally resistant to erythromycin and clindamycin.

ST30-IV [2B] (SWP CA-MRSA) and ST45-V [5C2&5] (WA84) accounted for 8.3% and 7.8% of CA-MRSA respectively and were isolated primarily in the eastern regions of Australia (Table 5). Typically PVL positive, ST30-IV [2B] (SWP CA-MRSA) was typically resistant to the ß-lactams only (50%, 9/18). Isolates were additionally non-susceptible to nitrofurantoin (6 isolates); resistant to cotrimoxazole (1); erythromycin (1); clindamycin (1); tetracycline and nitrofurantoin (1); or clindamycin, fusidic acid, nitrofurantoin and high-level mupirocin (1). All PVL negative ST45-V [5C2&5] (WA84) isolates were resistant to the ß-lactams and ciprofloxacin. Isolates were additionally resistant to erythromycin and tetracycline (2 isolates); erythromycin, gentamicin and tetracycline (2); erythromycin and clindamycin (2); erythromycin (1); erythromycin and gentamicin (1); erythromycin, clindamycin and tetracycline (1); erythromycin, clindamycin and gentamicin (1); or erythromycin, clindamycin, gentamicin and tetracycline (1).

Overall 90.8% of CA-MRSA were non-multiresistant and 51.6% were resistant to the ß-lactams only. However, 20 CA-MRSA isolates were multiresistant.

Panton-Valentine leucocidin

Overall 20.9% (77) of MRSA were PVL positive, all were CA-MRSA (Table 3). PVL positive CA-MRSA clones included the international CA-MRSA clone ST8-IV [2B] USA300.

Discussion

The Australian Group on Antimicrobial Resistance Targeted Resistance Surveillance program (AGAR-TRS) collects data on antimicrobial resistance, focussing on bloodstream infections caused by *S. aureus*, *Enterococcus* and *Enterobacteriaceae*. All data being collected in the AGAR-TRS programs are generated as part of routine patient care in Australia with most being available through labo-

Table 4: Number and proportion of healthcare-associated methicillin-resistant *Staphylococcus aureus* multilocus sequence types, Australia, 2013, by state or territory

Type	ACT		NSW		NT		Qld		SA		Tas.		Vic.		WA		Aus.	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
ST22-IV [2B] (EMRSA-15)	3	42.9	35	56.5	0	0.0	14	70.0	13	81.3	1	100.0	14	45.2	8	88.9	88	58.3
ST239-III (3A] (Aus-2/3 EMRSA)	4	47.1	26	41.9	5	100.0	6	30.0	3	18.7	0	0.0	14	45.2	1	11.1	59	39.1
ST5-II [2A] (USA100)	0	0.0	1	1.6	0	0.0	0	0.0	0	0.0	0	0.0	3	9.6	0	0.0	4	2.6
Total	7	100.0	62	100.0	5	100.0	20	100.0	16	100.0	1	100.0	31	100.0	9	100.0	151	100.0

Table 5: Number and proportion of the major community-associated methicillin-resistant *Staphylococcus aureus* multilocus sequence types, Australia (> 10 isolates), 2013, by state or territory

Type	ACT		NSW		NT		Qld		SA		Tas.		Vic.		WA		Aus.	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
ST93-IV [2B] (Qld)	1	25.0	10	30.3	9	47.4	8	17.1	9	32.1	1	100.0	4	12.1	8	15.4	50	23.0
ST1-IV [2B] (WA1)	0	0.0	4	12.1	4	21.1	12	25.5	5	17.9	0	0.0	6	18.2	14	26.9	45	20.7
ST5-IV [2B] (WA3)	0	0.0	2	6.1	1	5.3	6	12.8	5	17.9	0	0.0	3	9.1	8	15.4	25	11.5
ST78-IV [2B] (WA2)	0	0.0	1	3.0	0	0.0	1	2.1	2	7.1	0	0.0	1	3.0	15	28.8	20	9.2
ST30-IV [2B] (SWP)	0	0.0	3	9.1	3	15.8	6	12.8	2	7.1	0	0.0	3	9.1	1	1.9	18	8.3
ST45-V [5C2&5] (WA84)	2	50.0	6	18.2	0	0.0	0	0.0	1	3.6	0	0.0	8	24.2	0	0.0	17	7.8
Other	1	25.0	7	21.2	2	10.5	14	29.7	4	14.3	0	0.0	8	24.2	6	11.5	42	19.4
Total	4	100.0	33	100.0	19	100.0	47	100.0	28	100.0	1	100.0	33	100.0	52	100.0	217	100.0

ratory and hospital bed management information systems. Isolates are referred to a central laboratory where strain and antimicrobial resistance determinant characterisation is performed. As the programs are similar to those conducted in Europe, comparison of Australian antimicrobial resistance data with other countries is possible.[20]

In the 2012 European Centre for Disease Prevention and Control and Prevention SAB surveillance program, the European Union/European Economic Area (EU/EEA) population-weighted mean percentage of *S. aureus* resistant to methicillin was 17.8%, ranging from 0.7% in Sweden to 53.9% in Romania.[21] In ASSOP 2013, 19.1% (95% CI 17.5%–21.0%) of the 2,010 SAB episodes were methicillin resistant. Five European countries reported a similar percentage to Australia, including Bulgaria (19.8%; 95% CI, 15%–26%), Croatia (22%, 95% CI 18%–26%), France (19.2%, 95% CI 18%–20%), Ireland (22.6%, 95% CI 20%–25%) and Slovakia (21.7%, 95% CI 18%–26%). However, for 16 of the 30 European countries (primarily northern Europe countries including Germany and the United Kingdom) the percentage of SAB isolates resistant to methicillin was less than that reported in ASSOP 2013. Similar to Europe, which has seen the EU/EEA population-weighted mean percentage decrease significantly from 23.2% in 2009 to 17.8% in 2012, the percentage of methicillin resistant SAB in Australia has decreased from 23.8% (95% CI 21.4%–26.4%) in 2007 to 19.1% (95%CI 17.5%–21.0%) in 2013 ($P < 0.0001$).[20] The decrease in methicillin resistant SAB is consistent with what has been reported elsewhere[21,22] and is believed to be attributed to the implementation of antimicrobial stewardship and a package of improved infection control procedures including hand hygiene, MRSA screening and decolonisation, patient isolation and infection prevention care bundles.[23–27] However, unlike Europe, Australia has a high prevalence of CA-MRSA and so further reduction in the proportion of SAB due to MRSA may prove problematic.

In ASSOP 2013, the all cause mortality at 30-days was 14.4% (95% CI 12.8%–16.2%). In comparison, the 2008 Australian New Zealand Cooperative on Outcome in Staphylococcal Sepsis reported a significantly higher figure of 20.6% (95% CI 18.8%–22.5%, $P < 0.0001$), and when adjusted for Australian institutions only was 25.9% (personal communication). Although the SAB 30-day mortality appears to be falling in Australia, MRSA-associated SAB mortality remains high (20.1%, 95% CI,15.9%–24.7%, 67/334) and was significantly higher than MSSA-associated SAB mortality (13%, 95% CI 11.3%–14.9%, 179/1378, $P < 0.0001$). Although it has recently been shown that invasive MRSA infection may be more life-threatening, partially because of the inferior efficacy of the standard treatment, vancomycin,[9] the emergence of hyper-virulent multi-resistant CA-MRSA clones such as ST93-IV [2B] (Queensland CA-MRSA) causing healthcare-associated SAB is of concern.[30]

With the exception of the ß-lactams and erythromycin, antimicrobial resistance in MSSA remains rare. However, in addition to the ß-lactams, approximately 50% of MRSA were resistant to erythromycin and ciprofloxacin and approximately 20% were resistant to co-trimoxazole, tetracycline and gentamicin. Resistance was largely attributable to 2 healthcare associated MRSA clones, ST22-IV [2B] (EMRSA-15), which is typically ciprofloxacin and erythromycin resistant, and ST239-III [3A] (Aus-2/3 EMRSA) which is typically erythromycin, clindamycin, ciprofloxacin, co-trimoxazole, tetracycline and gentamicin resistant. Since the early 1980s the multi-resistant ST239-III [3A] (Aus-2/3 EMRSA) was the dominant HA-MRSA clone in Australian hospitals. However, ST22-IV [2B] (EMRSA-15) has recently replaced it as the most prevalent HA-MRSA isolated from clinical specimens and this change has occurred throughout the country.[31] In the current survey, ST239-III [3A] was the only HA-MRSA clone in the Northern Territory. In ASSOP 2013, approximately 24% of MRSA were characterised as ST22-IV [2B] (EMRSA-15). CA-MRSA, in particular the ST45-V [5C2&5] (WA84) clone, has acquired multiple antimicrobial resistance determinants including ciprofloxacin, erythromycin, clindamycin, gentamicin and tetracycline. Linezolid, daptomycin and teicoplanin resistance was detected in a small number of *S. aureus* isolates. Resistance was not detected for vancomycin.

Approximately 30% of SAB caused by CA-MRSA were healthcare onset cases. Although in several parts of the United States of America the CA-MRSA clone USA300 has replaced the HA-MRSA clone ST5-II [2A] (USA100) as a cause of healthcare associated MRSA infection,[28] transmission of CA-MRSA in Australian hospitals is thought to be rare.[33,34] Consequently, it is likely that many of the healthcare onset CA-MRSA SAB infections reported in ASSOP 2013 were caused by the patient's own colonising strains acquired prior to admission. In Australia, CA-MRSA clones such as PVL-positive ST93-IV [2B] (Queensland CA-MRSA) and PVL-negative ST1-IV [2B] (WA1) are well established in the community and therefore it is important to monitor antimicrobial resistance patterns in both community and healthcare associated SAB as this information will guide therapeutic practices in treating *S. aureus* sepsis.

In conclusion, ASSOP 2013 has demonstrated that antimicrobial resistance in SAB in Australia is a

significant problem and continues to be associated with a high mortality. This may be due, in part, to the high prevalence of methicillin resistant SAB in Australia, which is significantly higher than most EU/EEA countries. Consequently, MRSA must remain a public health priority and continuous surveillance of SAB and its outcomes and the implementation of comprehensive MRSA strategies targeting hospitals and long-term care facilities are essential.

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Australian Enterococcal Sepsis Outcome Programme annual report, 2013

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Abstract

From 1 January to 31 December 2013, 26 institutions around Australia participated in the Australian Enterococcal Sepsis Outcome Programme (AESOP). The aim of AESOP 2013 was to determine the proportion of enterococcal bacteraemia isolates in Australia that are antimicrobial resistant, and to characterise the molecular epidemiology of the *Enterococcus faecium* isolates. Of the 826 unique episodes of bacteraemia investigated, 94.6% were caused by either *E. faecalis* (56.1%) or *E. faecium* (38.5%). Ampicillin resistance was not detected in *E. faecalis* but was detected in over 90% of *E. faecium*. Vancomycin non-susceptibility was reported in 0.2% and 40.9% of *E. faecalis* and *E. faecium* respectively and was predominately due to the acquisition of the *vanB* operon. Overall, 41.6% of *E. faecium* harboured *vanA* or *vanB* genes. The percentage of *E. faecium* bacteraemia isolates resistant to vancomycin in Australia is significantly higher than that seen in most European countries. *E. faecium* isolates consisted of 81 pulsed-field gel electrophoresis pulsotypes of which 72.3% were classified into 14 major pulsotypes containing five or more isolates. Multilocus sequence typing grouped the 14 major pulsotypes into clonal cluster 17, a major hospital-adapted polyclonal *E. faecium* cluster. Of the 2 predominant sequence types, ST203 (80 isolates) was identified across Australia and ST555 (40 isolates) was isolated primarily in the western and central regions (Northern Territory, South Australia and Western Australia) respectively. In conclusion, the AESOP 2013 has shown enterococcal bacteraemias in Australia are frequently caused by polyclonal ampicillin-resistant high-level gentamicin resistant *vanB E. faecium*, which have limited treatment options. *Commun Dis Intell* 2014;38(4):E320–E326.

Keywords: antimicrobial resistance surveillance; *Enterococcus faecium, Enterococcus faecalis*, vancomycin resistant enterococci, bacteraemia

Introduction

Globally, enterococci are thought to account for approximately 10% of all bacteraemias, and in North America and Europe are the 4th and 5th leading cause of sepsis respectively.[1,2] Although in the 1970s healthcare-associated enterococcal infections were primarily due to *Enterococcus faecalis*, there has been a steadily increasing prevalence of *E. faecium* nosocomial infections.[3–5] While innately resistant to many classes of antibiotics, *E. faecium* has demonstrated a remarkable capacity to evolve new antimicrobial resistances. In 2009 the Infectious Diseases Society of America highlighted *E. faecium* as one of the key problem bacteria or ESKAPE (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumanii*, *Pseudomonas aeruginosa*, and *Enterobacter* species) pathogens requiring new therapies.[6]

The Australian Group on Antimicrobial Resistance (AGAR) is a network of laboratories located across Australia that commenced surveillance of antimicrobial resistance in *Enterococcus* species in 1995.[7] In 2011, AGAR commenced the Australian Enterococcal Sepsis Outcome Programme (AESOP).[8] The objective of AESOP 2013 is to determine the proportion of *E. faecalis* and *E. faecium* bacteraemia isolates demonstrating antimicrobial resistance with particular emphasis on:

1. assessing susceptibility to ampicillin;
2. assessing susceptibility to glycopeptides; and
3. molecular epidemiology of *E. faecium*.

Methods

Participants

Twenty-six laboratories from all 8 Australian states and territories participated in the program.

Collection period

From 1 January to 31 December 2013, the 26 laboratories collected all enterococcal species isolated from blood cultures. Enterococci with the same species and antimicrobial susceptibility profiles isolated from a patient's blood culture within 14 days of the 1st positive culture were excluded. A new enterococcal sepsis episode in the same patient was recorded if it was confirmed by a further culture of blood taken more than 14 days after the initial positive culture. Data were collected on age, sex, date of admission and discharge (if admitted), and mortality at 30 days from the date of blood

culture collection. To avoid interpretive bias, no attempt was made to assign attributable mortality. Each episode of bacteraemia was designated as 'hospital onset' if the 1st positive blood culture(s) in an episode was collected more than 48 hours after admission.

Laboratory testing

Enterococcal isolates were identified to the species level by the participating laboratories using one of the following methods: API 20S (bioMérieux), API ID32Strep (bio-Mérieux), Vitek2® (bioMérieux), Phoenix (BD), matrix-assisted laser desorption ionization Biotyper (Bruker Daltonics), Vitek-MS (bioMérieux), polymerase chain reaction (PCR), or conventional biochemical tests. Antimicrobial susceptibility testing was performed by using the Vitek2® (bioMérieux, France) or the Phoenix™ (BD, USA) automated microbiology systems according to the manufacturer's instructions. Minimum inhibitory concentration (MIC) data and isolates were referred to the Australian Collaborating Centre for *Enterococcus* and *Staphylococcus* Species (*ACCESS*) Typing and Research. Clinical and Laboratory Standards Institute (CLSI) and European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints were utilised for interpretation.[9,10] Isolates with either a resistant or an intermediate category were classified as non-susceptible. Molecular testing including *vanA/B* PCR, pulsed-field gel electrophoresis (PFGE) and multilocus sequence typing was performed as previously described.[11–13]

A chi-square test for comparison of 2 proportions was performed and 95% confidence intervals (95%CI) were determined using MedCalc for Windows, version 12.7 (Medcalc Software, Ostend Belgium).

Approval to conduct the prospective data collection was given by the research ethics committee associated with each participating laboratory.

Results

From 1 January to 31 December 2013, 826 unique episodes of enterococcal bacteraemia were identified. Males comprised a significantly higher proportion of cases than females (*P* = 0.02) with 551 (66.7%) being male (95% CI, 63.4–69.9). The average age of patients was 62 years ranging from 0–99 years with a median age of 67 years. The place of onset was recorded for 804 of the 826 episodes, of which 426 (53.0%) were hospital onset (95% CI, 49.8–56.5). All cause mortality at 30 days was 18.9% (95% CI, 16.1–21.9).

Although 9 *Enterococcus* species were identified, 56.1% (463 isolates) were *E. faecalis* and 38.5% (318) were *E. faecium*. Forty-five enterococci were identified either as *Enterococcus casseliflavus* (16 isolates), *E. gallinarum* (10), *E. avium* (5), *E. hirae* (5) *E. raffinosus* (3), *E. durans* (3) or *E. gilvus* (1). Two isolates could not be identified to the species level.

Enterococcus faecalis phenotypic susceptibility

Apart from erythromycin, tetracycline, ciprofloxacin and high-level gentamicin, resistance was rare among *E. faecalis* (Table 1). Ampicillin resistance was not detected and only 1 isolate was vancomycin non-susceptible. Of concern, 29 (6.3%) *E. faecalis*, isolated across Australia, were linezolid non-susceptible (MIC = 4 mg/L). Less than 1% of isolates were non-susceptible to daptomycin and teicoplanin.

Enterococcus faecium phenotypic susceptibility

The majority of *E. faecium* were non-susceptible to multiple antimicrobials (Table 2). Most isolates were non-susceptible to ampicillin, erythromycin, tetracycline, ciprofloxacin, nitrofurantoin and high-level gentamicin. Overall, 130 (40.9%) of the 318 *E. faecium* were phenotypically vancomycin non-susceptible (MIC > 4 mg/L). Fifteen (4.7%) and 8 (2.5%) isolates were teicoplanin and linezolid non-susceptible respectively.

Genotypic vancomycin susceptibility

The vancomycin non-susceptible *E. faecalis* isolate (MIC ≥ 32 mg/L) harboured a *vanB* gene. *VanA/B* PCR was performed on 129 isolates of the 130 vancomycin non-susceptible *E. faecium* isolates. *VanA* was detected in 8 isolates (vancomycin and teicoplanin MICs ≥ 32 mg/L) and *vanB* in 121 isolates (vancomycin MICs 8 [4 isolates] and ≥ 32 mg/L [117 isolates]). Seven of the 8 *vanA E. faecium* isolates were from New South Wales. Of the 121 *vanB E. faecium* isolates, seven were teicoplanin resistant by EUCAST criteria (MIC > 32 mg/L). *VanA/B* PCR was performed on 181 of the 188 vancomycin susceptible *E. faecium* isolates of which eight (4.4%) harboured a *vanB* gene.

Enterocoocus faecium molecular epidemiology

By PFGE, 301 of the 318 *E. faecium* were classified into 81 pulsotypes, including 14 major pulsotypes with five or more isolates (Table 3). Of the 67 pulsotypes with less than 5 isolates, 58 had only 1 isolate. Overall, 219 (72.8%) of the 301 isolates were grouped into the 14 major pulsotypes from which

Table 1: The number and proportion of *Enterococcus faecalis* non-susceptible to ampicillin and the non-ß-lactam antimicrobials, Australia, 2013

Antimicrobial	Tested	Breakpoint (mg/L)	Non-susceptible	
			n	%
Ampicillin	463	>8*	0	
		>4†	0	
Vancomycin	463	>4‡	1	0.2
Erythromycin	451	>0.5‡	375	83.2
Tetracycline	419	>4‡	314	74.9
Ciprofloxacin	424	>1‡	91	21.5
Daptomycin	397	>4‡	1	0.3
Teicoplanin	462	>8*	3	0.6
		>2†	4	0.9
Linezolid	462	>2‡	29	6.3
Nitrofurantoin	454	>32*	8	1.8
		>64†	4	0.9
High level gentamicin	463	>128*	150	32.4

* Clinical and Laboratory Standards Institute (CLSI) non-susceptible breakpoint.

† European Committee on Antimicrobial Susceptibility Testing (EUCAST) non-susceptible breakpoint.

‡ CLSI and EUCAST non-susceptible breakpoint.

Table 2: The number and proportion of *Enterococcus faecium* non-susceptible to ampicillin and the non-ß-lactam antimicrobials, Australia, 2013

Antimicrobial	Tested	Breakpoint (mg/L)	Non-susceptible	
			n	%
Ampicillin	318	>8*	295	92.8
		>4†	296	93.1
Vancomycin	318	>4c‡	130	40.9
Erythromycin	309	>0.5‡	296	95.8
Tetracycline	294	>4‡	146	49.7
Ciprofloxacin	305	>1‡	290	95.1
Teicoplanin	318	>8*	15	4.7
		>2†	15	4.7
Linezolid	315	>2‡	8	2.5
Nitrofurantoin	315	>32*	259	82.2
		>64†	114	36.2
High level gentamicin	317	>128*	196	61.8

* Clinical and Laboratory Standards Institute (CLSI) non-susceptible breakpoint.

† European Committee on Antimicrobial Susceptibility Testing (EUCAST) non-susceptible breakpoint.

‡ CLSI and EUCAST non-susceptible breakpoint.

8 multilocus sequence types (STs) were identified. Using eBURST, the 8 STs were grouped into clonal complex (CC) 17.

Of the 2 predominant sequence types, ST203 (80 isolates) was identified across Australia and ST555 (40 isolates), was isolated primarily in the western and central regions (Northern Territory, South Australia and Western Australia). ST796 (32 isolates) was only identified in Victoria while ST17 (23 isolates) was identified on the eastern coast (Queensland, New South Wales, Victoria) and in Western Australia. ST341 (19 isolates), ST192 (12 isolates) and ST18 (8 isolates) were

primarily identified in New South Wales, Victoria and Queensland respectively. ST761 (5 isolates) was identified only in New South Wales.

*Van*A or *vanB* genes were identified in 2 (5 isolates) and 10 (113 isolates) major pulsotypes respectively (Table 4). Efm22 (ST18) harboured *vanA* and *vanB* genes. Twelve minor pulsotypes (13 isolates) and 1 non-typed *E. faecium* isolates also harboured

Table 3: The number and proportion of major *Enterococcus faecium* pulsed-field gel electrophoresis pulsotypes, Australia, 2013, by state or territory

Type	ST	ACT		NSW		NT		Qld		SA		Tas.		Vic.		WA		Aus.	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Efm1		1	5.5	3	3.0	0		3	8.1	0		1	20.0	0		2	4.8	10	3.1
Efm2		0		0		0		11	29.7	15	46.9	0		5	6.3	0		31	9.8
Efm75	ST203	7	38.9	4	4.0	0		7	18.9	0		0		2	2.5	0		20	6.3
Efm76		0		13	12.9	0		0		0		0		0		0		13	4.1
Efm6		0		3	3.0	0		0		0		0		3	3.8	0		6	1.9
Efm4	ST555	0		0		0		0		8	25.0	0		1	1.3	22	52.4	31	9.8
Efm77		0		1	1.0	3	100	0		4	12.5	0		0		1	2.4	9	2.8
Efm74	ST796	0		0		0		0		0		0		32	40.0	0		32	10.1
Efm5	ST17	1	5.5	8	7.9	0		2	5.4	0		0		2	2.5	5	11.9	18	5.7
Efm18		0		5	5.0	0		0		0		0		0		0		5	1.6
Efm3	ST341	3	16.7	14	13.9	0		2	5.4	0		0		0		0		19	6.0
Efm24	ST192	0		2	1.9	0		0		0		0		10	12.7	0		12	3.8
Efm22	ST18	0		2	2.0	0		5	13.5	1	3.1	0		0		0		8	2.5
Efm78	ST761	0		5	5.0	0		0		0		0		0		0		5	1.6
Other	ND	6	33.3	29	28.7	0		6	16.2	4	12.5	4	80.0	22	27.9	11	26.2	82	25.9
ND	ND	0		12	11.9	0		1	2.7	0		0		3	3.8	1	2.4	17	5.4
Total		18		101		3		37		32		5		80		42		318	

ND = Not done

Table 4: Number and proportion of major *Enterococcus faecium* pulsed-field gel electrophoresis pulsotypes harbouring *vanA/B* genes, Australia, 2013

Pulsotypes	ST	Number	vanA		vanB		Not detected	
			n	%	n	%	n	%
Efm1		10	0		1	10.0	9	90.0
Efm2		31	0		31	100.0	0	
Efm75	ST203	20	0		2	10.0	18	90.0
Efm76		13	0		12	92.3	1	7.7
Efm6		6	0		0		6	100.0
Efm4	ST555	31	0		0		31	100.0
Efm77		9	0		9	100.0	0	
Efm74	ST796	32	0		32	100.0	0	
Efm5	ST17	18	0		3	16.7	15	83.3
Efm18		5	4	80.0	0		1	20.0
Efm3	ST341	19	0		19	100.0	0	
Efm24	ST192	12	0		3	25.0	9	75.0
Efm22	ST18	8	1	12.5	2	25.0	5	62.5
Efm78	ST761	5	0		0		5	100.0
Total		219	5	2.3	114	52.0	100	45.7

vanB genes. In addition, *vanA* genes were detected in 3 minor pulsotypes (3 isolates). Over 90% of Efm2 (ST203), Efm76 (ST203), Efm77 (ST555), Efm74 (ST796) and Efm3 (ST341) harboured *vanB* genes. In contrast, at least 90% of Efm1 (ST203), Efm75 (ST203), Efm6 (ST203), Efm4 (ST555) and Efm78 (ST761) did not harbour *van* genes. Four of the 8 *vanA E. faecium* isolates were characterised as Efm18 pulsotype (ST17).

Discussion

Enterococci are intrinsically resistant to a broad range of antimicrobials including the cephalosporins and sulphonamides. Through their ability to acquire additional resistance through the transfer of plasmids and transposons and to disseminate easily in the hospital environment, enterococci have become difficult to treat and provide major infection control challenges.

All data being collected in the AGAR sepsis programs are generated as part of routine patient care in Australia with most being available through laboratory and hospital bed management information systems. Isolates are referred to a central laboratory where strain and antimicrobial resistance determinant characterisation is performed. As the programs are similar to those conducted in Europe comparison of Australian antimicrobial resistance data with other countries is possible.[14]

In the 2012 European Centre for Disease Prevention and Control and Prevention Enterococci surveillance program the European Union/European Economic Area (EU/EEA) population-weighted mean percentage of *E. faecium* resistant to vancomycin was 8.1%. This ranged from 0.0% in Bulgaria, Croatia, Estonia, Iceland, Luxembourg, Netherlands, Slovenia and Sweden to 44.0% in Ireland. Germany (16.2%), Greece (17.2%) and Portugal (23.3%) were the only other EU/EEA countries to report levels above 15%.[15]

In AESOP 2013, approximately 40% of enterococcal bacteraemias were due to *E. faecium* of which 40.9% (95% CI, 35.4–46.5) were vancomycin non-susceptible. Unlike Europe, where vancomycin resistance has predominately been due to the acquisition of the *vanA* operon, almost all AESOP 2013 *E. faecium* isolates harbouring *van* genes carried the *vanB* operon. In addition to vancomycin resistance, the majority of *E. faecium* isolates were non-susceptible to multiple antimicrobials including ampicillin (92.8%, 95% CI, 89.4–95.4), and high level gentamicin (61.8%, 95%CI 56.2–67.2). In the previous AGAR enterococcal sepsis study, AESOP 2011, 37% and 90% of *E. faecium* harboured *vanA/B* genes and were ampicillin resistant respectively; suggesting the incidence of multi-drug-resistant *E. faecium* bacteraemia in Australia is increasing.

Eight (6.2%) of the 129 *vanB E. faecium* isolates had a vancomycin MIC at or below the CLSI and the EUCAST susceptible breakpoint (≤ 4 mg/L) and would not have been identified using routine phenotypic antimicrobial susceptibility methods.

With the use of PFGE, *E. faecium* was shown to be very polyclonal, consistent with the known plasticity of the enterococcal genome. The 14 major *E. faecium* pulsotypes formed part of CC17, a global hospital-derived lineage that has successfully adapted to hospital environments. CC17 is characteristically ampicillin and quinolone resistant and subsequent acquisition of *vanA*– or *vanB*-containing transposons by horizontal transfer in CC17 clones has resulted in vancomycin resistant enterococci with pandemic potential. In AESOP 2013, 5 major pulsotypes not characterised in AESOP 2011 were identified, including: Efm74 (32 isolates), Efm75 (20 isolates), Efm76 (13 isolates), Efm77 (9 isolates) and Efm78 (5 isolates). Pulsotypes Efm 76 and Efm78 were identified in New South Wales and Efm74 in Victoria. Efm75 was identified in several regions on the east coast of Australia, while Efm77 was primarily in the central regions.

Conclusion

The AESOP 2013 study has shown that although predominately caused by *E. faecalis,* enterococcal bacteraemia in Australia is frequently caused by ampicillin-resistant high-level gentamicin-resistant *vanB E. faecium*. Furthermore the percentage of *E. faecium* bacteraemia isolates resistant to vancomycin in Australia is significantly higher than that seen in almost all European countries. In addition to being a significant cause of healthcare-associated sepsis, the emergence of multiple multi-resistant hospital-adapted *E. faecium* strains has become a major infection control issue in Australian hospitals. Further studies on the enterococcal genome will contribute to our understanding of the rapid and ongoing evolution of enterococci in the hospital environment and assist in preventing their nosocomial transmission.

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Enterobacteriaceae Sepsis Outcome Programme annual report, 2013

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Abstract

The Australian Group on Antimicrobial Resistance performs regular period-prevalence studies to monitor changes in antimicrobial resistance in selected enteric Gram-negative pathogens. The 2013 survey focussed for the first time on blood stream infections. Four thousand nine hundred and fifty-eight *Enterobacteriaceae* species were tested using commercial automated methods (Vitek® 2, BioMérieux; Phoenix™, BD). The results were analysed using Clinical and Laboratory Standards Institute (CLSI) and European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints (January 2014). Of the key resistances, non-susceptibility to the third-generation cephalosporin, ceftriaxone, was found in 7.5%/7.5% (CLSI/EUCAST criteria respectively) of *Escherichia coli*; 6.3%/6.3% of *Klebsiella pneumoniae*, and 7.4%/7.4% of *K. oxytoca*. Non-susceptibility rates to ciprofloxacin were 10.3%/11.3% for *E. coli*, 4.6%/7.5% for *K. pneumoniae*, 0.6%/0.6% for *K. oxytoca*, and 3.6%/6.1% in *Enterobacter cloacae*. Resistance rates to piperacillin-tazobactam were 3.1%/6.2%, 4.2%/7.0%, 11.9% /12.6%, and 17.3% /22.2% for the same 4 species respectively. Fourteen isolates were shown to harbour a carbapenemase gene, 9 bla_{IMP}, 3 bla_{KPC}, and 2 bla_{NDM}. *Commun Dis Intell* 2014;38(4):E327–E333.

Keywords: antibiotic resistance; bacteraemia; gram-negative; *Escherichia coli; Enterobacter; Klebsiella*

Introduction

Emerging resistance in common pathogenic members of the Enterobacteriaceae family is a worldwide phenomenon, and presents therapeutic problems for practitioners in both the community and in hospital practice. The Australian Group on Antimicrobial Resistance (AGAR) commenced surveillance of the key Gram-negative pathogens, *Escherichia coli* and *Klebsiella* species in 1992. Surveys were conducted biennially until 2008 when annual surveys commenced alternating between community– and hospital-onset infections (http://www.agargroup.org/surveys). In 2004, another genus of Gram-negative pathogens in which resistance can be of clinical importance, *Enterobacter* species, was added. *E. coli* is the most common cause of community-onset urinary tract infection, while *Klebsiella* species are less common but are known to harbour important resistances. *Enterobacter* species are less common in the community, but of high importance due to intrinsic resistance to first-line antimicrobials in the community. Taken together, the 3 groups of species surveyed are considered to be valuable sentinels for multi-resistance and emerging resistance in enteric Gram-negative bacilli. In 2013, AGAR commenced the Enterobacteriaceae Sepsis Outcome Programme, which focuses on the collection of resistance and some demographic data on all isolates prospectively from patients with bacteraemia.

Resistances of particular interest include resistance to ß-lactams due to ß-lactamases, especially extended-spectrum ß-lactamases (ESBL). These inactivate the third-generation cephalosporins that are normally considered reserve antimicrobials. Other resistances of interest are to agents important for treatment of these serious infections, such as gentamicin; and resistance to reserve agents such as ciprofloxacin and meropenem.

The objectives of the 2013 surveillance program were to:

1. monitor resistance in Enterobacteriaceae isolated from blood;
2. examine the extent of co-resistance and multi-resistance; and
3. detect emerging resistance to newer last-line agents such as carbapenems.

Methods

Study design

From 1 January to 31 December 2013, 25 institutions across Australia collected either all or up to 200 isolates from different patient episodes of bacteraemia.

Species identification

Isolates were identified using the routine method for each institution; Vitek®, Phoenix™ Automated Microbiology System, or where available, mass spectrometry (MALDI-TOF).

Susceptibility testing

Testing was performed by 2 commercial semi-automated methods, Vitek ® 2 (BioMérieux) or

Phoenix™ (BD), which are calibrated to the ISO reference standard method of broth microdilution. Commercially available Vitek AST-N246, Vitek AST-N247, Phoenix NMIC/ID-80 or Phoenix NMIC-203 cards were utilised by all participants throughout the survey period. The Clinical and Laboratory Standards Institute (CLSI) M100[1] and European Committee on Antimicrobial Susceptibility Testing (EUCAST) v4.0[2] breakpoints from January 2014 have been employed in the analysis. For analysis of cefazolin, breakpoints of ≤ 4 for susceptible and ≥ 8 for resistant were applied due to the restricted minimum inhibitory concentration (MIC) range available on the commercial cards, recognising that the January 2014 breakpoint is actually susceptible (≤ 2 mg/L).

Molecular confirmation of resistances

E. coli and *Klebsiella* isolates with ceftazidime or ceftriaxone MIC > 1 mg/L, or cefoxitin MIC > 8 mg/L; *Enterobacter* spp. with cefepime MIC > 1 mg/L; all isolates with ciprofloxacin MIC > 0.25 mg/L; and all isolates with meropenem MIC > 0.25 mg/L were referred to a central laboratory (SA Pathology) for molecular confirmation of resistance.

All referred isolates were screened for the presence of the bla_{TEM}, and bla_{SHV} genes using a real-time polymerase chain reaction (PCR) platform (LC-480) and published primers.[3,4] A multiplex real-time TaqMan PCR was used to detect CTX-M-type genes.[5] Strains were probed for plasmid-borne AmpC enzymes using the method described by Pérez-Pérez and Hanson,[6] and subjected to molecular tests for MBL (bla_{VIM}, bla_{IMP}, and bla_{NDM}), bla_{KPC}, and $bla_{OXA\text{-}48\text{-}like}$ genes using real-time PCR.[7,8] Known plasmid mediated quinolone resistance mechanisms (Qnr, efflux (*qepA*, *oqxAB*), and aac(6')-Ib-cr) were examined by PCR on all referred isolates with ciprofloxacin MIC > 0.25 mg/L using published methods.[9,10] All *E. coli* were examined for the presence of the O25b-ST131 clone and its *H30*- and *H30*-Rx subclones.[11-13]

Results

A total of 4,958 Enterobacteriaceae species were tested. The species isolated and the numbers of each are listed in Table 1. Three genera, *E. coli*, *Klebsiella* spp. and *Enterobacter* spp. contributed 86.3% of all isolates. Major resistances and non-susceptibilities for the top 6 ranked species are listed in Table 2. Non-susceptibility, which includes intermediately resistant and resistant strains, has been included for some agents because these figures provide information about important emerging acquired resistances. Multiple acquired resistances by species are shown in Table 3. Multiresistance was detected in 11.7% of *E. coli* isolates, 7.0% of *K. pneumoniae*, and 12.6% of *Enterobacter cloacae*. A more detailed breakdown of resistances and non-susceptibilities by state and territory is provided in the online report from the group (http://www.agargroup.org/surveys).

Table 1: Species tested

Species	Total	%
Escherichia coli	2,958	59.7
Klebsiella pneumoniae	727	14.7
Enterobacter cloacae	311	6.3
Proteus mirabilis	184	3.7
Klebsiella oxytoca	163	3.3
Serratia marcescens	156	3.1
Enterobacter aerogenes	98	2.0
Salmonella species (non Typhi)	78	1.6
Morganella morganii	54	1.1
Citrobacter koseri	51	1.0
Citrobacter freundii	38	0.8
Salmonella Typhi/paratyphi	23	0.5
Pantoea agglomerans	13	0.3
Raoultella ornithinolytica	11	0.2
Enterobacter asburiae	11	0.2
Other species (n=31)	82	1.7
All species	4,958	

Escherichia coli

Moderately high levels of resistance to ampicillin (and therefore amoxycillin) were observed (50.2%/52.2%, CLSI/EUCAST criteria), with lower rates for amoxycillin-clavulanate (12.7%/– intermediate, 8.8%/21.5% resistant). Non-susceptibility to third-generation cephalosporins was low (ceftriaxone 7.5%/7.5%, ceftazidime 4.1%/7.0%). Moderate levels of resistance were detected to cefazolin (19.1%/–) and trimethoprim (26.9%/28.7%). Ciprofloxacin non-susceptibility was found in 10.3%/11.3% of *E. coli* isolates. Resistance to ticarcillin-clavulanate (8.1%/18.3%), gentamicin (7.7%/7.9%), piperacillin-tazobactam (3.1%/6.2%), cefepime (1.9%/2.8%) were low. Four isolates had elevated meropenem MICs (≥ 0.5 mg/L). For the ESBL-producing strains. ciprofloxacin and gentamicin resistance was found in 57.3%/59.0% and 41.0%/41.4% respectively.

In line with international trends among community strains of *E. coli*, most of the strains with ESBL genes harboured genes of the CTX-M type (171/229 = 75%). Over half of the *E. coli* with CTX-M group 1 types were found to belong to sequence type 131 (O25b-ST131). ST131 accounted

Table 2: Non-susceptibility and resistance rates for the top 6 ranked species tested

Antimicrobial	Category*	*Escherichia coli* (%)		*Klebsiella pneumoniae* (%)		*Klebsiella oxytoca* (%)		*Enterobacter cloacae* (%)		*Proteus mirabilis* (%)		*Serritia marcescens* (%)	
		CLSI	EUCAST	CLSI	EUCAST	CLSI	EUCAST	CLSI	EUCAST	CLSI	EUCAST	CLSI	EUCAST
Ampicillin	I	2.0	-	†	†	†	†	†	†	2.8	-	†	†
Ampicillin	R	50.2	52.2	†	†	†	†	†	†	17.0	19.8	†	†
Amoxycillinclavulanate	I	12.7	-	5.5	-	4.3	-	†	†	5.5	-	†	†
Amoxycillinclavulanate	R	8.8	21.5	6.0	11.5	8.7	13.0	†	†	5.0	10.5	†	†
Ticarcillin-clavulanate	R	8.1	18.3	5.9	9.6	10.6	12.5	23.3	27.5	0.6	1.7	1.9	5.1
Piperacillintazobactam	R	3.1	6.2	4.2	7.0	11.9	12.6	17.3	22.2	0.6	1.1	0.0	2.1
Cefazolin	R	19.1	/	10.0	/	62.1	/	†	†	24.2	/	†	†
Cefoxitin	R	2.9	/	4.2	/	0.0	/	†	†	1.1	/	†	†
Ceftriaxone	NS	7.5	7.5	6.3	6.3	7.4	7.4	26.8	26.8	1.6	1.6	5.1	5.1
Ceftazidime	NS	4.1	7.0	4.9	6.6	1.3	1.9	23.3	26.9	0.5	1.1	0.6	1.9
Cefepime	NS	3.5	6.0	2.8	5.0	0.6	0.6	4.5	12.0	0.5	1.1	0.6	1.3
Meropenem	NS	0.1	0.1	0.7	0.5	0.0	0.0	4.2	3.9	0.0	0.0	1.3	1.3
Ciprofloxacin	NS	10.3	11.3	4.6	7.5	0.6	0.6	3.6	6.1	2.2	3.8	1.3	2.6
Norfloxacin	NS	10.0	17.0	4.0	13.0	0.7	1.4	2.8	13.8	1.7	4.7	0.7	5.6
Gentamicin	NS	7.9	8.4	3.9	4.2	0.6	0.6	9.4	9.7	3.8	7.1	1.3	1.9
Trimethoprim	R	26.9	28.7	14.1	15.9	3.2	3.8	19.7	21.4	20.8	21.4	1.3	1.3
Nitrofurantoin	NS	6.1	1.3	81.6	36.7	41.0	2.5	73.4	20.1	†	†	†	†

CLSI Clinical and Laboratory Standards Institute.

EUCAST European Committee on Antimicrobial Susceptibility Testing.

* R = resistant, I = intermediate, NS = non-susceptible (intermediate + resistant), using criteria as published by the CLSI [2014] and EUCAST [2014].

† Considered largely intrinsically resistant due to natural β-lactamases; - no intermediate category; / no breakpoints defined.

Table 3: Multiple acquired resistances, by species

Species	Total	Number of acquired resistances (CLSI breakpoints)														
		Non-multi-resistant					Multi-resistant									
		0	1	2	3	Cumulative %	4	5	6	7	8	9	10	11	12	Cumulative %
Escherichia coli	2,434	1,031	490	431	197		101	54	65	37	19	7	2			
	%	42.4	20.1	17.7	8.1	88.3	4.1	2.2	2.7	1.5	0.8	0.3	0.1			11.7
Klebsiella pneumonia	598	328	163	53	12		7	13	8	5	2	2	1	2	2	
	%	54.8	27.3	8.9	2.0	93.0	1.2	2.2	1.3	0.8	0.3	0.3	0.2	0.3	0.3	7.0
Enterobacter cloacae†	301	162	55	13	33		16	13	4	2	3					
	%	53.8	18.3	4.3	11.0	87.4	5.3	4.3	1.3	0.7	1.0					12.6
Proteus mirabilis	151	8	78	41	12		9	1	0	0	1	0	1			
	%	5.3	51.7	27.2	7.9	92.1	6.0	0.7	0.0	0.0	0.7	0.0	0.7			7.9
Serritia marcescens†	142	1	134	5	1		0	0	1							
	%	0.7	94.4	3.5	0.7	99.3	0.0	0.0	0.7							0.7
*Klebsiella oxytoca**	139	47	70	10	5		7									
	%	33.8	50.4	7.2	3.6	95.0	5.0									5.0
Enterobacter aerogenes†	94	30	36	4	14		10									
	%	31.9	38.3	4.3	14.9	89.4	10.6									10.6
Salmonella spp. (non Typhi)	65	53	8	2	1		1									
	%	81.5	12.3	3.1	1.5	98.5	1.5									1.5

CLSI Clinical and Laboratory Standards Institute.

* Antibiotics included: amoxycillin-clavulanate, piperacillin-tazobactam, cefazolin, cefoxitin, ceftriaxone, ceftazidime, cefepime, gentamicin, amikacin, ciprofloxacin, nitrofurantoin, trimethoprim, meropenem;.
Antibiotics excluded: ampicillin (intrinsic resistance), ticarcillin-clavulanate, tobramycin, norfloxacin, nalidixic acid, sulfamethoxazole-trimethoprim (high correlation with antibiotics in the included list).

† Antibiotics included: piperacillin-tazobactam, ceftriaxone, ceftazidime, cefepime, gentamicin, amikacin, ciprofloxacin, nitrofurantoin, trimethoprim, meropenem
Antibiotics excluded: ampicillin, amoxycillin-clavulanate, cefazolin, and cefoxitin, (all four due to intrinsic resistance); also excluded were ticarcillin-clavulanate, tobramycin, norfloxacin, nalidixic acid, sulfamethoxazole-trimethoprim (high correlation with antibiotics in the included list).

for 66% of *E. coli* ESBL phenotypes that were ciprofloxacin resistant (MIC > 1 mg/L), and only 2% of ciprofloxacin susceptible ESBL phenotypes. Ninety-eight per cent and 57% of O25b-ST131 were associated with the H30 and *H30-Rx* subclones, respectively, with their reported association with more antibiotic resistances and greater virulence potential.[12]

Klebsiella pneumoniae

K. pneumoniae showed slightly higher levels of resistance to piperacillin-tazobactam and ceftazidime compared with *E. coli*, but lower rates of resistance to amoxycillin-clavulanate, ticarcillin-clavulanate, cefazolin, ceftriaxone ciprofloxacin, gentamicin, and trimethoprim. Four *K. pneumoniae* isolates had elevated meropenem MICs (see below). ESBLs were present in 38 of 45 (84%) presumptively ESBL-positive isolates of *K. pneumoniae*, 31 of which proved to be of the CTX-M type.

Enterobacter species

Acquired resistance was common to ticarcillin-clavulanate (23.3%/27.5% and 27.8%/32.0%), piperacillin-tazobactam (17.3%/22.2% and 20.6%/28.9%), ceftriaxone (26.5%/26.5% and 28.9%/28.9%), ceftazidime (22.7%/23.3% and 28.9%/28.9%) and trimethoprim (19.7/21.4% and 3.2%/3.2%) for *Ent. cloacae* and *Ent. aerogenes*, respectively. Cefepime, ciprofloxacin, and gentamicin resistance were all less than 10%. Fifteen of 33 *Ent. cloacae* tested for ESBLs based on a suspicious phenotype, harboured ESBL-encoding genes. Thirteen *Ent. cloacae* strains had elevated meropenem MICs.

Carbapenemase resistance

Overall, 14 isolates from 12 patients were found to harbour a carbapenemase gene. bla_{IMP} was detected in 9 strains (*Ent. cloacae* (4), *Citrobacter* spp. (2) *E. coli* (1), *S. marcescens* (1), *K. pneumoniae* (1); bla_{KPC} was detected in 3 *K. pneumoniae* isolates (1 patient with multiple admission); and bla_{NDM} in 1 patient with 2 bacteraemic episodes.

Discussion

AGAR has been tracking resistance in sentinel enteric Gram-negative bacteria since 1992. From 2008, surveillance was segregated into hospital- versus community-onset infections. The last year of hospital-onset only surveillance was 2011.[14] This is the first comprehensive survey of antimicrobial resistance among Enterobacteriaceae isolates from bacteraemic patients throughout Australia, using an approach similar to that conducted by the European EARS-Net program (http://www.ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/database/Pages/database.aspx).

CTX-M-producing *E. coli* and *Klebsiella* species and gentamicin- and ciprofloxacin-resistant *E. coli* are well established among bacteraemic patients. Of concern is the high proportion of *E. coli* that belong to the ST131 *H30-Rx* subclone, and its reported association with more antibiotic resistance and greater virulence potential.[12] Carbapenem resistance attributable to acquired carbapenemases are still rare in patients with bacteraemia in Australia, although 3 different types (IMP, KPC, and NDM) were detected from seven of the participating institutions. Compared with many other countries in our region, resistance rates in Australian Gram-negative bacteria are still relatively low,[15] but similar to those observed in 2012 in many Western European countries (http://ecdc.europa.eu/en/publications/Publications/antimicrobial-resistance-surveillance-europe-2012.pdf).

Multi-resistance is being increasingly observed, especially in *E. coli* and *Ent. cloacae*, both of which have multi-resistance rates (as defined by AGAR) above 10%. This is likely to drive more broad-spectrum antibiotic use, and increase the resistance selection pressure for important reserve classes, especially the carbapenemases.

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Australian Rotavirus Surveillance Program annual report, 2013

Carl D Kirkwood, Susie Roczo-Farkas, and the Australian Rotavirus Surveillance Group

Abstract

This report from the Australian Rotavirus Surveillance Program, together with collaborating laboratories Australia-wide, describes the rotavirus genotypes responsible for the hospitalisation of children with acute gastroenteritis during the period 1 January to 31 December 2013. During the survey period, 1,035 faecal samples were referred for rotavirus G and P genotype analysis. Of these 828 were confirmed as rotavirus positive. A total of 503 specimens were collected from children under 5 years of age, while 325 were from older children and adults. Genotype analysis of the 828 rotavirus samples collected from both children and adults revealed that G12P[8] was the dominant genotype in this reporting period, identified in 33% of strains nationally. Genotype G3P[8] was the second most common strain nationally, representing 31% of samples, followed by genotype G2P[4] (14%). This represents the first report where G12P[8] strains are the major cause of disease in this population. The genotype distribution was slightly altered when the analysis was restricted to samples collected from children under 5 years of age, with G3P[8] being the dominant genotype (39.2%) followed by G12P[8] as the second most common genotype (31%). Fluctuations in genotype distribution were also observed based on the vaccine type in use. Genotype G12P[8] was more common in states and territories using RotaTeq, while G3P[8] was more common in the locations using Rotarix. This survey highlights the yearly fluctuations in rotavirus genotypes observed since vaccine introduction, with changes in dominant genotypes an annual event. The emergence of G12P[8] as the dominant genotype further illustrates the ongoing changes in the wild type rotavirus population evident in the Australian population since vaccine introduction. *Commun Dis Intell* 2014;38(4):E334–E342.

Keywords: rotavirus, gastroenteritis, genotypes, disease surveillance

Introduction

Rotaviruses are triple layered dsRNA viruses that belong to the *Reoviridae* family. They contain 11 gene segments that encode the 6 structural proteins found in the virion and 6 non-structural proteins produced inside cells during viral replication.[1]

Rotaviruses are the most common cause of severe diarrhoea in young children worldwide.[2] Vaccines have been developed to reduce the significant morbidity and mortality associated with infection. Two live attenuated oral rotavirus vaccines; Rotarix® [GlaxoSmithKline] and RotaTeq® [Merck], have been shown to be safe and highly effective in the prevention of severe diarrhoea due to rotavirus infection.[3,4] Both vaccines were included into the funded National Immunisation Program of Australia from 1 July 2007. RotaTeq is administered in Victoria, South Australia, Western Australia and Queensland, while Rotarix is administered in New South Wales, the Northern Territory, Tasmania and the Australian Capital Territory. Since 2006, rotavirus vaccines have been licensed in over 125 countries and included in the national vaccination schedules of 59 predominantly high and middle-income countries worldwide.[5]

Historically in Australia, rotavirus infection accounted for up to 10,000 childhood hospitalisations for diarrhoea each year.[6] The introduction of rotavirus vaccines has seen a significant impact on the disease burden, with state based studies in New South Wales, Queensland, South Australia and Victoria showing a substantial decline in both rotavirus coded and non-rotavirus coded hospitalisations and emergency room visits since vaccine introduction.[7–10]

The annual circulation patterns of rotavirus genotypes causing disease in Australian children has been documented by the Australian Rotavirus Surveillance Program since 1997. The strain diversity and temporal and geographic changes observed each year provides the baseline information vital to assist vaccine introduction and ongoing evaluation.[11] Vaccine introduction has increased the population immunity to wild type rotavirus strains, which is likely to impact on the epidemiology of circulating strains. Therefore, characterisation of circulating rotavirus genotypes will provide insight into whether vaccine introduction has impacted on virus epidemiology, and altered circulating strains, which could have ongoing consequences for the success of the vaccination programs.

In this report we describe the genotype of rotavirus strains causing severe gastroenteritis in Australia for the period 1 January to 31 December, 2013.

Methods

Rotavirus positive specimens detected by enzyme immunoassay (EIA) or latex agglutination in collaborating laboratories across Australia were collected, stored frozen and forwarded to the Australian Rotavirus Reference Centre Melbourne, together with relevant age and sex details. The laboratories contributing samples were;

- ACT Pathology, Canberra, Australian Capital Territory
- The Virology Division, South Eastern Area Laboratory Services, Prince of Wales Hospital, New South Wales
- Virology Department, The Children's Hospital at Westmead, New South Wales
- Centre for Infectious Diseases and Microbiology, Westmead, New South Wales
- The Microbiology Department, John Hunter Hospital, Newcastle, New South Wales
- The Microbiology Department, Royal Darwin Hospital, Casuarina, Northern Territory
- The Microbiology Department, Alice Springs Hospital, Alice Springs, Northern Territory
- Forensic and Scientific Services, Queensland Health, Herston, Queensland
- Microbiology division, Pathology Queensland, Herston, Queensland
- The Queensland Paediatric Infectious Diseases Laboratory, Royal Children's Hospital, Brisbane, Queensland
- Queensland Health laboratories in Townsville, Cairns and Gold Coast, Queensland
- Microbiology and Infectious Diseases Laboratory, SA Pathology, Adelaide, South Australia
- The Serology Department, Royal Children's Hospital, Parkville, Victoria
- Princess Margaret Hospital for Children, Subiaco, Western Australia
- Division of Microbiology, PathWest Laboratory Medical WA, The Queen Elizabeth II Medical Centre, Nedlands, Western Australia

Viral RNA was extracted from 10%–20% faecal extracts of each specimen using the QIAamp Viral RNA mini extraction kit (Qiagen) according to the manufacturer's instructions. The rotavirus G and P genotype were determined for each sample by the application of independent hemi-nested multiplex reverse transcription polymerase chain reaction (RT-PCR) assays. The first round RT-PCR assays were performed using the Qiagen one step RT-PCR kit, using VP7 conserved primers VP7F and VP7R, or VP4 conserved primers VP4F and VP4R. The second round genotyping PCR reactions were conducted using specific oligonucleotide primers for G types 1, 2, 3, 4, 8, 9 and 12 or P types [4], [6], [8], [9], [10] and [11].[12–16] Two new G3 primers were included in the G typing assay: EQ3 fwd-ctgcatacgctaattctacacaagg, and EQ3 rev-gatcgtacaagtagccgtagtaac. The G and P genotype of each sample was assigned using agarose gel analysis of second round PCR products.

Any samples that provided a discordant result between the initial antigen detection and genotype assay were further tested using the commercial rotavirus enzyme linked immunosorbent assay ProSpecT (Thermo Fisher, Aus), as per the manufacturer's instructions to confirm the presence of rotavirus antigen.

Results

Number of isolates

During the period 1 January to 31 December 2013, a total of 1,035 faecal specimens were collected for analysis from 18 collaborating centres across Australia; located in Victoria, Western Australia, the Northern Territory, New South Wales, Queensland, South Australia, and the Australian Capital Territory.

Of these, 828 were confirmed as rotavirus positive by EIA (ProSpecT, OXOID) or RT-PCR analysis. Of these, 503 samples were collected from children under 5 years of age, and 325 samples were from older children and adults. An additional 207 specimens contained either insufficient specimen for genotyping (n= 3), or the specimen was not confirmed to be positive for rotavirus (n= 204) and these were not analysed further.

Age distribution

During the reporting period, 61% of samples were obtained from children under 5 years of age (Table 1). Overall, 17.9% of isolates were from infants 0–6 months of age, 9.9% were from infants 7–12 months of age, 16.1% were from children 13–24 months of age, and 9.4% were from children 25–36 months of age. A total of 14.4% of samples were from children 5 years and 1 month to 10 years of age, and 21.3% of samples were from individuals older than 21 years of age, which included 5.6% from adults over the age of 80 years.

Genotype distribution

All of the 828 confirmed rotavirus samples collected from children and adults from 7 locations in New South Wales, the Northern Territory, Queensland, Western Australia, South Australia,

Table 1: Age distribution of gastroenteritis cases

Age range (months)	n	% of total
0–6	148	17.9
7–12	82	9.9
13–24	133	16.1
25–36	78	9.4
37–48	31	3.7
49–60	30	3.6
61–120	119	14.4
121–240	28	3.4
241–960	130	15.7
961+	46	5.6
Unknown	3	0.4
Total	828	na

Victoria and the Australian Capital Territory, underwent genotype analysis (Table 2). G12P[8] strains were the most common genotype identified nationally, representing 33% of all specimens analysed. This genotype was identified as the dominant type in 3 states, Queensland, Victoria and South Australia, representing 42%, 68% and 61% of strains respectively. Genotype G12P[8] strains were only identified in one other location, Western Australia, during this survey period and represented 9% of strains.

G3P[8] strains were the 2nd most common genotype identified nationally, representing 31% of all specimens. This genotype was identified in all 7 states and territories, and was the dominant type in the Northern Territory and Western Australia, where it represented 93% and 44% respectively.

G2P[4] strains were the 3rd most common genotype nationally, representing 14% of all specimens. It was identified in 5 states and was the dominant type in New South Wales, representing 59% of strains.

In this survey period, G1P[8] was the 4th most common genotype representing only 10% of strains analysed; however it was identified in all states and territories.

Genotypes G4P[8] and G9P[8] each represented less than 2% of the total specimens typed. Several rare or uncommon genotype combinations were identified, including 3 G12P[6] strains in Western Australia, 2 G9P[9] strains in South Australia, and single G3P[14], G2P[8] and G6P[8] strains in Queensland, Western Australia and South Australia. Of 10 samples that contained multiple G and/or P genotypes, 7 were identified as being vaccine component strains by sequence analysis. A total of 32 samples contained a non-typeable G– and/or P genotype. The non-typeable samples are likely to be samples that contain low virus amounts, below the limits of our typing assays, or could have contained inhibitors in extracted RNA to prevent the function of the enzymes used in RT and/or PCR steps.

Twenty-nine faecal specimens collected through routine surveillance were identified that contained a component of the RotaTeq vaccine; these were from Western Australia and South Australia. In addition, faecal specimens were received from 15 children who developed gastroenteritis after being vaccinated. A RotaTeq vaccine component was identified in 5 samples, while a G9P[8] strain was identified in a single sample. The RotaTeq vaccine virus components were identified by RT-PCR and sequence analysis.

Analysis of genotypes identified in samples from children less than 5 years of age

A total of 503 rotavirus samples were collected from children under 5 years of age. Genotype G3P[8] strains were the most commonly identified; found in 39.2% of samples, and G12P[8] strains were the 2nd most common genotype; identified in 31% of samples. G1P[8] was the 3rd most common genotype; identified in 11.3% of samples. G2P[4], G4P[8] and G9P[8] all represented minor genotypes in children in this study, and were identified in 4.6%, 2.4% and 1.6% of samples respectively (Table 3).

Analysis of G and P genotyping results revealed that in states where RotaTeq is in use, G12P[8] was the dominant genotype in children less than 5 years of age, identified in 42.5% of samples, while G3P[8] was the 2nd most common, identified in 22.3% of strains (Figure). G1P[8] was the 3rd most common genotype representing 13.6% of samples. In states where Rotarix is used, G3P[8] strains were dominant, identified in 84.6%, while genotype G1P[8] and G2P[4] were identified in 5.1% of strains.

A degree of consistency in genotype distribution within each vaccine type was observed, for example, in 3 of the 4 RotaTeq states (Queensland, Victoria and South Australia) G12P[8] was the dominant genotype. However, in states using Rotarix (New South Wales, Northern Territory and Australian Capital Territory), G3P[8] was dominant only in the Northern Territory. The small number of samples (n=138) from locations using Rotarix may have influenced these comparisons.

Table 2: Rotavirus G and P genotype distribution in Australian infants, children and adults, 1 January to 31 December 2013

Centre	Total	G1P[8]		G2P[4]		G3P[8]		G4P[8]		G9P[8]		G9P[9]		G12P[8]		G12P[6]		G6P[8]		G3P[14]		G2P[8]		Mix*		Non-type†		Vaccine		Neg	Insuff
		%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	n	n
Australian Capital Territory																															
ACT	3	33	1	0	0	33	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	33	1	0	0	11	0
New South Wales																															
Sydney (POW)	33	15	5	52	17	24	8	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	9	3	0	0	7	0
Sydney (Westmead)	16	6	1	75	12	0	0	0	0	0	0	0	0	6	1	0	0	0	0	0	0	0	0	0	0	13	2	0	0	1	0
Newcastle (JH)	2	50	1	50	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	10	1
Northern Territory																															
Alice Springs	53	0	0	0	0	94	50	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	1	4	2	0	0	5	0
Darwin	68	3	2	0	0	96	65	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	7	0
Other‡	4	25	1	0	0	75	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
Queensland																															
Pathology (Brisbane)	53	17	9	19	10	13	7	0	0	0	0	0	0	47	25	0	0	0	0	2	1	0	0	0	0	2	1	0	0	13	0
Qld regional	25	24	6	16	4	12	3	0	0	8	2	0	0	36	9	0	0	0	0	0	0	0	0	0	0	4	1	0	0	46	0
Pathology (Townsville)	9	33	3	0	0	33	3	0	0	0	0	0	0	33	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	15	0
Pathology (Gold Coast	4	50	2	0	0	0	0	25	1	0	0	0	0	25	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	12	0
South Australia																															
Adelaide	231	6	14	10	22	6	14	3	8	0	0	1	2	61	140	0	0	0	1	0	0	0	0	0	0	7	16	6	14	8	0
Victoria																															
RCH	87	10	9	13	11	10	9	1	1	1	1	0	0	64	56	0	0	0	0	0	0	0	0	0	0	0	0	0	0	19	0
Monash	23	13	3	0	0	4	1	0	0	0	0	0	0	83	19	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Western Australia																															
PathWest WA	202	12	25	17	35	44	88	1	2	5	11	0	0	9	18	1	3	0	0	0	0	0	1	0	0	2	5	7	14	15	2
Perth (P Marg)	15	20	3	0	0	47	7	0	0	7	1	0	0	7	1	0	0	0	0	0	0	0	0	7	1	7	1	7	1	34	0
Total	828	10	85	14	112	31	259	1	12	2	15	0	2	33	273	0	3	0	1	0	1	0	1	0	3	4	32	4	29	204	3

207 specimens were omitted from analysis due to insufficient sample or because the specimen was not confirmed to be rotavirus positive

Non-typeables:

ACT: 1x NT/NT

Perth: 8x G-non typeable P[8]

SA: 1x NT/NT (EIA +ve), 1x G2 P[non typeable], 7x G1 P[non typeable], 6x G4P[non typeable], 4x G12 P[non typeable], 1x G-non typeable P[4], 6x G-non typeable P[8], 1x G-non typeable P[9]?

A.S. (NT): 2x G-non typeable P[8]

POW G3 P[non typeable], G-non typeable P[8], NT/NT

Westmead: 1x G2 P[non typeable], 1x G3 P[non typeable]

Table 3: Rotavirus G and P genotype distribution in Australian children ≤ 5 years, 1 January to 31 December 2013

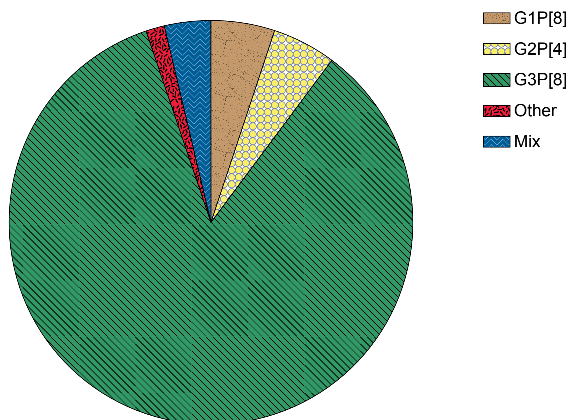
Centre	Total	G1P[8]		G2P[4]		G3P[8]		G4P[8]		G9P[8]		G12P[8]		G12P[6]		G6P[8]		G3P[14]		G2P[8]		Mix*		Non-type[†]		Vaccine		Neg	Insuff
		%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	n	n
Australian Capital Territory																													
ACT	1	100	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	-	-	9	0
New South Wales																													
Sydney (POW)	13	15	2	38	5	31	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	15	2	-	-	1	0
Sydney Westmead	4	25	1	50	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	25	1	-	-	1	0
Newcastle (JH)	1	100	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	-	-	5	0
Northern Territory																													
Alice Springs	52	0	0	0	0	94	49	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	1	4	2	-	-	5	0
Darwin	62	3	2	0	0	95	59	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	1	0	0	-	-	5	0
Other[‡]	3	0	0	0	0	100	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	-	-	0	0
Queensland																													
Pathology (Brisbane)	24	25	6	8	2	21	5	0	0	0	0	46	11	0	0	0	0	0	0	0	0	0	0	0	0	0	0	9	0
Qld regional	10	20	2	20	2	0	0	0	0	0	0	50	5	0	0	0	0	0	0	0	0	0	0	10	1	0	0	23	0
Pathology Townsville	5	60	3	0	0	20	1	0	0	0	0	20	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	9	0
Pathology (Gold Coast)	2	0	0	0	0	0	0	50	1	0	0	50	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	8	0
South Australia																													
Adelaide	123	8	10	5	6	2	2	7	8	0	0	61	75	0	0	1	1	0	0	0	0	0	0	6	7	11	14	3	0
Victoria																													
RCH	56	11	6	5	3	13	7	2	1	2	1	68	38	0		0		0		0		0		0	0	0		7	0
Monash	15	13	2	0	0	0	0	0	0	0	0	87	13	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Western Australia																													
PathWest WA	119	15	18	3	3	52	62	2	2	5	6	9	11	0	0	0	0	0	0	1	1	0	0	2	2	12	14	6	2
Perth (P Marg)	13	23	3	0	0	38	5	0	0	8	1	8	1	0	0	0	0	0	0	0	0	8	1	8	1	8	1	30	0
Total	503	11.3	57	4.6	23	39.2	197	2.4	12	1.6	8	31	156	0	0	0.2	1	0	0	0.2	1	0.6	3	3.2	16	5.8	29	-	-

Discussion

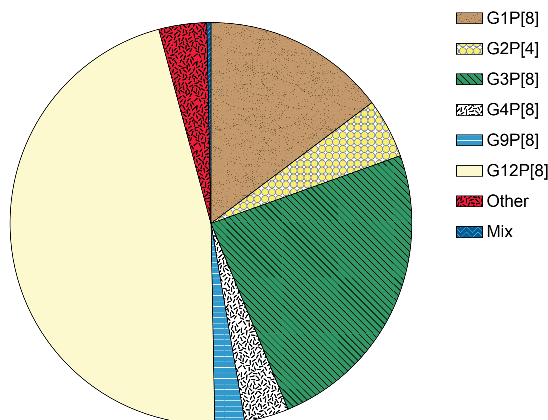
The Australian Rotavirus Surveillance Program report for the period 1 January to 31 December 2013 describes the annual distribution of rotavirus genotypes and geographic differences in genotypes causing disease in Australia. In 2013, the surveillance program identified that genotype G12P[8] emerged as the dominant genotype nationally, representing 33% of all strains, being the dominant genotype in 3 states; Queensland, Victoria and South Australia. Genotype G3P[8] was the 2nd most common genotype nationally, comprising 28% of all strains, but was the dominant genotype in 2 locations, Western Australia and the Northern Territory. Genotype G2P[4] represented the 3rd most common genotype, representing more than 14% of strains nationally, and was the dominant genotype in New South Wales.

Figure: Overall distribution of rotavirus G and P genotypes identified in Australian children based on vaccine usage for period 1 January to 31 December, 2013

Rotarix states



RotaTeq states



Since 2007–2008, genotypes G1P[8] and G2P[4] have alternated as the dominant genotype causing disease across Australia.[17–20] The identification of G12P[8] as the dominant genotype this year is the first time since vaccine introduction that neither of these genotypes were dominant. In 2012, the emergence of G12P[8] strains represented more than 20% of strains, being identified as the 3rd most common genotype, and were observed circulating in Western Australia, the Northern Territory, Queensland and South Australia.[20] This report found that G12P[8] did not spread across the country, rather it continued to emerge in two of the locations (Queensland and South Australia) and cause a greater proportion of disease in those settings. Victoria was the only new location where G12P[8] strains emerged in 2013. Prior to 2012, G12P[8] strains only represented a sporadic and rare cause of disease in Australia. In other countries, G12P[8] generally continues to represent an uncommon cause of disease.[21] However, similar to Australia, a few countries have seen the emergence of G12 in recent years. In West Africa, G12 strains represented more than 80% of strains in 2011–2012,[22] while in the Basque Country of Spain, G12P[8] was the predominant genotype, causing 65% of rotavirus gastroenteritis.[23] This Spanish outbreak was characterised by a broad geographical distribution (rural and urban) and affected both infants and children.[23] The sudden emergence and predominance of G12P[8] rotaviruses in several locations suggest that they may soon become a major human rotavirus genotype. Importantly, in an efficacy trial of Rotarix conducted in South Africa and Malawi, vaccination was shown to provide comparable protection against a range of circulating genotypes including G12 strains.[24] The presence of the P[8] VP4 protein in the G12 strains suggests that both rotavirus vaccines are likely to be effective against the emergence of G12P[8] strains.

This report saw the emergence of G3P[8] strains as the 2nd most common genotype across Australia. In previous years, G3P[8] strains have been observed as generally the 3rd most common type, representing 4%–11% of strains in any given year, and only on 2 occasions was it the most common type in one location; Melbourne 2006–07 and 2009–10.[17–20] The identification of G3P[8] as the dominant type in 2 locations within the same year is unique. In part, its emergence may be due to its unusual G3 VP7 protein, which on preliminary sequence analysis is genetically more similar to equine G3 strains than other human strains (unpublished observations, C Kirkwood). Further sequence analysis of the whole genome of this genotype is required to determine whether other genes are unique.

In the previous surveillance report in 2012, a single genotype G3P[14] rotavirus strain was identified in a 12-year-old child presenting to the Emergency Department of the Royal Children's Hospital, Melbourne, with gastroenteritis. Full genome sequence analysis revealed that the strain contained the novel genome constellation G3-P[14]-I2-R3-C3-M3-A9-N2-T6-E2-H3.[25] The genome was genetically divergent from previously characterised lapine viruses and the genes were distantly related to a range of human bovine-like strains and animal strains of bovine, bat and canine/feline characteristics.[25] This highlights that novel strains are capable of causing disease in Australian children, and an interest in uncommon rotavirus genotypes continues because of the possible impact they could have on rotavirus vaccination programs.

The use of different vaccines in Australian states and territories provides a unique opportunity to compare the effect of each vaccine on the circulating wild type strains. In the current survey, G12P[8] strains were the most common in locations using RotaTeq vaccine, however, none were observed in locations using Rotarix vaccine. In contrast, G3P[8] represented the most common type in Rotarix locations, and was second most common in RotaTeq locations. Differences in genotype distribution based on vaccine usage have been observed each year since vaccine introduction.[26] During the post vaccine years 1, 2 and 5, G2P[4] strains were more common in states and territories using Rotarix, and during year 4, in states using RotaTeq. G1P[8] strains were more common in the other 4 years in locations using Rotarix. G3P[8] were more common in RotaTeq states in years 2008––09, and 2009–10, after which they occurred at similar rates in years 4 and 5.[17–20] Thus consistent differences in genotype distribution linked to a particular vaccine may be starting to emerge.

This survey of rotavirus strains causing disease between 1 January and 31 December 2013 highlights the emergence of G12P[8] rotavirus as the dominant genotype in Australia. The emergence of G12P[8] and to a lesser extent G3P[8] illustrates a unique change to the genotype patterns in Australia, further highlighting the continual changes in the wild type virus population and suggest a more dynamic virus population is present in the current post vaccine era than observed in the pre-vaccine era.

Whether the introduction of vaccine is exerting an increase due to immune pressure or whether the increase is simply due to natural variation is still unclear, but the identification of G12 and unusual G3 strains strengthens the need to continue rotavirus surveillance in both humans and animals. Therefore, continued surveillance of the wild type strains circulating in Australia is required to monitor any changes that may emerge and impact vaccine effectiveness.

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Australian Paediatric Surveillance Unit annual report, 2013

Marie Deverell, Yvonne A Zurynski, Elizabeth J Elliott, and all chief investigators of APSU surveillance studies

Introduction

This report provides an update on the surveillance conducted by the Australian Paediatric Surveillance Unit (APSU) during the period January to December 2013. The APSU facilitates national active surveillance of uncommon diseases of childhood including selected communicable diseases. This report includes data on the following conditions: acute flaccid paralysis (AFP), congenital cytomegalovirus (cCMV), congenital rubella, perinatal exposure to HIV and paediatric HIV infection, neonatal herpes simplex virus (HSV), congenital varicella, neonatal varicella, severe complications of varicella and juvenile onset recurrent respiratory papillomatosis (JoRRP). Surveillance of severe complications of influenza was undertaken during the influenza season (July to September 2013).

Methods

Australian Paediatric Surveillance Unit

The APSU study protocols and case definitions are developed with collaborating study investigators who provide specialised clinical and research expertise for each condition studied and listed in the Table. Conditions under surveillance are listed on the APSU report card, which is sent to approximately 1,400 practising paediatricians and child health specialists every month. Response rates to the APSU monthly report card have remained over 90% for the last 20 years, and were 90% in 2013.

Over 85% of contributors report via email. Contributors respond each month whether or not they have a case to report for any of the conditions listed on the report card. The APSU collects de-identified clinical and/or laboratory data via a case report form completed by the doctor looking after the child. Completed case report forms are forwarded to study investigators. All study protocols and case report forms are available on the APSU website (www.apsu.org.au).

Paediatric Active Enhanced Disease Surveillance

The Paediatric Active Enhanced Disease Surveillance (PAEDS) system was initiated in 2007 by the APSU and the National Centre for Immunisation Research and Surveillance of Vaccine Preventable Diseases.[1] PAEDS (www.paeds.edu.au) is a hospital-based surveillance system reliant on active case ascertainment by specialist surveillance nurses. PAEDS operates in 5 tertiary hospitals in the capital cities of 5 states; New South Wales, Victoria, South Australia, Western Australia and Queensland. PAEDS complements surveillance conducted by the APSU for AFP and varicella complications.

Results

Acute flaccid paralysis

Pooled data from the APSU and PAEDS systems are submitted regularly to the Polio Expert Panel. In 2013, there were 62 confirmed cases of AFP: 28 ascertained by PAEDS, 12 by APSU and 22 by both systems. The target of a non-polio AFP rate of ≥ 1 per 100,000 children under 15 years of age has been consistently reached for the last 6 years (2008–2013). PAEDS nurses ascertain the majority of AFP cases from the 5 tertiary paediatric hospitals where PAEDS operates. The APSU mainly contributes cases from non-PAEDS hospitals such as Sydney Children's Hospital, John Hunter Children's Hospital, Geelong Hospital, Toowoomba Hospital etc. These data contribute towards Australia fulfilling its requirements as stipulated by the World Health Organization (WHO) required AFP surveillance as part of the Global Polio Elimination Strategy and maintenance of the Polio-Free Certification by WHO. All cases are reviewed by the Polio Expert Panel. In 2013, 61 cases of AFP were classified as non-polio AFP and 1 case was classified as polio compatible. The main diagnoses associated with reported cases of AFP were Guillain-Barrè syndrome, transverse myelitis and acute disseminated encephalomyelitis.

Congenital cytomegalovirus

The total number of reports of cCMV continue at approximately 16–17 cases per year. In 2013, a total of 16 confirmed cases and 3 probable cases were reported to the APSU. There was a total of 247 confirmed cases reported during the study period 1999–2013. The number of reports suggest a continuing under-recognition and underreporting of cCMV, as the investigators reported in 2011,[3] and as continues today. Testing for cCMV after detection of sensorineural hearing loss (SNHL) on neonatal hearing screening is not routine in all

Table: Confirmed cases identified to December 2013 and for the total study period, and reported rates per 100,000 of the relevant child population

Condition	Date surveillance commenced	Questionnaire returned (%)	Number of confirmed cases 2013	Reported rate for 2013 (per 100,000)	Number of confirmed cases for total study period	Reported rate for total study period (per 100,000 per annum)
Acute flaccid paralysis	Mar 1995	100	62*	1.42†	779	1.01†
Congenital cytomegalovirus	Jan 1999	91	16	5.17‡	247	6.48‡
Congenital rubella (with defects)§	May 1993	100	3	0.06‖	54	0.07‖
Perinatal exposure to HIV	May 1993	90	43	13.89‡	587	10.99‡
HIV Infection	May 1993	100	1	0.02‖	84	0.10‖
Neonatal – herpes simplex virus infection	Jan 1997	91	14	4.52‡	154	3.57‡
Infant – herpes simplex virus infection	Jan 2012	91	3	0.96¶	3	0.50¶
Congenital varicella	May 2006	No notifications	Nil	Nil	2	0.10‡
Neonatal varicella	May 2006	75	3	0.97‡	22	1.07‡
Severe complications of varicella	May 2006	50	1	0.02†	50	0.15†
Juvenile onset recurrent respiratory papillomatosis**	Data for 2012	91	7	0.16†	7	0.16†
	Data for 2013	100	3	0.07†	10	0.12†
Severe complications of influenza††	Influenza season each year since 2008	93	13	0.30†	289	1.13†

* Includes all cases of acute flaccid paralysis reported via the Australian Paediatric Surveillance Unit or Paediatric Active Enhanced Disease Surveillance. All cases have been classified by the Polio Expert Panel as 'non-polio AFP' according to World Health Organization criteria.

¶ Notification was received by the Australian Paediatric Surveillance Unit, clinical data had not been returned at the time of submission.

† Influenza surveillance was conducted each year since 2008 during the influenza season, July to September except in the pandemic year (2009) when surveillance occurred from June to October.

‡ Based on population of children aged less than 15 years.

§ Based on number of births.

|| Based on population of children aged less than 16 years.

†† Based on population aged less than 12 months.

** Confirmed cases and probable cases are reported; a probable case is defined as a papilloma visualised by endoscopy but the histology results are pending.

All reported rates are based on child population estimates published by the Australian Bureau of Statistics.[2]

All of the figures were correct at the time of submission and agreed by the chief investigators for each condition.

jurisdictions despite cCMV being an important cause of SNHL. cCMV is found in 5%–10% of neonates with SNHL of an otherwise unknown cause,[4] including in Sydney (Rawlinson 2014 personal communication),[5] although screening of children failing universal hearing screening is often practically difficult.[5] Potential treatment with antiviral therapy to prevent long-term neurodevelopmental sequelae is limited by the lack of routine screening for CMV in pregnant women and in neonates,[3] although this may change with recent efficacy analyses.[6]

Congenital rubella

There were four notifications of congenital rubella to the APSU during 2013. One was a duplicate notification. Three cases met the case definition criteria for congenital rubella with defects (microcephaly, hearing and vision impairments) and were consistent with congenital rubella syndrome. Two of the confirmed cases were children born in Australia (1 child born in 2013 in Victoria and 1 child born in 2012 in the Northern Territory) to mothers who had been born overseas (Thailand and Indonesia). Another child reported in 2013 was born overseas (in 2012) and diagnosed after arrival in South Australia at about 12 months of age. Prior to this, the last confirmed case of congenital rubella was reported in 2008. These recent cases highlight the need to remain vigilant by continuing surveillance efforts, continuing prevention of congenital rubella by screening all women (especially immigrant women) of childbearing age for rubella antibodies, and by maintaining high coverage of rubella vaccination in children.

Perinatal exposure to HIV and HIV infection

There was a total of 43 confirmed cases of perinatal exposure to HIV reported to the APSU in 2013. In addition, there was 1 case of HIV infection reported to the APSU in 2013. Over the total study period (1993–2013) 556 cases of perinatal exposure to HIV and 84 cases of neonatal HIV infection have been reported. The number of HIV perinatal exposures has remained relatively steady, but fewer infants acquire HIV infection as women take up interventions including avoiding breastfeeding, antiretroviral therapies and caesarean section.

Neonatal herpes simplex virus

In 2012, the case definition was amended to include disease in the new-born as well as in infants aged 1 month to up to 1 year of age. In 2013, a total of 17 cases were reported to the APSU; 14 in neonates and 3 in infants aged over 1 month of age. Since 1997, a total of 154 cases of HSV were reported by the end of 2013.

Congenital, neonatal and severe complications of varicella

No cases of congenital varicella were reported to the APSU during 2013. The last reported case of congenital varicella was in 2007. There were 4 cases of neonatal varicella reported to the APSU; completed cases reports were received for three of these and all three met the case definition criteria. All 3 infants were exposed to varicella after birth; the details of the infective contact were unknown for 2 infants; the other one was exposed to a sibling who had chickenpox. All infants required hospitalisation due to the varicella infection (3–6 days), and all were treated with Aciclovir. Of the 2 notifications of children hospitalised with severe complications of varicella, 1 completed case report was received. The child was 10 years of age and spent 15 days in hospital with encephalitis and ataxia. This child had mild ataxia at discharge from hospital. A history of contact with a person known to have varicella was not provided.

Juvenile onset recurrent respiratory papillomatosis

JoRRP is a rare condition that develops in childhood and is typically found in children aged less than 12 years. It is the most common cause of benign neoplasms of the larynx in children and is caused by persistent infection of the upper airways with human papillomavirus (HPV) genotypes HPV 6 or HPV 11 acquired via vertical transmission before or during birth. HPV6 and HPV11 are targeted by the prophylactic quadrivalent HPV vaccine, meaning that JoRRP is now potentially a vaccine preventable disease, with high vaccination coverage achieved among Australian women aged 12–26 years by 2009.[7,8] There were 15 notifications during the total study period (2012–2013) with completed case reports received for 14 notifications (93%). Of these 14 completed case reports there were 3 duplicate notifications and 1 error, leaving 10 cases. Of these 10, there were 6 confirmed cases and 1 probable case in 2012 (total 7) and one confirmed case and 2 probable cases in 2013 (total 3). There has been a decrease in the number of cases of JoRRP reported to the APSU in 2013.

Severe complications of influenza

The data for 2013 showed a marked reduction in the number of cases of influenza with severe complications reported to the APSU. There was a total of 13 confirmed cases of influenza with severe complications in children less than 15 years of age reported to the APSU in 2013, compared with 56 confirmed case reports during 2012. Eight cases had influenza B, and 5 cases had influenza A. The median age was 4.3 years (range from 10 days

to 14.4 years). Complications included the following: pneumonia with oxygen requirement, need for mechanical ventilation, seizures, myocarditis, pericarditis, shock, acute encephalopathy and rhabdomyolysis. Similar complications have previously been reported in children with pre-existing chronic conditions as well as in previously healthy children.[9] Eight cases had not been vaccinated for influenza in the previous 12 months and the vaccination status of a further 5 cases was unknown.

Of the 13 cases, five were admitted to the Paediatric Intensive Care Unit. Of these 5 cases, four had not been vaccinated for influenza and the vaccination status was not known for 1 case. Underlying chronic conditions of these patients included: neuromuscular disorder with intellectual disability, lung disease (with and without intellectual disability) and asthma. There were 2 deaths reported during 2013.

Conclusions and future directions

The APSU has conducted national surveillance of rare diseases for 20 years and continues to provide a valuable data on a number of serious rare childhood diseases. The APSU 20 year annual report is available for download on the APSU web site (www.apsu.org.au).

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Chief Investigators of APSU surveillance studies:

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Creutzfeldt-Jakob disease surveillance in Australia, update to December 2013

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Abstract

Nation-wide surveillance of transmissible spongiform encephalopathies including Creutzfeldt-Jakob disease, is performed by the Australian National Creutzfeldt-Jakob Disease Registry, based at the University of Melbourne. Surveillance has been undertaken since 1993. Over this dynamic period in transmissible spongiform encephalopathy research and understanding, the unit has evolved and adapted to changes in surveillance practices and requirements, the emergence of new disease subtypes, improvements in diagnostic capabilities and the overall heightened awareness and understanding of Creutzfeldt-Jakob disease and other transmissible spongiform encephalopathies in the health care setting. In 2013, routine surveillance continued and this brief report provides an update of the surveillance data collected by the Australian National Creutzfeldt-Jakob Disease Registry prospectively from 1993 to December 2013, and retrospectively to 1970. The report highlights the recent multi-national collaborative study published that has verified the correlation between surveillance intensity and reported disease incidence. *Commun Dis Intell* 2014;38(4):E348–E355.

Keywords: Creutzfeldt-Jakob disease, prion disease, transmissible spongiform encephalopathy, disease surveillance

Introduction

In 1993, the Allars inquiry[1] into the use of cadaver-derived pituitary hormones under the Australian Human Pituitary Hormone Program and the association with 4 medically acquired (iatrogenic) Creutzfeldt-Jakob disease (CJD) deaths recommended the formation of an Australian surveillance unit to monitor further cases of iatrogenic CJD in Australia. The Australian National Creutzfeldt-Jakob disease Registry (ANCJDR) was established in October 1993 within the department of pathology at the University of Melbourne. The monitoring of further Australian iatrogenic CJD cases related to pituitary hormone treatment for infertility or short stature and contaminated dura mater grafts remains one of the core objectives of the ANCJDR; however, the ANCJDR's activities have changed to encompass the surveillance of all types of CJD including sporadic, genetic and variant CJD and other transmissible spongiform encephalopathies (TSEs) such as Gerstmann Sträussler-Sheinker syndrome and fatal familial insomnia.

As described previously,[2] human prion disease can arise sporadically or from genetic or iatrogenic aetiologies. Detailed evaluation of each suspected case added to the register is undertaken to determine whether a case can be excluded from suspicion or classified as a definite, probable or possible TSE case according to World Health Organization (WHO) diagnostic criteria.[3] CJD was made a notifiable disease in all states and territories of Australia as of June 2006. Most initial notifications to the ANCJDR arise through diagnostic testing available through the Registry and this occurs prior to health department notification.

The global incidence of CJD is commonly reported to be 1 case per million per year; however, in most countries with long-standing surveillance systems in place such as France and Switzerland, annual incidence has been reported above this quoted figure.[4] Incidence rates as high as 1.2–2.4 cases per million per year have been reported.[4] Temporally, human prion disease incidence has increased in most countries including Australia, as surveillance mechanisms have evolved, diagnostic testing capabilities have improved and there is generally greater awareness of this rare disease in the health care setting. A recent multi-national collaborative study has verified that surveillance intensity positively correlates with reported disease incidence.[5]

In 2013, several changes have occurred that have or will influence the level of suspected case notifications and possibly future incidence rates of CJD in Australia. These include more discerning practices in relation to suspected case referrals, in part due to ever increasing demands through the diagnostic testing; the suspension of the Queensland autopsy service since January 2013; and an increased number of genetic prion diseases classified in 2013 returning the proportion of genetic cases closer to expected levels. In this report, updated surveillance figures to 31 December 2013 are provided for all retrospective (to 1970) and prospective cases ascertained from 1993 onwards and discussed in relation to these changes and how these may influence case notifications, classifications and overall incidence.

Methods

Patients with a suspected human prion disease are notified to the ANCJDR predominantly through referral for diagnostic cerebrospinal fluid (CSF) 14-3-3 protein detection. Other mechanisms include personal communication with clinicians, families, hospitals and CJD-related groups, and health record searches through hospitals or health departments. Once notified to the ANCJDR, referrals are assessed and if the suspicion of prion disease is supported, the case will be added to the register as a suspected case for continued investigation with the aim of exclusion or classification according to World Health Organization diagnostic criteria. Investigation of register cases can be prolonged as the ANCJDR requires the next-of-kin consent to access and compile the appropriate clinical information from various health information sources for comprehensive evaluation. Response times can vary as the information can be extensive or sources numerous. Medico-demographic questionnaires are offered and forwarded to families if they are willing to contribute, providing valuable information for analysis and evaluation.

The classification of a register case remains as 'incomplete' until the investigation is completed or a definitive result from neuropathological assessment is obtained. Cases may be excluded from the register on the basis of neuropathological examination or after thorough clinical history evaluation. A 'definite' classification requires brain tissue examination, including immunohistochemically and 'probable' and 'possible' cases are reliant on specific clinical profile and diagnostic test outcomes being met as previously described.[3] In this report, the total number of confirmed CJD cases include those that have been classified during 2013.

In conjunction with the ANCJDR's surveillance responsibilities, the Registry provides a diagnostic platform for ante- and post-mortem diagnostic testing for human prion diseases. The testing of CSF for the presence of a family of low molecular weight proteins called 14-3-3 is performed weekly by the ANCJDR. This test, first introduced in 1997, has been readily utilised by the health community and since its introduction referrals have increased substantially to around 400 referrals each year. As described previously, the test provides an increasingly larger proportion of initial notifications of suspected human prion disease to the ANCJDR each year. The ANCJDR also offers services for genetic testing, and Western blot analysis of tonsil and brain tissue from biopsies or autopsies to supplement immunohistochemical assessment. The ANCJDR actively promotes these diagnostic tests so that these options are available to clinicians and families to facilitate the most accurate diagnosis and classification of suspected cases should they wish to pursue these avenues of investigation.

Annual human prion disease incidence rates were calculated using direct age-standardisation, based on the Australian Bureau of Statistics 2000 estimated resident population for Australia and for each state and territory.[6] Population based rates of post-mortem examination in suspected human prion disease were calculated using the Australian Bureau of Statistics 1993–2013 Australia demographic statistics for specific states.[7–11] Health information is collected through a combination of public health and surveillance responsibilities, based on the national notification of communicable diseases. Surveillance activities for the period reported were conducted under ethical approval granted by The University of Melbourne Human Research Ethics Committee.

Statistical analysis (Log-Rank test) was performed using Stata (Intercooled Stata 7, Stata Corporation, College Station, TX).

Results

Fifty-two suspected human prion disease cases were added to the CJD surveillance register in 2013. Cases were notified via request for 14-3-3 CSF test (40 cases), personal communication from clinicians (7 cases), hospitals (2 cases), the CJD Support group network (1 case), and direct health department notifications (2 cases). The proportions of these initial notification sources are consistent with those in previous years and the overall trends for all register cases (Table 1).

While the suspected case notifications added to the register in 2013 were consistent with those observed in 2012 (n=53 cases), notifications were 37% lower compared with the long-term average for the years 1993 to 2012. By the same comparison, fewer notifications from Victoria, Western Australia and Tasmania were received during 2013 (Figure 1), continuing the trend observed during the previous year. Notifications were also lower in Queensland in 2013. Although lower notifications than the long-term average were observed in New South Wales in 2013, there was a modest increase from the previous year returning notifications closer to expected levels. The remaining states and territories remained unchanged from the previous year. Overall, it is estimated that the number of cases added to the register in 2013 was about 20 cases lower than the long-term average of case notifications for 1993 to 2013 (about 70 case notifications per year). While fluctuations are to be expected with annual CJD notifications, it should be noted that since 2009, notifications have been consist-

Table 1: Source of initial notification of suspected transmissible spongiform encephalopathies cases ascertained between 1993 and 2013

Method	Register cases* (%)	Cases removed from the register† (%)	Overall
CSF 14-3-3 protein test request (Since September 1997)	51.8	49.3	50.8
Personal communications			
Neurologists	13.5	12.4	13.0
Neurologists (mail-out reply cards)	2.8	1.8	2.4
Neuropathologists	8.4	8.5	8.4
Neuropathologists (mail-out reply cards)	0.6		0.4
Pituitary Hormones Task Force	1.8	3.2	2.3
Family	3.0	2.5	2.8
Molecular biologist	0.1		0.1
Hospital	0.4	1.3	0.8
Death certificates	9.9	5.6	8.2
Hospital and health department searches			
Hospital medical records	4.8	11.5	7.4
Health department search/state	3.4	7.9	5.1
Morbidity data	1.4	3.6	2.3
Direct health department notification	1.4	0.3	1.0
CJD counselling service	0.4	0.6	0.5
Combined CSF/genetic test request	0.4	0.9	0.6
Genetic test request	0.3	1.7	0.8
Victorian brain bank network		0.2	0.2
Coroner's post mortem request	0.1	0.2	0.1
CJD support group	0.1		0.1
Press	0.1		0.05
UK surveillance unit	0.1		0.05
Total	100.0	100.0	100.0

CSF Cerebrospinal fluid

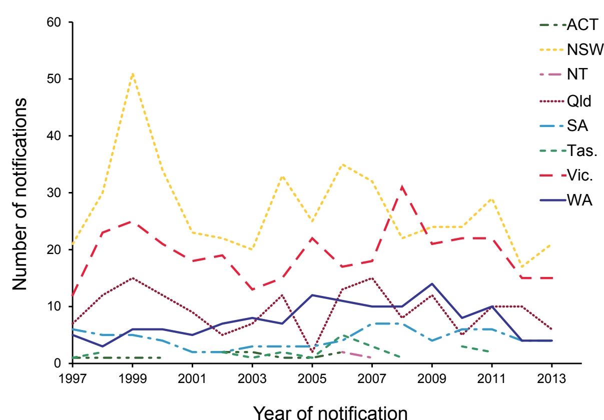
* Register cases; includes all cases currently on the register as classified cases or cases still under investigation.

† Cases removed from the register; includes all suspected cases excluded from the register after detailed investigation.

ently declining in Western Australia. During this period, CSF 14-3-3 protein testing referrals from Western Australia have remained stable; however, there have been fewer cases within this referral group where the suspicion for CJD warrants formal addition to the register and therefore lower case notifications.

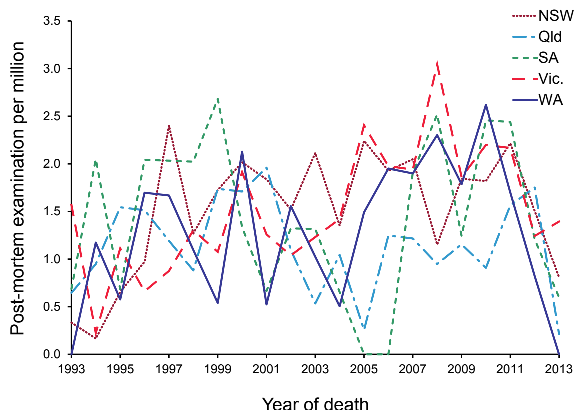
As of 31 December 2013, the majority of the 52 suspected cases added to the register in 2013 were classified as incomplete. Eleven cases were excluded after detailed clinical follow-up (2 cases) or neuropathological examination (9 cases); 9 cases were classified as definite and 1 as probable prion disease.

Figure 1: Prospective notifications of suspected transmissible spongiform encephalopathies cases notified to the ANCJDR, 1997 to 2013, by state or territory and year



Excluding the post-mortem rate in 2013 where figures are still provisional, the average post-mortem rate for all suspected cases on the register who died between 1993 and 2012 is 62%. Over this period, the rate of post-mortems being performed has steadily increased from around 50% during 1993 to 1995 to 70% since 2005. This high post-mortem rate underpins the strong and consistent number of confirmed Australian human prion disease cases recorded since 2005. A comparison of the post-mortem rates in the 5 most populous states in Australia indicates that the overall trend in post-mortem rates has been positive from 1993 to 2012 (Figure 2) with the exception of South Australia where rates have been variable over this period. Excluding the rates shown for 2013, where results are provisional as some post-mortem results are still pending, it is apparent that the post-mortem rate has been declining in Western Australia since 2010. While decreases in New South Wales, South Australia and Victoria are also seen in 2012, they are not as substantial as in Western Australia.

Figure 2: Rate of post-mortem examination in transmissible spongiform encephalopathies suspected case deaths per million population in New South Wales, Queensland, South Australia, Victoria, and Western Australia



Queensland post-mortem rates in contrast, continued to increase from 2005 to 2012 until the CJD autopsy service in that state was suspended. In the other states and territories, post-mortem rates are variable over the surveillance period and show no clear trends due to low population and low numbers of post-mortems being performed.

As of 31 December 2013, there were 989 cases on the register with 757 of these being classified as probable or definite CJD cases. An additional definite iatrogenic case who was treated in Australia, and died in the United Kingdom is included in Table 2; however this case is not classified as an Australian case due to the location at death and is thereby excluded from the overall statistical analysis of Australian CJD cases. Since the start of surveillance, 663 suspected prion disease cases have been excluded from the register after detailed follow-up, with 25 of these being excluded in 2013 (19 after neuropathological examination).

In 2013, 20 cases were re-classified from incomplete to definite prion disease, 4 cases to probable and a single case who died in 2002 was re-classified as possible sporadic CJD, bringing the total number of possible cases to 15. Fourteen of these cases were sporadic and one was iatrogenic CJD (Table 2). Of the 216 incomplete cases, 136 are presently alive. In 2013, the number of incomplete cases under evaluation by the ANCJDR has remained consistent with the number of incomplete cases in 2012. In contrast, there has been a 50% reduction in the number of cases excluded from the register and a 35% reduction in the number of cases classified from incomplete to definite, probable or possible in 2013 compared with 2012.

Age-standardised mortality rates show that the rate of human prion disease mortality in Australia during the period of 1970 to 2013 is increasing, except in 2013, where case evaluation is pending for the majority of deaths (Figure 3) and incidence

Table 2: Classification of Australian National Creutzfeldt-Jakob Disease Register cases, Australia, 1970 to 2013

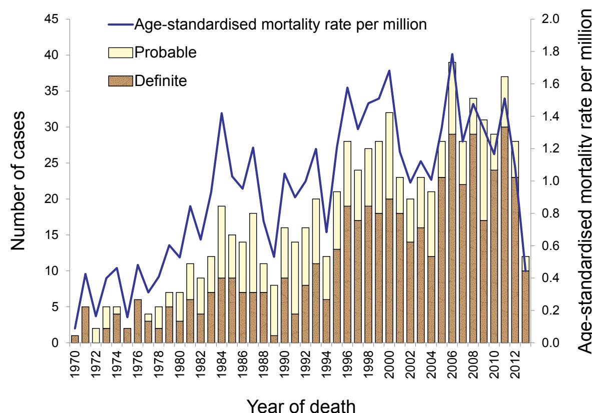
Classification	Sporadic	Familial	Iatrogenic	Variant CJD	Unclassified	Total
Definite	448	49	5*	0	0	502
Probable	241	11	4	0	0	256
Possible	14	0	1	0	0	15
Incomplete					216†	216
Total	703	60	10	0	216	989

* Includes 1 definite iatrogenic case who received pituitary hormone treatment in Australia but disease onset and death occurred while a resident of the United Kingdom. This case is not included in statistical analysis since morbidity and mortality did not occur within Australia.

† includes 136 living cases.

is therefore provisional. In 2013, the age-adjusted mortality rate was 0.44 deaths per million per year and this would be expected to increase after further investigation and classification of incomplete cases. The mean annual age-adjusted mortality rate during the period from 1970 to 2012 was 1.0 death per million (range, 0.1–1.8). For the prospective surveillance period of 1993 to 2012, the mean annual rate is 1.3 deaths per million (range, 0.7–1.8). By state and territory, the majority of regions in Australia have a mean age-adjusted mortality rate above 1 case per million per year between 1993 and 2012 (range, 1.0–1.5). The exceptions are Tasmania and the Northern Territory with 0.7 and 0.9 deaths per million respectively. Restriction of the surveillance data to the period between 2003 and 2012 allows comparisons between states and territories during a timeframe of relatively consistent surveillance practices, diagnostic capabilities and utility with the exception of MRI diagnostics. (Table 3). During this period, Tasmania, the Northern Territory and Queensland have lower than expected mean mortality rates, while Western Australia and Victoria have the highest TSE mortality in Australia.

Figure 3: Number of definite and probable transmissible spongiform encephalopathies cases and age-standardised mortality rate,* Australia, 1970 to 2013, by classification and year



* Age-standardised mortality rates were calculated using the Australian Bureau of Statistics 2000 estimated resident population for Australia.

The proportions of human prion disease aetiologies represented on the register have remained similar to previous years, with the exception of genetic cases. Previously we have reported that the annual number of genetic cases had declined in recent years.[2] In 2013, 6 cases were classified as genetic definite or probable prion disease. Two of these were new cases confirmed as definite genetic cases in 2013, whereas the remaining four were re-classified from definite or probable sporadic cases to genetic cases after further investigation or information was provided to the ANCJDR. The classification of these cases has returned the proportion of genetic TSE closer to the levels expected in the Australian population (Figure 4). Overall, the vast majority of human prion disease cases are sporadic (91.0%) while genetic and iatrogenic cases represent 7.9 and 1.1% respectively of all definite and probable cases.

Based on 757 definite and probable human prion disease cases, 53% per cent were female. Similar proportions for gender exist for all human prion disease aetiologies. Median ages at death for the overall case group or by specific aetiology are largely unchanged from the previous reporting

Table 3: Transmissible spongiform encephalopathies deaths and age-adjusted mortality rates, 2003 to 2012, by year and state or territory

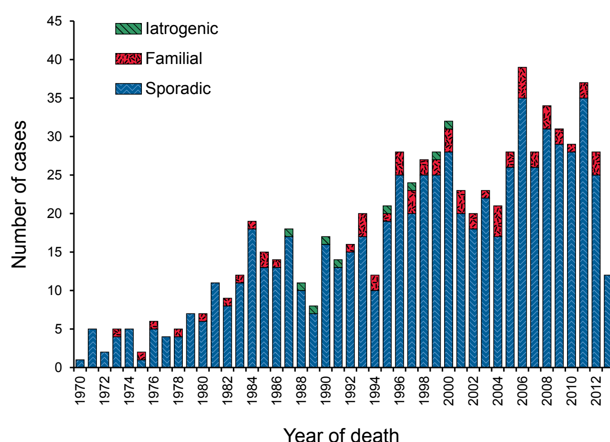
Year	03	04	05	06	07	08	09	10	11	12	13*	Total	Mean age-adjusted mortality rate† (deaths/million/year)
ACT		1		1		2		1				5	1.35
NSW	7	11	10	12	10	6	11	5	14	6	5	97	1.24
NT				2	1							3	0.97
Qld	3			7	2	4	4	2	5	6	2	35	0.68
SA	1	2	1	1	3	5	2	4	4	2	1	26	1.46
Tas.			1	2						1		4	0.71
Vic.	9	5	11	10	6	13	9	13	9	10	4	99	1.71
WA	3	2	5	4	6	4	5	4	5	3		41	1.68
Aus.	23	21	28	39	28	34	31	29	37	28	12	310	1.30

* Provisional figures.

† Age-standardised mortality rates (2003–2012) were calculated using the Australian Bureau of Statistics 2000 estimated resident population for Australian states and territories.

period. Sixty-six years is the median age at death for all cases overall with only a single year difference between males (66 years) and females (67 years). For sporadic cases, 67 years is the median age at death overall and for both males and females. For genetic prion disease, there is a 4 year age difference between males (58 years) and females (62 years) and overall the median age of death from genetic prion disease is 60 years. As there have been no further iatrogenic cases identified since the last reporting period at 31 December 2012, there has been no change to the previously reported median age at death for iatrogenic cases.[2]

Figure 4: Definite and probable human prion disease cases, 1970 to 2013, by aetiology and year



Duration of illness is typically short for human prion disease, especially sporadic CJD, with the median length of illness duration for all cases combined being 3.9 months. By aetiology, median duration was found to be 3.5 months for sporadic cases (range, 0.9–60 months), 6.25 months for iatrogenic cases (range, 2–25 months) and 5.8 months for genetic cases (range, 1.25–192 months). Within 6 months of disease onset, 70% of all TSE cases were deceased. By aetiology, 72% of sporadic, 53% of genetic and 56% of iatrogenic human prion disease were deceased 6 months after the onset of symptoms. Survival is significantly shorter in sporadic CJD than the genetic form ($P < 0.0001$ by Log Rank Test).

Between 1 January and 31 December 2013, no variant CJD or further iatrogenic CJD cases were identified in Australia.

Discussion

The reduced numbers of formal prion disease notifications to the ANCJDR observed in 2012 and 2013 has prompted a review of internal and external factors that may be contributing to the lower number of notifications. One likely factor is a more clinically discerning approach by the ANCJDR before formally adding cases to the register for investigation. This has been necessary due to improved clinician awareness of diagnostic capacity with consequent increased number of suspected case notifications based on suggestive diagnostic investigation results. These include notifications received by the ANCJDR through CSF 14-3-3 protein detection but especially MRI, straining human resources. It is also clear that there are fewer notifications from some states and territories, specifically Victoria, Western Australia and Tasmania in both 2012 and 2013. It is unclear why the numbers from Victoria have decreased and this will be closely monitored in 2014.

In Western Australia, a greater reliance on local health services to manage case investigation and in particular those cases that proceed to post-mortem examination, may contribute to the reduced number of notifications. This may limit the involvement and ability of the ANCJDR to ascertain the true level of suspicion for these cases. The ANCJDR will assess options for improving ascertainment in Western Australia during 2014.

Another important and possibly contributing factor to declining notifications is the suspension of the Queensland CJD autopsy service, which ceased in January 2013 and still remains suspended as of 31 December 2013. It is unclear when the service may be resumed. During 2013, the ANCJDR was aware of several suspected CJD cases in Queensland where autopsies were requested by clinicians and/or families. The effect of this suspension will be marked, particularly on incidence rates in Queensland but also on the overall Australian incidence rates in 2013. Furthermore, notification rates may be lowered as a consequence. As there is only a single year of data with lower notifications in Queensland, notification rates will need to be reviewed during 2014 to determine whether the 2013 data was an isolated fluctuation.

Monitoring annual suspected human prion disease notifications is of importance due to the relationship of this parameter with overall incidence. The ANCJDR led a multi-national collaborative study and demonstrated that greater surveillance intensity incorporating suspected case notifications, referrals for diagnostic testing and post-mortem examination correlates with increased reported disease incidence.[5] In 2013, the ANCJDR published an analysis of datasets from 10 countries with similar surveillance systems and determined a predictive relationship between surveillance intensity and disease incidence. It is therefore of concern that there has

been a sustained change to notification levels and these need to be monitored and assessed carefully in the context of the ANCJDR and local state services activities and processes.

The number of cases classified as definite and probable prion diseases in 2013 (24 cases) is smaller than the number classified in 2012 (39 cases). Definite case classification declined marginally (16% decrease) in 2013 and probable case classifications were 70% lower. An explanation for the lower levels of classifications and exclusion of register cases is in part due to the inflation of the number of cases classified or excluded in 2012 due to concerted efforts by the ANCJDR to classify outstanding cases. After an exceptional year of case classification in 2012, classifications were expected to be lower in 2013 in comparison and return to pre-2012 levels. The ANCJDR aims to maintain a consistent level of case classification with attention focused on probable case classification in 2014.

Despite the decrease in suspected case notifications in 2012, the incidence rate in 2012 has been maintained at expected levels (1.1 cases per million per year). This provides some reassurance that while case notifications have been lower in 2012, the ANCJDR has maintained the ability to detect the expected annual number of prion disease cases in the Australian population despite changes to ANCJDR approaches. No firm conclusions can be made regarding whether these trends will continue in 2013 as the incidence rates are provisional at the time of reporting; however the number of definite cases are predicted to be lower than expected in 2013 due to the suspension of the Queensland autopsy service.

The proportion of annual TSE cases due to genetic prion disease has returned to expected levels during 2013. This is pleasing given the concerns in 2012 that genetic prion disease was under-ascertained between 2009 and 2012, possibly due to the de-centralisation of genetic services to external laboratories and a disconnect with the ANCJDR regarding genetic testing outcomes. Processes have been established in order to redress this issue by genetic services (in conjunction with the CJD support group network), and this has in part contributed to an increased number of genetic prion disease cases classified in 2013. While these processes will prove valuable for case classification in future, the majority of the genetic prion disease identified in 2013 was classified after case investigation, underscoring the utility and importance of comprehensive case evaluation by the ANCJDR.

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The ANCJDR wishes to thank families, as well as medical practitioners and associated staff for their generous support of Australian CJD surveillance. The ANCJDR also thanks Dr Handan Wand, Dr Matthew Law and Professor John Kaldor (The Kirby Centre at the University of New South Wales) for their expert epidemiological and statistical support, as well as the CJD Support Group Network for their assistance in surveillance activities.

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Tuberculosis notifications in Australia, 2011

Christina Bareja, Justin Waring, Richard Stapledon, Cindy Toms, Paul Douglas and the National Tuberculosis Advisory Committee, for the Communicable Diseases Network Australia

Abstract

The National Notifiable Diseases Surveillance System received 1,385 tuberculosis (TB) notifications in 2011, representing a rate of 6.2 cases per 100,000 population. While Australia has maintained a rate of 5 to 6 cases per 100,000 for TB since the mid-1980s, there has been a steady increase in incidence over the past decade. In 2011, Australia's overseas-born population continued to represent the majority of TB notifications (88%) with a notification rate of 20.2 per 100,000. The incidence of TB in the Australian-born Indigenous population has fluctuated over the last decade and showed no clear trend; however, in 2011 the notification rate was 4.9 per 100,000, which is a notable decrease from the 7.5 per 100,000 recorded in 2010. The incidence of TB in the Australian-born non-Indigenous population has continued to remain low at 0.9 per 100,000. Australia continued to record only a small number of multi-drug-resistant TB (MDR-TB) cases nationally (n=25), all of which were identified in the overseas-born population. To ensure that Australia can retain its low TB rate and work toward reducing rates further, it is essential that Australia maintains good centralised national TB reporting to monitor trends and identify at-risk populations, and continues to contribute to global TB control initiatives. *Commun Dis Intell* 2014;38(4):E356–E368.

Keywords: Australia, epidemiology, annual report, *Mycobacterium tuberculosis,* disease surveillance

Introduction

Like many low-incidence countries, Australia's biggest challenge in maintaining good tuberculosis (TB) control is to manage TB rates in its migrant population. Throughout the 19th and 20th centuries, the majority of Australia's migrant population has originated from European countries. Over the last decade, the proportion of migrants coming from European countries has declined from 52% in 2001 to 40% in 2011, while the proportion of migrants coming from Asian countries increased from 24% in 2001 to 33% in 2011.[1] Given this change in migration patterns as well as Australia's close proximity to the South East Asia and Western Pacific regions where 60% of the world's TB cases are located,[2] Australia's ability to maintain good TB control domestically will rely on the ongoing success of the Stop TB Strategy to reduce the TB burden in these regions.

The National Tuberculosis Advisory Committee (NTAC), a subcommittee of the Communicable Diseases Network Australia (CDNA), oversees the surveillance of TB in Australia. NTAC also has the key role of providing strategic, expert advice to CDNA and the Australian Government, on a coordinated national approach to TB control. NTAC also has the role of developing and reviewing nationally agreed strategic plans and guiding their implementation for the prevention and control of TB in Australia.

This report describes the epidemiology of notified cases of TB in Australia in 2011 and should be considered in conjunction with the annual Australian Mycobacterium Reference Laboratory Network (MRLN) report on bacteriologically confirmed cases.[3]

Methods

TB is a nationally notifiable disease in Australia and is monitored using the National Notifiable Disease Surveillance System (NNDSS). Under state and territory public health legislation medical practitioners, public health laboratories and other health professionals are required to report to jurisdictional health authorities, cases of TB that fit the national case definition.[4] The *National Health Security Act 2007* provides the legislative basis for the national notification of communicable diseases and authorises the exchange of health information between the Commonwealth and states and territories. State and territory health departments transfer these notifications regularly to the NNDSS. The primary responsibility for public health action resulting from notification resides with state and territory health departments.

The Tuberculosis Data Quality Working Group (TBDQWG), a working group of NTAC with representation from states and territories, the Commonwealth and the MRLN, ensures routine and timely reporting of trends and emerging issues in TB. The TBDQWG is responsible for maintaining national consistency in data standards and systems for national TB reporting.

Data presented in this report represent a point in time analysis of notified cases of TB. This report presents data extracted from NNDSS during February 2014. Due to the dynamic nature of the NNDSS, data in this report may vary from data reported in other NNDSS reports and reports of

TB notifications at the state or territory level. The details on case definition, data collection, quality control and the categorisation of population sub-groups are available in the 2007 annual report.[5]

This report presents data analysed by date of diagnosis, a derived field within the NNDSS. The methodology for the date of diagnosis changed in January 2014 and was applied to notifications retrospectively, including for this 2011 report. Diagnosis date for TB is equivalent to the notification received date. This is the date the notification of the disease was received by the communicable disease section of the health authority. Crude rates for the overall population were calculated using the 2011 mid-year estimated resident population from the Australian Bureau of Statistics (ABS) *Australian Demographic Statistics*.[6] Crude rates for the overseas-born population were calculated using the 2011 mid-year estimated resident population from the ABS *Migration, Australia, 2011–12 and 2012–13* tables.[7]

Results

Epidemiological situation in 2011

In 2011, there were 1,385 cases of TB reported to the NNDSS, representing a rate of 6.2 cases per 100,000 population (Figure 1, Table 1). This was an increase of 1% in the number of notified cases compared with 2010 (n=1,368). While a relatively low rate of TB has been maintained since the mid-1980s, there has been a steady and sustained increase in incidence over the decade leading up to 2011 (Figure 1).

A case classification was reported in almost all cases (n=1,381) reported in 2011. Of those with a case classification, the majority of cases were classified as new (95%, n=1,314); that is a patient who has never been treated for TB or a patient treated previously for less than 1 month (Table 1). Relapse was reported in 67 cases, with 17 of those cases reported as relapsing following full treatment in Australia, 12 following partial treatment in Australia and 38 following full or partial treatment overseas.

Geographic distribution

As in previous years, New South Wales accounted for the largest number of cases notified by a state or territory (n=541, Table 1). In 2011, the lowest number of notifications and the lowest jurisdiction-specific rate was reported in Tasmania (n=17, Table 1) while the highest jurisdiction-specific rate was reported in the Northern Territory (15.1 per 100,000).

Figure 1: Notification rate for tuberculosis, Australia, 1960 to 2011

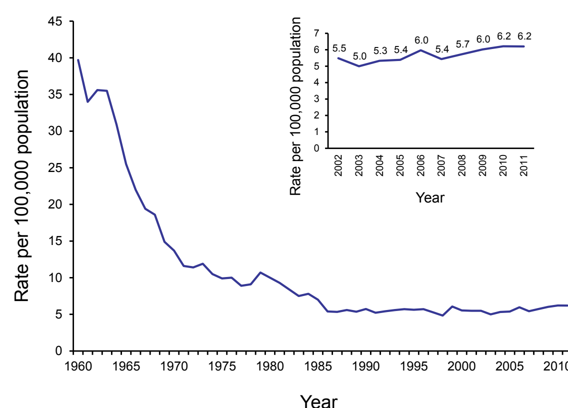


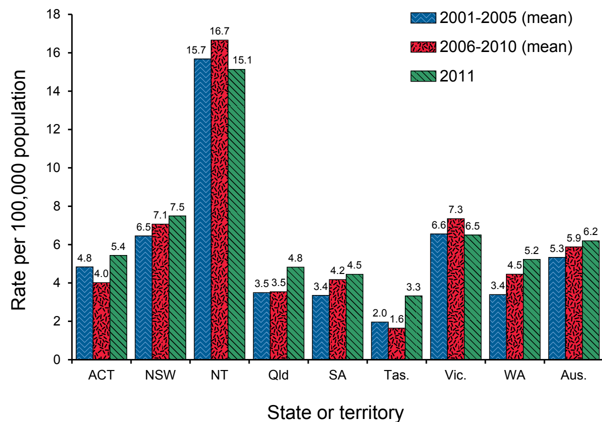
Table 1: Notified cases and rates for tuberculosis, Australia, 2011, by case classification and state or territory

State or territory	New cases Notifications	New cases Rate	Relapse cases Notifications	Relapse cases Rate	Total* Notifications	Total* Rate
ACT	20	5.4	0	–	20	5.4
NSW	505	7.0	33	0.5	541	7.5
NT	32	13.8	2	0.9	35	15.1
Qld	204	4.6	12	0.3	216	4.8
SA	71	4.3	2	0.1	73	4.5
Tas.	16	3.1	1	0.2	17	3.3
Vic.	347	6.3	13	0.2	360	6.5
WA	119	5.1	4	0.2	123	5.2
Aust.	1,314	5.9	67	0.3	1,385	6.2

* Total includes 4 cases reported without a case classification (NSW: 3; NT: 1).

In 2011, all jurisdictions except for Victoria and the Northern Territory, recorded a jurisdiction-specific rate higher than the 5-year mean jurisdiction-specific rates of the 2 preceding 5-year intervals (Figure 2).

Figure 2: Notification rate for tuberculosis, Australia, 2001 to 2011, by state or territory

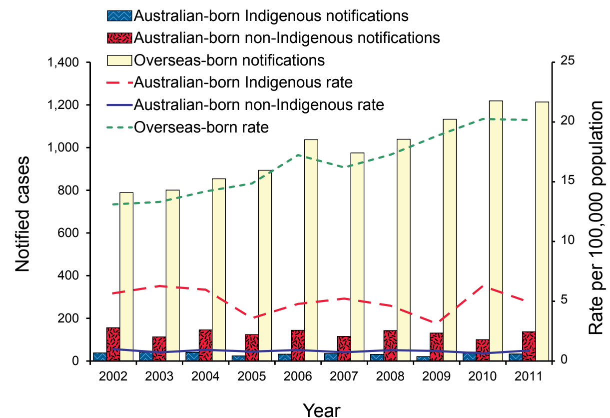


Tuberculosis in the Australian-born population

The overall rate of TB in the Australia-born population in 2011 was 1.0 per 100,000 (Table 2). The rate in the Australian-born Indigenous population (4.9 per 100,000) was more than 5 times the rate reported in the Australian-born non-Indigenous population (0.9 per 100,000). The rate in the Australian-born population however, meets the pre-elimination target set by the World Health Organization (WHO) to be achieved by 2035, reflecting the need to concentrate additional control strategies on the Indigenous and migrant population.[8]

The rate of TB in Australian-born non-Indigenous people has remained relatively stable since 2002, while the rate in Australian-born Indigenous peoples has demonstrated no clear trend, ranging from 3.1 to 6.3 cases per 100,000 over this period (Figure 3).

Figure 3: Notified cases and rate for tuberculosis, Australia, 2002 to 2011, by population subgroup



Tuberculosis in the overseas-born population

All but 1 case of TB diagnosed in 2011 were reported with country of birth information, with 88% (n=1,214) of cases reported as overseas-born (Table 2). The proportion of cases that were reported as overseas-born varied across states and territories, ranging from 46% (n=16) in the Northern Territory to 91% (n=112) in Western Australia.

Table 2: Notified cases and rates for tuberculosis, Australia, 2011, by population subgroup and state or territory

	Australian-born							
	Indigenous		Non-Indigenous		Total		Overseas-born	
State/ territory	Notifications	Rate	Notifications	Rate	Notifications	Rate	Notifications	Rate
ACT	0	–	3	1.1	3	1.1	17	17.7
NSW	7	3.4	56	1.1	63	1.2	478	23.4
NT	12	17.4	7	5.9	19	10.1	16	36.7
Qld	10	5.3	19	0.6	29	0.8	186	18.5
SA	2	5.3	5	0.4	7	0.6	66	17.0
Tas.	0	–	2	0.5	2	0.4	15	23.4
Vic.	0	–	36	0.9	36	0.9	324	20.4
WA	2	2.3	9	0.6	11	0.7	112	14.2
Aust.	33	4.9	137	0.9	170	1.0	1,214	20.2

In 2011, the rate of TB among overseas-born people was more than 19 times the rate in Australian-born and maintained the peak reported in this population group in the previous year. TB in overseas-born people has increased steadily since this subgroup was first reported in 2002 (Figure 3). This figure should be interpreted with caution, given that completeness of reporting the country of birth has improved over this time.

Among overseas-born cases notified in 2011, the most frequently reported country of birth was India (n=276), followed by Vietnam (n=99), the Philippines (n=99) and China (n=82) (Table 3). Among the most frequently reported countries of birth, the highest estimated rates were for those born in Nepal (284 per 100,000), Ethiopia (260 per 100,000) and Papua New Guinea (238 cases per 100,000). These estimated rates must be interpreted with caution as temporary residents are included in Australia's TB notifications (the numerator) but may not be included in the ABS estimated resident population (the denominator).

Residency status was available for 97% (n=1,174) of TB cases reported as overseas born in 2011. Residency status is self-reported at the time of diagnosis and is not verified against migration records. The majority of overseas-born cases reported with a residency status were reported as permanent residents (n=635) followed by overseas students (n=224) (Table 4). This was seen across all states and territories except South Australia, where overseas-born cases were most likely to be reported as overseas visitors (n=17).

There were 47 cases of TB notified among Papua New Guinea (PNG) nationals accessing health care in the Torres Strait Protected Zone (TSPZ) in 2011, a 42% increase on the 33 cases reported in 2010. Treating PNG nationals in the TSPZ

Table 3: Notified cases and rates for tuberculosis for frequently reported countries of birth, Australia, 2011, by case classification

Country of birth	New cases	Relapse cases	Total cases*	Estimated resident population†	Estimated rate (per 100,000 population)	WHO country rate (per 100,000 population) ‡
India	265	9	276	337,120	82	181
Vietnam	93	6	99	207,620	48	151
Philippines	98	1	99	193,030	51	270
China§	75	7	82	387,420	21	75
Nepal	77	2	79	27,810	284	163
Papua New Guinea	66	7	73	30,650	238	346
Indonesia	42	2	44	73,060	60	187
Sudan	25	1	26	22,000	118	117
Ethiopia	22	3	25	9,630	260	258
Thailand	23	1	24	52,990	45	124
Afghanistan	22	2	24	32,970	73	189
Bangladesh	18	5	23	31,620	73	225
Myanmar	21	1	22	24,430	90	381
Pakistan	21	1	22	34,150	64	231
Malaysia	21	0	21	134,140	16	81
Cambodia	17	0	18	32,510	55	424
Sri Lanka	15	1	16	99,740	16	66
Other overseas-born	231	9	241			
Total overseas-born	1,152	58	1,214			
Australian-born	161	9	170			
Total‖	1,314	67	1,385			

* Total includes cases reported without a case classification.

† The Australian Bureau of Statistics estimated resident population at 30 June 2011, Cat 3412.0.

‡ Rates from the World Health Organization TB Burden Estimates, 2011.

§ China excludes Special Administrative Regions and Taiwan.

|| Total includes cases reported without a country of birth.

Table 4: Notified cases of tuberculosis in overseas-born people, Australia, 2011 by residency status and state or territory

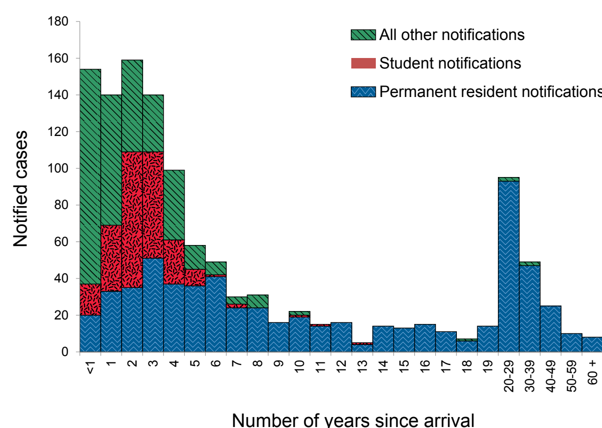
Residency status	ACT	NSW	NT	Qld	SA	Tas.	Vic.	WA	Aust.
Refugee/humanitarian	0	1	0	10	7	2	12	12	44
Permanent resident	10	287	8	57	8	5	196	64	635
Overseas visitor	2	25	1	19	17	3	10	14	91
Overseas student	5	101	2	32	8	2	63	11	224
Unauthorised person	0	7	2	0	0	1	1	4	15
Other	0	52	2	20	1	2	34	6	117
Illegal foreign fisher	0	0	1	0	0	0	0	0	1
Residents of the TSPZ accessing tuberculosis treatment in Queensland	N/A	N/A	N/A	47	N/A	N/A	N/A	N/A	47
Unknown or not reported	0	5	0	1	25	0	8	1	40
Total overseas-born cases	17	478	16	186	66	15	324	112	1,214

TSPZ Torres Strait Protected Zone.

accounted for 22% of Queensland's total caseload in 2011. There was only 1 illegal foreign fisher reported with TB in 2011, the same as in 2010.

In 2011, data on the year of arrival were available for 98% (n=1195) of the cases reported as overseas born. Fifty per cent (593/1195) of these cases were diagnosed with active TB within 4 years of arrival in Australia and 31% (185/593) of those cases reported were in the overseas student population (Figure 4). This high figure primarily reflects reactivation of latent TB infection (LTBI) indicating the potential need to target this in control strategies.

Figure 4: Notified cases of tuberculosis in the overseas-born population, Australia, 2011, by residency status and number of years since arrival in Australia



Premigration health screening

The *Migration Regulations 1994,* enabled by the *Migration Act 1958*, stipulate that visa applicants must meet certain Public Interest Criteria; and these criteria include visa applicants must be "… free from TB" and/or not be a "… threat to public health in Australia or a danger to the Australian community".[9] Therefore, permanent resident visa applicants, some temporary resident visa applicants, and children aged 11 years or over are required to undergo an offshore medical examination, including a chest x-ray, to screen for active TB. Children aged less than 11 years are required to undergo a physical examination.

In 2011, 287 cases of active TB were documented through the premigration health screening process offshore. This represents an estimated incidence rate in those undertaking premigration medical examinations of 80 per 100,000. Approximately 60% of these cases were identified in those applying for temporary resident visa categories; mostly student and short-term visitor visas. These cases include visa applicants who were either newly diagnosed through the premigration health screening process or who were already on treatment at the time of screening. Similar to the onshore NNDSS data, a large proportion (63%) of active TB cases identified in the premigration health screening process were in visa applicants from the Philippines, India, Vietnam and China. Visa applicants who are identified as having active TB during premigration screening are required to undergo treatment for the disease prior to entry to Australia.

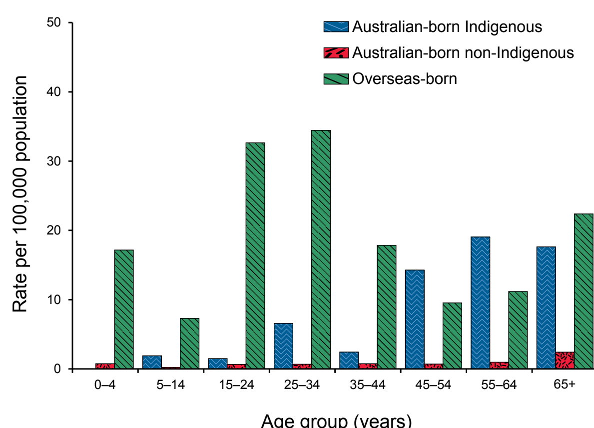
Further information on premigration health screening process and related statistics can be obtained from the Australian Government Department of Immigration and Border Protection, Global Health Branch.

Age and sex distribution

Age and sex were reported for all TB cases notified in 2011. Continuing the trend reported in previous years, there were more males than females notified with TB, with a male to female ratio of 1.2:1.

In 2011, TB was predominantly seen in young adults aged 25–34 years. This was driven by high rates in overseas-born cases in this age group (Figure 5). In cases reported as Australian-born Indigenous and Australian-born non-Indigenous, the burden of disease increased with age.

Figure 5: Notification rates for tuberculosis, Australia, 2011, by population subgroup and age group



One of the most important aspects of TB control is the monitoring of incidence in children aged less than 15 years because these cases represent recent TB infection. TB was notified in 51 children aged less than 15 years in 2011, 4% of the total notified cases. Of these, 15 were Australian-born non-Indigenous children including 8 cases reported as having one or more parents born in a high-risk country. An additional 3 cases were Australian-born Indigenous and 33 cases were children born overseas.

Selected risk factors for tuberculosis

Selected risk factor data were provided for 99% (n=1,370) of notified cases in 2011. Overall, the most frequently reported risk factor was past travel to or residence in a high-risk country (n=1,145, Table 5). The increase seen in the reporting of this risk factor, compared with previous reporting periods, is in part due to Victoria initiating reporting of this risk factor to the national dataset from 2011. Interpretation of this risk factor in overseas-born cases is problematic. At the time these data were collected there were inconsistent practices across states and territories as to the inclusion of a case's country of birth in the assessment of this risk factor. NTAC has agreed that this risk factor is to identify travel-related TB and as such is intended to be exclusive of a case's country of birth. Reporting of this risk factor from 2013 should be clearer.

Table 5: Notified cases of tuberculosis, Australia, 2011 by population subgroup and selected risk factors*

Risk factor*	Australian-born Indigenous	Australian-born non-Indigenous	Overseas-born	Total
Household or other close contact with TB	16	35	120	171
Ever resided in a correctional facility†	2	0	7	9
Ever resided in an aged care facility†	1	2	6	9
Ever employed in an institution†,‡	1	0	12	13
Currently or previously† employed in health industry in Australia or overseas	0	5	93	98
Ever homeless	0	1	3	4
Past travel to or residence in a high-risk country	2	35	1,107	1,145
Chest x-ray suggestive of old untreated TB	1	1	14	16
Currently receiving immunosuppressive therapy	1	7	13	21
Australian-born child with one or more parent born in a high-risk country	0	9	0	9
None of the above risk factors	9	52	65	126
Total cases assessed for risk factors	30	133	1,206	1,370

* More than 1 risk factor may be reported for each notified case of tuberculosis.

† Within the preceding 5 years.

‡ Institution is defined as a correctional facility, aged care facility or homeless shelter.

Having a household member or close contact with TB was the most common risk factor reported by Australian-born Indigenous cases (n=16). Whereas, it was equally common as a risk factor reported for Australian-born non-Indigenous cases as past travel to or residence in a high-risk country (n=35) and the second most common risk factor reported by overseas-born cases (n=120).

A total of 98 cases of TB in 2011 were reported in people who were currently or had previously worked in a health care setting. Of these, 44 were working in a health care setting in Australia at the time of diagnosis or within 12 months of diagnosis. More than half (n=24) of these cases presented with extrapulmonary disease only, which is generally not communicable. None of these notified cases were deemed to have acquired TB in an Australian health care setting, nor were there any reports of active TB transmission to patients from health care workers in Australia in 2011. Nine per cent (n=126) of TB cases were reported as having no risk factors identified.

Tuberculosis and HIV status

The HIV testing history of notified cases of TB was reported in 98% of cases (n=1,351, Table 6). More than half of these cases (n=779) were reported with a known HIV status, of which 2.6% (n=20) were reported as HIV positive. Australian-born non-Indigenous cases were reported more frequently as HIV positive (5.0%) than Australian-born Indigenous (0%) and overseas-born cases (2.5%). One-fifth (n=280) of cases with an HIV testing history were reported as being tested for HIV but the result of that test was unknown. These cases were almost entirely reported by Victoria, where current policy prevents the HIV status of an individual being reported against their TB notification.

Anatomical site of disease

The anatomical site of TB disease was recorded in all notified cases in 2011 (Table 7). Pulmonary disease was the most frequently reported site of disease (61%, n=848), with most of these cases reported as having pulmonary disease only. Cases presenting with disease focused in extrapulmonary sites accounted for 39% (n=537) of cases, with lymph nodes (n=291) and pleura (n=82) reported as the most frequent extrapulmonary sites. Of the more severe forms of TB, there were 6 cases classified as miliary and 6 cases classified as meningeal.

Bacteriologically-confirmed cases and drug resistance

Cases confirmed bacteriologically including the drug susceptibility profiles of culture isolates are reported in the annual MRLN report.[3]

The number of cases confirmed by culture of the *Mycobacterium tuberculosis complex* from clinical samples was 1,057 (76%). Of the 848 pulmonary cases, 682 (80.4%) were culture positive and of these 289 (42.3%) were smear positive. Specimens obtained by bronchoscopy established the diagnosis in 148 (21.7%) of the confirmed cases of which 37 (25.0%) were smear positive. Three cases had multi-drug-resistant TB (MDR-TB) isolated from bronchoscopy samples; 1 smear positive. Extrapulmonary disease was culture confirmed in 374 (53%) cases.

In vitro drug susceptibility testing of culture isolates demonstrated resistance to at least one of the standard first line anti-tuberculosis agents in 107 (10.0%) cases. Mono-resistance to isoniazid was reported in 45 cases and mono-resistance to rifampicin was reported in 1 case only. Resistance to at least isoniazid and rifampicin (MDR-TB) was confirmed in 25 (2.4%) cases with overseas-born persons accounting for 100% of these. Ten patients with MDR-TB accessed health services in the TSPZ. In 2011, 2.4% of all bacteriologically-confirmed cases were MDR-TB, but only 1.4% when the TSPZ cases were excluded.

Table 6: Notified cases of tuberculosis, Australia, 2011 by population subgroup and HIV status

HIV testing history	Australian-born Indigenous	Australian-born non-Indigenous	Overseas-born	Total
HIV positive	0	3	17	20
HIV negative	30	57	671	759
HIV tested, result unknown	0	24	256	280
Not tested	3	47	233	283
Refused testing	0	3	6	9
HIV testing history unknown	0	3	31	34
Total	33	137	1,214	1,385

Table 7: Notified cases of tuberculosis, Australia, 2011 by case classification and site of disease

Site of disease	New cases	Relapse cases	Total*	Per cent of cases
Total pulmonary disease	802	46	848	61.2
Pulmonary only	642	39	681	49.2
Pulmonary plus other sites	160	7	167	12.1
Total extrapulmonary only†	512	21	537	38.8
Pleural	82	0	82	5.9
Lymph nodes	275	15	291	21.0
Bone/joint	48	1	50	3.6
Genito/urinary	25	1	26	1.9
Miliary	6	0	6	0.4
Meningeal	6	0	6	0.4
Peritoneal	32	2	35	2.5
Other	126	4	131	9.5
Unknown extrapulmonary site	0	0	0	0.0

* Total includes four extrapulmonary cases reported without a case classification.

† More than one extrapulmonary site may be reported for each notified case of extrapulmonary tuberculosis.

Treatment outcomes of 2010 tuberculosis patient cohort

The treatment outcomes of an annual patient cohort are reported in the following year's annual report. This allows adequate time for all cases notified in a single year to begin treatment and for the treatment outcomes to be recorded in the NNDSS. Treatment outcomes for the 2011 patient cohort will be reported in the 2012 annual report.

In 2010, treatment success, which includes those cured (bacteriologically-confirmed) and those who completed treatment, was reported in 96% (1185/1233) of cases with assessable outcomes (Table 8). Treatment success ranged from 89.5% in Australian-born Indigenous cases to 96.8% Australian-born non-Indigenous cases. In 2010, there was 1 case of a treatment failure reported in an overseas-born case and a total of 10 (0.8%) cases were reported to have died due to TB.

National performance indicators

Performance criteria for incidence (less than 1 per 100,000) were met only for the incidence rates in Australian-born non-Indigenous cases (Table 9). Incidence rates in children exceeded the performance criteria (less than 0.1 case per 100,000) in all population groups. The reporting of HIV testing history has improved on the previous year and is close to reaching the target of 100%. Outcome reporting fell short of meeting the target of 100% for the 2010 patient cohorts, with 1% of cases with assessable outcomes reported with an unknown outcome. The performance indicator for cases that reported treatment success was met in 2010 (Table 9). Additionally in 2010, this performance indicator was met for Australian-born non-Indigenous cases and overseas-born cases, but fell slightly short for Australian-born Indigenous cases (Table 8).

Discussion

The incidence of TB in Australia continues to be one of the lowest for any country in the world. The rate of 6.2 per 100,000 population is equivalent to rates in recent years,[10,11] indicating that the 1% increase in notifications is as expected for migrant population growth. However, when this rate is compared with the mean of the 2 preceding intervals of 5 years there is a slight increase. This upward trend is particularly evident in New South Wales, Queensland, Western Australia and Tasmania, whereas the relatively higher rates in Victoria and Northern Territory seem to have stabilised.

The rate of TB in Australia reported in 2011 compares favourably with equivalent countries with well-developed and resourced health care systems e.g. New Zealand (7 per 100,000)[12] and the United Kingdom (14.4 per 100,000).[13] However, as reported in 2010, Australia's upward trend is in contrast with the downward trend seen in the United States of America (USA). The USA has seen a steady decline in rates over the last 10 years and in 2011 recorded a rate of 3.4 per 100,000.[14] It is possible that this contrasting trend is a result of the USA's differing approach to Australia in both premigration screening and LTBI screening policies. For example, since 2009 the USA's premigration screening policy has included insisting on a sputum culture as well as

Table 8: Notified cases of tuberculosis, Australia, 2010, by population subgroup and treatment outcome

Treatment outcome	Australian-born Indigenous		Australian-born non-Indigenous		Overseas-born		Total cases*	
	Notifications	% assessable	Notifications	% assessable	Notifications	% assessable	Notifications	% assessable
Assessable outcomes								
Treatment success	34	89.5	91	96.8	1,055	96.4	1,185	96.1
Cured (bacteriologically confirmed) †	6	15.8	5	5.3	58	5.3	69	5.6
Completed treatment	28	73.7	86	91.5	997	91.1	1,116	90.5
Interrupted treatment‡	0	0.0	0	0.0	4	0.4	5	0.4
Died of tuberculosis	0	0.0	1	1.1	9	0.8	10	0.8
Defaulted§	4	10.5	1	1.1	15	1.4	20	1.6
Failure‖	0	0.0	0	0.0	1	0.1	1	0.1
Not followed up, outcome unknown	0	0.0	1	1.1	10	0.9	12	1.0
Total assessable	38	100.0	94	100.0	1,094	100.0	1,233	100.0
Non-assessable outcomes								
Transferred out of Australia	0	0.0	3	3.0	87	7.1	90	6.6
Died of other causes	2	4.8	3	3.0	29	2.4	34	2.5
Still under treatment	2	4.8	0	0.0	9	0.7	11	0.8
Total	42	100.0	100	100.0	1,219	100.0	1,368	100.0

* Total includes 7 cases reported with an unknown population subgroup.

† Cured is defined as the bacteriologically-confirmed sputum smear– and culture-positive at the start of treatment and culture-negative in the final month of treatment and on at least 1 previous occasion.

‡ Interrupted treatment is defined as treatment interrupted for 2 months or more but completed.

§ Defaulted is defined as failed to complete treatment.

|| Failure is defined as sputum culture positive at 5 months or later.

Table 9: National tuberculosis performance indicators, performance criteria* and the current status of tuberculosis, Australia, 2010 and 2011

National tuberculosis performance indicator	Performance criteria	2010	2011
Annual incidence of TB (cases per 100,000 population)			
Australian-born Indigenous Australians	<1	6.3	4.9
Australian-born non-Indigenous Australians	<1	0.6	0.9
Overseas-born persons	*	20.3	20.2
Incidence in children <15 years, by risk group (per 100,000 population)			
Australian-born Indigenous Australians	<0.1	2.5	1.2
Australian-born non-Indigenous Australians	<0.1	0.5	0.4
Overseas-born persons	*	6.6	9.0
Collection of HIV status			
Collection of HIV status in all tuberculosis cases	100%	95%	98%
Treatment outcome measures (%)			
Cases evaluated for outcomes	100%	99	TBA
Cases that have treatment completed and are cured (treatment success)	>90%	96	TBA
Cases recorded as treatment failures	<2%	0.1	TBA

* Performance criteria currently under review.

TBA To be assessed; treatment outcomes for 2011 patient cohort to be reported in the 2012 annual report.

sputum microscopy to exclude TB in prospective migrants.[15] Furthermore, since 2000 the USA has engaged in targeted tuberculin testing in high risk groups, including recent migrants from high-burden TB countries, to identify and treat LTBI.[15,16] In addition, the USA has introduced LTBI premigration screening for all children under 15 years of age. Other contributing factors could include that previously in the USA, prospective migrants diagnosed with TB on screening were allowed entry and thus were counted in USA notification data, whereas more recently these migrants have been excluded from entry and are therefore no longer counted in USA's notification data. Also, the USA receives more migrants from medium burden TB regions, such as the Americas, than Australia does, thereby lowering the risk of TB reactivation after migration.[17]

TB notifications classified as relapsed remain unusual in Australia, though slightly more cases were reported in 2011 than in 2010 (4.8% and 3.8% of cases respectively). Of the 67 relapse cases reported in 2011, 29 (51%) had been treated in Australia. Current notification data does not clarify whether this is related to inadequate treatment, poor adherence to or supervision of the initial treatment or whether the relapsed TB is associated with drug resistance or whether re-infection is a consideration.

The incidence rate of TB in Australian-born people remains very low and stable; however, Aboriginal and Torres Strait Islander people remain disproportionately more affected, with a 5 times higher incidence rate in 2011 than Australian-born non-Indigenous people. The 2011 rate in Aboriginal and Torres Strait Islander people is an improvement on that reported in 2010, which was 11 times higher. Over the last 10 years the rate of TB in Aboriginal and Torres Strait Islander people has neither improved nor deteriorated.

The incidence of TB in Australia continues to be largely determined by migration, with nearly 90% of notifications in 2011 being in overseas-born people. There has been a steady rise in the number of TB notifications in this group for the last 10 years. India continues to contribute the largest number of TB cases (20%), reflecting its status as the most common country of origin for new permanent residents in Australia as well as being a high TB burden country.[18] Vietnam, the Philippines and China are also high TB burden countries and significantly contribute to new permanent residents in Australia, accounting for another 20% of TB notifications in Australia. Nepal was first recognised as a significant contributor to Australian TB notifications in 2010, particularly among students undertaking tertiary education in Australia. In 2011, Nepal again was in the top 5 countries that contributed to TB notifications in Australia with a high proportion of notifications reported as overseas students studying in Australia.

While residency status is self-reported and unverified, the reported data show 44% of TB notifications among overseas-born people are not permanent residents. In 2011, among temporary residents notified with TB, the largest group remains overseas students who contributed to 16% of all TB notifications, 18% of TB notifications in overseas-born people, and 31% of all overseas-born cases diagnosed within 4 years of arrival. This is a lower proportion of notifications than in 2010, though the change is likely to be more a function of the number of students than any change to their risk of TB. NTAC continues to work towards engaging relevant stakeholders in the tertiary education and immigration sectors to undertake active case finding and treatment of LTBI and increase awareness of TB in this population.

In 2011, TB notifications among PNG nationals accessing health care in the TSPZ increased by 42% compared with 2010. PNG nationals accessing health care in the TSPZ represented 22% of all TB notifications. The 2010 initiated collaboration between the TB Control Programs of the PNG, Queensland, and Australian Governments, initiated and funded by the Australian Government in 2010, continued to work toward improving the joint capacity to manage TB in the Western Province of PNG. While it is expected that this collaboration will reduce TB notifications in this group in Australia in future years, the outcome of the enhanced program in the Western Province will be monitored due to its importance.

The other group of migrants arriving by sea that contribute to TB in Australia are illegal maritime arrivals (IMAs), either those seeking asylum or the vessel's crew members. As reported in 2010, the current enhanced dataset does not specifically collect this information, so the exact number of IMA-related cases is not reported here. In 2011, the Department of Immigration and Citizenship (now the Department of Immigration and Border Protection) reported an increased number of boats arriving.[19] Given that this group originated in countries with a high TB burden, it is also likely that the group has contributed to the number of TB notifications in 2011. Nearly all of the TB cases in this migrant group are detected in either Western Australia or the Northern Territory as this is where most IMAs arrive and are then first screened for TB. In a separate report, yet to be published, Western Australia and the Northern Territory together reported 14 cases in this group in 2011, at a rate of 296 per 100,000 people screened.

One of the most frequently reported risk factors for both Australian-born Indigenous (n=16) and Australian-born non-Indigenous cases (n=35) was a history of a household or other close contact with TB. This is important as, in the absence of any other risk factor it is possibly an indicator that local transmission of TB is occurring. In the Australian-born Indigenous cases, 53% of notifications, with risk factor information available, reported a history of household or other close contact with TB. This proportion is less than 2010, but still significant enough to indicate that household transmission is likely continuing to be the main reason for persistently higher rates of TB among Indigenous Australians.

Another marker of transmission of TB within Australian is the incidence of TB in children aged under 15 years. Most cases in this age group were reported as being overseas-born (n=33, 65%) with the remaining 35% of TB cases in this age group being in Australian-born children (n=18). This proportion of Australian-born cases is 3 times higher than the Australian-born proportion of all TB notifications (12%). Fifty-three per cent of the Australian-born children with TB were reported to have at least 1 parent born in a high incidence country. With 'circulatory migration', that is residents returning frequently to their country of origin, this pattern of disease in children may be expected to rise. It may also reflect the absence of a thorough premigration screening process in this cohort. In 2011, there were 3 cases reported in Australian-born Indigenous children. Overcrowding and late presentation may contribute to this transmission in the Indigenous Australian setting and childhood cases are therefore not unexpected. It is important that thorough and timely contact tracing is carried out to identify childhood cases early and to offer observed curative treatment. Reporting on methods of diagnosis for TB in children overall and their risk factors for disease may be useful performance indicators for TB programs and TB control.

People who had previously or are currently working in the healthcare industry were again an important group being notified with TB, making up 7% of the total notifications. This contribution to TB notifications from this group has been increasing over recent years. Less than half of these healthcare workers had recently been working in the sector at the time of diagnosis and only 20% had pulmonary TB and would therefore have been potentially infectious. There were no reported cases of transmission of TB from a healthcare worker to patients. Virtually all healthcare workers (95%) with TB were born overseas and none were considered to have acquired TB from their work in Australia. These data, therefore, do not indicate a lack of infection control in healthcare facilities. However, healthcare workers remain an important risk group for active surveillance for TB.

According to Australia's *2011 National HIV Testing Policy version 1.3*, 'all people with HIV should be tested for tuberculosis, and all people with tuber-

culosis should be tested for HIV'.[20] In 2011, 98% of cases had a HIV test history* reported and of those cases 77% were tested for HIV. HIV co-infection with TB remains uncommon in Australia and at similar levels to previous years.

The outcome of TB treatment remains very good with consistently more than 95% of cases with assessable outcomes in recent years being successfully treated. Both the case fatality rate (0.8%) and the treatment default rate (1.6%) in 2010 were very low and slightly better than results from 2009. In 2010, the outcomes for treatment of TB in Australian-born Indigenous cases were poorer than for other groups, with an overall success of 90%.

This report demonstrates good and sustained TB control in Australia. The crude incidence rate in Australian-born non-Indigenous people is consistently better than the target of less than 1 per 100,000, and achieves the WHO's pre-elimination target of less than 10 notified TB cases per million population.[21] Australia also reports very good outcomes for treatment of TB and in 2010 met targets in all subgroups. Conversely, this assessment against performance indicators does highlight potential challenges, and therefore the future targets for future work to improve TB control in Australia. Notifications and the rate of TB in overseas-born people continues to rise and be the main driver of overall TB incidence; the incidence in children in all subgroups did not meet the performance targets, possibly indicating low grade transmission of TB in Australia; and incidence and outcomes for Indigenous Australians continues to indicate a lower level of control. The key to sustaining the achievements in TB control in Australia that are reported here will be the maintenance of jurisdictional TB control programs at the current high standard, an increasing focus on both pre- and post-migration strategies including for children, and nationally agreed and coordinated strategic activity toward improving detection and outcomes in the at-risk subgroups identified by epidemiological reports such as this one.

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* HIV test history means knowing whether or not the person was tested for HIV, not tested for HIV or refused testing for HIV testing.

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Tuberculosis in Australia: bacteriologically-confirmed cases and drug resistance, 2011

A report of the Australian Mycobacterium Reference Laboratory Network

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Abstract

The Australian Mycobacterium Reference Laboratory Network collects and analyses laboratory data on new cases of disease caused by the *Mycobacterium tuberculosis* complex. In 2011, a total of 1,057 cases were identified bacteriologically; an annual reporting rate of 4.6 cases per 100,000 population. Eighteen children aged less than 15 years plus an additional 11 children from the Torres Strait Protected Zone had bacteriologically-confirmed tuberculosis. Results of *in vitro* drug susceptibility testing were available for 1,056 isolates for isoniazid, rifampicin, ethambutol, and pyrazinamide. A total of 107 (10.0%) isolates of *M. tuberculosis* were resistant to at least one of these anti-tuberculosis agents. Resistance to at least isoniazid and rifampicin (defined as multi-drug resistance, MDR) was detected in 25 (2.4%) isolates; 18 were from the respiratory tract (sputum n=14, bronchoscopy n=3, tissue n=1). Ten (55.6%) of the MDR-TB-positive sputum specimens were smear-positive, as was a single sample from a lymph node. Ten patients with MDR-TB were Papua New Guinea (PNG) nationals in the Torres Strait Protected Zone. If these PNG nationals are excluded from the analysis, the underlying MDR-TB rate in Australia was 1.4%. No cases of extensively drug-resistant TB (defined as MDR-TB with additional resistance to a fluoroquinolone and an injectable agent) were detected in 2011. *Commun Dis Intell* 2014;38(4):E369–E375.

Keywords: *Mycobacterium tuberculosis, Mycobacterium bovis,* multi-drug-resistant, laboratory diagnosis, drug resistance,

Introduction

In the 2012 Global Tuberculosis Report, The World Health Organization (WHO), declared that the 2015 Millennium Development goal of halting and reversing tuberculosis (TB) incidence had been achieved with global TB incidence falling for several years and declining at a rate of 2.2% in 2010 and 2011.[1] However, in 2011, there were still an estimated 8.7 million cases of TB globally, of which 5.8 million (67%) were notified to national TB control programs. India and China account for almost 40% of the global burden. By WHO region, South East Asia and the Western Pacific regions combined account for almost 60% of the cases globally.

Australia continues to record one of the lowest notification rates (5–6 cases per 100,000 population) of TB in the world. For non-Indigenous persons born in Australia, the notification rate was around 0.7 per 100,000 population.[2,3] In recent years, more than 85% of notified cases occurred in the overseas-born population with international students representing almost 20% of all overseas-born cases notified in 2011.[4] The current epidemiology of TB in Australia is largely a direct effect of past residence in a high burden TB country.

Since 1991, the National Notifiable Diseases Surveillance System (NNDSS) has provided data on TB notifications reported to public health authorities in Australia's states and territories. The Australian Tuberculosis Reporting Scheme has been conducted by the Australian Mycobacterium Reference Laboratory Network (AMRLN) since 1986. Data compiled by the AMRLN relate to cases of bacteriologically-confirmed tuberculosis whereas NNDSS data also includes cases identified on the basis of clinical and epidemiological information, or on non-bacteriological laboratory investigations. This report describes the bacteriologically-confirmed TB diagnoses for the year 2011. This report should be considered in conjunction with the National TB Advisory Committee (NTAC) TB notification report.[4]

Methods

The data were based on clinical specimens that were culture-positive for *Mycobacterium tuberculosis* complex (MTBC). Almost all isolates of MTBC were referred to one of the five laboratories comprising the AMRLN for species identification and drug susceptibility testing. Comparable methodologies were used in the reference laboratories. Relapse cases, as defined by the *National Strategic Plan for TB Control in Australia Beyond 2000* prepared by the NTAC,[5] were included in the laboratory data as laboratories are generally unable to differentiate relapse or failed cases from new cases. Data include temporary visitors to Australia, asylum seekers or overseas persons detained in Australia in correctional service facilities. For

each new bacteriologically-confirmed case, the following information was collected where available: demography: patient identifier, age, sex, HIV status and state of residence; specimen: type, site of collection, date of collection and microscopy result; isolate: *Mycobacterium* species and results of drug susceptibility testing, nucleic acid amplification testing results; and for drug resistant isolates: patient country of origin, and history of previous TB treatment, to determine whether resistance was initial or acquired. Data from contributing laboratories were submitted in standard format to the AMRLN coordinator for collation and analysis. Duplicate entries (indicated by identical patient identifier and date of birth) were deleted prior to analysis. Where more than one jurisdiction reported data for the same patient, the earlier collection date was used for including the result. Rates were calculated using mid-year estimates of the population for 2011 supplied by the Australian Bureau of Statistics.[6] For each case, the nature of the first clinical specimen that yielded an isolate of MTBC was used to record the nominal site of disease. Culture-positive specimens collected at bronchoscopy or by gastric lavage were counted as pulmonary disease. Patients with isolates recovered from multiple sites were counted as pulmonary disease (the most important category for public health purposes) if a sputum, bronchoscopy, or lung biopsy specimen was culture positive. Drug resistance among new cases (proxy for primary resistance) was defined as the presence of resistant isolates of *M. tuberculosis* in patients who, in response to direct questioning, denied having received any prior anti-TB treatment (for more than 1 month) and, in countries where adequate documentation was available, for whom there was no evidence of such a history.[7] Drug resistance among previously treated cases (proxy for acquired resistance) was defined as the presence of resistant isolates of *M. tuberculosis* in cases who, in response to direct questioning, report having been treated for 1 month or more or, in countries where adequate documentation was available, for whom there was evidence of such a history.[7] For 2009 onwards, the AMRLN has been requested by NTAC to provide laboratory data on bacteriologically confirmed isolation of *M. bovis* (bacille Calmette Guérin) (BCG).

Results

There were 1,057 bacteriologically-confirmed cases of tuberculosis in 2011 (Figure 1), representing an annual rate of 4.6 cases per 100,000 population. State-specific reporting rates varied from 2.5 (Tasmania) to 12.5 (Northern Territory) cases per 100,000 population (Table 1).

Figure 1: Comparison between tuberculosis notifications and laboratory data, Australia, 1990 to 2011

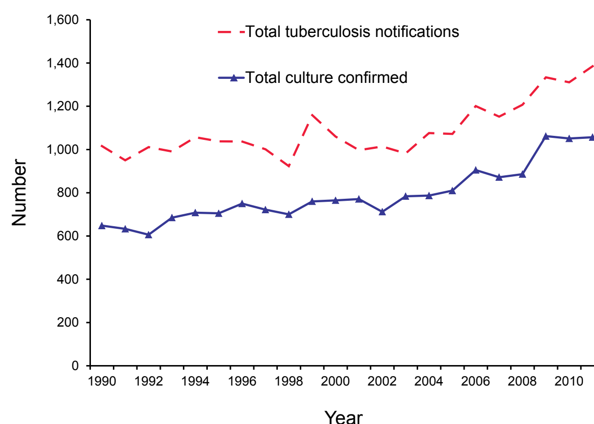


Table 1: Bacteriologically confirmed cases of tuberculosis and rate per 100,000 population, Australia, 2009 to 2011, by state or territory

State or territory	2011 n	2011 Rate	2010* n	2010* Rate	2009* n	2009* Rate	2008* n	2008* Rate
New South Wales†	384	4.9	370	4.9	409	5.5	327	4.5
Northern Territory	30	12.5	23	10.0	24	10.9	25	11.4
Queensland	194	4.2	166	3.7	153	3.4	111	2.6
South Australia	57	3.4	52	3.2	51	3.1	49	3.1
Tasmania	13	2.5	9	1.8	7	1.4	3	0.6
Victoria	280	4.9	344	6.2	331	6.1	299	5.6
Western Australia	99	3.9	87	3.8	87	3.9	72	3.3
Total	1,057	4.6	1,051	4.7	1,062	4.9	886	4.1

* Data from previous reports of the Australian Mycobacterium Reference Laboratory Network.

† Data from the Australian Capital Territory are included with those from New South Wales.

Causative organism

Almost all isolates were identified as *M. tuberculosis* (n=1053), the remaining isolates being *M. bovis* (n=2), *M. africanum* (n=1), and *M. orygis* (formerly known as the 'Oryx' bacillus; (n=1). In addition, a total of 24 *M. bovis* (BCG) were isolated from clinical samples.

Distribution by sex, age and site of disease

The site of disease was dependent upon age and sex. Complete information for sex and age was available for 1,055 patients; 455 (43.1%) were from females, 600 (56.9%) were from males, and sex was not recorded for 2 cases. The overall M:F ratio was 1.3:1. For respiratory isolates, the M:F ratio was 1.5:1. For TB lymphadenitis, the M:F ratio was 1.1:1. For males, there were 2 distinct peak age groups in bacteriologically-confirmed rates: 13.5 cases of TB per 100,000 population at 25–29 years and a 2nd peak in elderly males aged more than 84 years (more than 11.5 cases of TB per 100,000 population). The age distribution of female cases was similar, with 11.6 bacteriologically-confirmed TB cases per 100,000 population for the 25–29 year age group and a lower rate of 4.6 for women more than 84 years of age. The predominant culture-positive respiratory specimen was sputum (n=497), a further 148 were obtained from bronchoscopy, 11 from lung biopsies and 7 lung/nasogastric aspirates (Table 2). Sixty pleural specimens (32 fluid, 28 biopsy/tissue) were culture positive. The most commonly encountered extrapulmonary culture-positive specimen was lymph tissue (n=205) followed by pleural (n=60), bone/joint (n=34), genitourinary tract (n=18), and peritoneal (n=23)

Twenty-nine children aged under 15 years (male n=17, female n=12) had bacteriologically-confirmed tuberculosis (sputum n=15, gastric aspirate n=4, bronchoscopy n=2, lymph node n=5, and a single isolate each from a hip aspirate, tuberculoma of the brain, and tissue (site unknown)). Four respiratory specimens, a lymph node, hip aspirate, and a brain tuberculoma were smear positive. Eleven children (male n=6, female n=5) from the Torres Strait Protected Zone (TSPZ) were bacteriologically confirmed for TB (sputum n=7, gastric aspirate n=2, and an isolate each from lymph node and hip aspirate). Drug resistance was identified in children from the TSPZ, including MDR (n=1) and resistance to streptomycin and isoniazid (n=1).

Table 2: Site of specimens that were smear– and culture-positive for *Mycobacterium tuberculosis* complex, Australia, 2011

	N*	Smear positive	%
Sputum	497	247	49.6
Bronchoscopy	148	37	25.0
Lymph node	205	44	21.5
Pleural	60	4†	6.7
Genitourinary	18	‡	
Bone/joint	31	‡	
Peritoneal	24	‡	
Skin	3	‡	
Cerebrospinal fluid	2	‡	

* Based on specimens that reported a microscopy result and excludes (i) microscopy not performed or (ii) result unknown.

† Two pleural tissues and 2 pleural fluids were smear positive.

‡ Percentage of specimens smear positive not calculated due to the small number of cases.

Association with HIV

The AMRLN database recorded the HIV status of only 102 (9.6%) patients. No patient was identified as being HIV-seropositive.

Microscopy

Microscopy was available for 1,036 (98.0%) of the bacteriologically-confirmed cases in 2011. Microscopy was not performed on 7 specimens and no result was provided for the remaining 14 specimens. For specimens recording a smear result, 247 of 497 (49.7%) sputum and 37 of 148 (25.0%) bronchoscopy specimens were smear positive (Table 2). Of 60 pleural specimens (23 biopsy and 37 fluids) that were culture-positive for *M. tuberculosis* and reported a microscopy result, 2 fluids and 2 tissue samples were smear positive. Lymph node specimens were smear positive in only 44 of 205 (21.5%) cases.

Drug susceptibility testing

The five Australian Mycobacterium Reference laboratories are using the same automated liquid culture system for drug susceptibility testing (MGIT960) and using WHO guidelines for breakpoint drug concentrations (streptomycin 1.0 μg/ml; isoniazid 0.1 μg/ml; rifampicin 1.0 μg/ml; ethambutol 5.0 μg/ml, and pyrazinamide 100 μg/ml).

Results of *in vitro* drug susceptibility testing were available for all but 1 isolate (1,056/1,057) for isoniazid, rifampicin, ethambutol, and pyrazinamide Table 3). One other isolate did not have a pyrazinamide result recorded. A total of 107 (10.0%) *M. tuberculosis* isolates were resistant to at least one

of these first-line anti-TB drugs. Resistance to at least isoniazid and rifampicin (defined as MDR) was detected in 25 (2.4%) isolates. All of the MDR isolates were *M. tuberculosis* (Table 4). Of the 25 MDR-TB isolates, 18 were from the respiratory tract (sputum n=14, bronchoscopy n=3, tissue n=1). Isolates of MDR-TB were obtained from lymph node (n=7) also. Importantly, 10 sputum specimens from MDR-TB cases were smear positive.

A pyrazinamide result was missing from a single isolate and 2 *M. bovis* isolates were not included in the pyrazinamide analysis.

Table 3: Drug resistance profiles, 2011

	2011
DST not completed	1
Fully susceptible	941
Any resistance	
S	58
H	101
R	26
E	5
Z	13
Mono resistance	**(59)**
S	9
H	45
R	1
E	0
Z	4
MDR-TB	**(25)**
HR	3
HRE	1
HRZ	1
HREZ	0
SHR	13
SHRE	1
SHRZ	3
SHREZ	3
XDR-TB	**(0)**
	0
Poly resistance	**(31)**
SH	30
HZ	1
Total isolates	1,057

* The streptomycin result was included for this table.

H = isoniazid, R = rifampicin, E = ethambutol, Z = pyrazinamide, XDR-TB = extensively drug-resistant tuberculosis plus resistance to fluoroquinolone and an injectable agent

Table 4: Drug resistance patterns in multi-drug resistant strains of tuberculosis, Australia 1995 to 2011

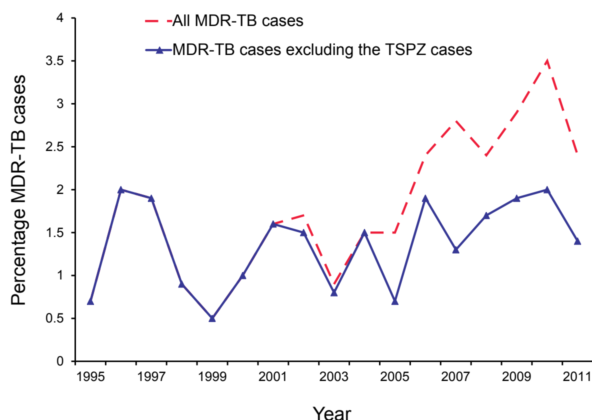
Resistance pattern (standard drugs)*	2011	2010	2009	2008	2007	2006	2005	2004	2003	2002	2001	2000	1999	1998	1997	1996	1995
H+R only	16	18	21	10	16	16	5	7	4	8	8	3	2	2	6	10	3
H+R+E	1	1	1	3	2	1	3	2	2	1	1	1	1	1	1	1	1
H+R+Z	4	15	7	3	5	0	1	1	1	1	3	3	1	2	5	4	1
H+R+E+Z	4	3	2	5	1	5	3	2	0	2	0	1	0	1	2	0	0
XDR-TB	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
Total (n)	25	37	31	21	24	22	12	12	7	12	12	8	4	6	14	15	5
Total (%)	2.4	3.5	2.9	2.4	2.8	2.4	1.5	1.5	0.9	1.7	1.6	1.0	0.5	0.9	1.9	2.0	0.7

* The streptomycin result was not considered for this table.

H = isoniazid, R = rifampicin, E = ethambutol, Z = pyrazinamide, XDR-TB = extensively drug-resistant tuberculosis plus resistance to fluoroquinolone and an injectable agent.

Ten patients with MDR-TB were Papua New Guinea (PNG) nationals from the TSPZ, and these patients access health services in the outer TSPZ. Of the 9 TSPZ patients with pulmonary TB, seven were smear positive. The impact of MDR-TB cases from the TSPZ has lifted the proportion of MDR-TB cases above the 0.5%–2.0% range (Figure 2). In 2011, 2.4% of all isolates were MDR-TB, but only 1.4% when the TSPZ isolates were excluded. When the TSPZ isolates were excluded, 15 MDR-TB cases were documented from patients born overseas but living in Australia. The 15 MDRTB patients originated from: India (n=3), Nepal (n=2), and single cases from Bangladesh, China, Ethiopia, Indonesia, Iraq, South Africa, South Korea, Sudan, Vietnam, and Zimbabwe. No Australian-born patients were identified with MDR-TB. No pre- XDR-TB (MDR-TB with additional resistance of quinolone or injectable but not both) or XDR-TB cases were reported in 2011.

Figure 2: Percentage of multi-drug-resistant tuberculosis in Australia: the impact of multi-drug-resistant tuberculosis cases in Papua New Guinea nationals from the Torres Strait Protected Zone



Mono-resistance to isoniazid was detected in 45 isolates; mono-resistance to rifampicin (n=1), and pyrazinamide (n=4) were also detected. One hundred and one isolates demonstrated resistance to isoniazid at a concentration of 0.1 mg/L. Of these, 25 (24.8%) demonstrated resistance to isoniazid at the higher level of 0.4 mg/L. Among MDR-TB strains, 6/25 (24.0%) demonstrated isoniazid resistance at the higher concentration (0.4 mg/L). Forty-one (38.7%) of 106 specimens culture-positive for drug resistant strains, including 36 of 64 (56.3%) sputum or bronchoscopy specimens, were smear-positive for acid-fast bacilli.

The 2 *M. bovis* isolates that are inherently resistant to pyrazinamide, were not included in the pyrazinamide analysis.

Results of testing for streptomycin were available for 380 of 1,056 (40.0%) isolates with 61 demonstrating resistance to at least streptomycin; 9 had mono-resistance, 30 were resistant to streptomycin and isoniazid, and 19 of 20 MDR-TB strains reporting a streptomycin result were also streptomycin-resistant.

New or previously treated cases, and country of birth

Of the 106 *M. tuberculosis* isolates resistant to at least one of the standard drugs, 63 (59.4%) were from new cases, 4 (3.8%) from previously treated cases, and no information was available on the remaining 39 cases. Two were Australian-born and the remaining 104 were overseas-born. The 104 overseas-born persons with drug resistant disease were from 25 countries; most frequently from India (n=27), Papua New Guinea (including Torres Strait Islands–PNG) (n=21), Vietnam (n=13), Nepal (n=5) and The Philippines (n=5).

Isolation of *Mycobacterium bovis* (bacille Calmette Guérin)

There were 24 isolations of *M. bovis* (BCG) in 2011. Ten were cultured from children aged 5 years or under (4 males; 6 females). Nine isolations were from the vaccination site or axilla, and there was a single isolation from an axillary lymph node. Nine adult males (age range: 63–83 years) had *M. bovis* (BCG) isolated from urine as did a single woman (aged 50 years). In addition, one male aged 68 years had *M. bovis* (BCG) isolated from blood. Three patients had no age or source of isolate documented.

Discussion

The detection of 1,057 laboratory-confirmed cases of TB in 2011 represented 4.6 cases per 100,000 population. In previous AMRLN reports, for the years 2000–2010, the average rate per 100,000 population was 4.6 with a range 3.6 (2002) to 4.9 (2009). As expected, the 1,385 cases notified to the NNDSS in 2011 was higher than the 1,057 (76.4%) cases of bacteriologically confirmed TB.[4] The most frequent reasons postulated for the extra cases reported in the NNDSS include diagnosis of childhood and extrapulmonary TB based on clinical, radiological and epidemiological information, and submission of extrapulmonary samples in formalin precluding bacteriological investigation. In the past decade, the proportion of notifications

confirmed by culture has been consistently within a range of 70%–80% of total NNDSS notifications (see previous AMRLN reports).

Importantly, there is little evidence of active transmission occurring to children within Australia. However, laboratory testing has a lower diagnostic yield in children and so laboratory-confirmed cases may not be sufficiently sensitive to detect low level transmission within this patient group.

MDR-TB remains at a consistently low level. Since the AMRLN began preparing annual reports in 1985, the proportion of patients with MDR-TB has stayed within a range of 0.5%–2.0%. Since 2000 however, the influence of MDR-TB cases occurring in PNG nationals moving within the TSPZ has pushed the percentage above 2%. In 2011, when the 10 TSPZ isolates are included, the MDR-TB rate was 2.4%. When the 10 TSPZ isolates were excluded, the proportion of MDR-TB isolates was 1.4%. All MDR-TB cases documented in 2011 were from persons born overseas; no Australian-born persons were diagnosed with MDR-TB.

For 2011, the indicated country of birth for 62 cases was Papua New Guinea; of these, at least 50 were from the TSPZ. Papua New Guinea is facing a national TB emergency.[8] In the WHO Western Pacific Region, the country ranks second in terms of estimated TB incidence, first in estimated HIV-sero-positive TB, and third in terms of estimated prevalence. The 2012 WHO global report documented an estimated incidence of 346 cases per 100,000 population and a prevalence of 534 per 100,000 population.[1] The AMRLN data showed that 13/62 (21.0%) cases were children less than 15 years of age and 35/62 (56.5%) cases were aged less than 30 years. Although the AMRLN data are small and patient selection bias is likely, there is clear evidence of active transmission occurring in communities, including transmission of drug-resistant TB.

For 2011, the WHO estimated that the MDR-TB rate in PNG among new cases was 4.9% and 23% among retreatment cases.[1] A drug resistance surveillance study is underway in PNG employing Xpert MTB/rifampicin for primary screening. This survey will provide invaluable guidance on the extent of rifampicin-resistant TB in PNG to inform the response of the PNG National TB Control Program, international organisations and donors (Dr Sushil Pandey: personal communication).

Acknowledgements

The Australian Mycobacterium Reference Laboratory Network comprises the Mycobacterium Reference Laboratories at the following facilities:

- SA Pathology, Adelaide, South Australia
- Pathology Services, Herston Hospitals Complex, Herston, Queensland
- Victorian Infectious Diseases Reference Laboratory, North Melbourne, Victoria
- PathWest Laboratory Medicine WA, Queen Elizabeth II Medical Centre, Nedlands, Western Australia
- Institute of Clinical Pathology and Medical Research, Westmead Hospital, Westmead, New South Wales.

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Future reporting of tuberculosis in Australia

In 1985, a decision was made by the Australian Mycobacterium Reference Laboratory Network (AMRLN) to report laboratory data on bacteriologically-confirmed cases of tuberculosis in persons living in Australia, and emphasising documentation of drug resistance. This was seen by the network as an important concern for Australian public health. The National Notifiable Diseases Surveillance System and AMRLN reports have been published in parallel.

In 1995, I attended a national tuberculosis (TB) meeting in Canberra; on the agenda was the topic of unifying the databases. Despite multiple attempts to merge the databases to allow a unified report to be prepared regarding Australian TB cases, success eluded the efforts to do so. Fast forward to 2014, and the roadblocks have been resolved. A report on the combined data for 2012 and 2013 will be published soon in CDI. It will allow for much faster publishing of annual Australian TB data. Furthermore, it should enable different questions to be answered, that hitherto, could not be, and will possibly provide useful information to high burden countries in our region.

On behalf of the AMRLN, we congratulate those involved in developing the unified database and look forward to reading more comprehensive reports on Australian tuberculosis cases.

Richard Lumb
Data Coordinator
Australian Mycobacterium Reference Laboratory Network
17 December 2014

Quarterly report

OzFoodNet quarterly report, 1 April to 30 June 2013

The OzFoodNet Working Group

Introduction

The Australian Government Department of Health established the OzFoodNet network in 2000 to collaborate nationally to investigate foodborne disease. In each Australian state and territory OzFoodNet epidemiologists investigate outbreaks of enteric infection. OzFoodNet conducts studies on the burden of illness and coordinates national investigations into outbreaks of foodborne disease. This quarterly report documents investigations of outbreaks of gastrointestinal illness and clusters of disease potentially related to food, that occurred in Australia between 1 April and 30 June 2013.

Data were received from OzFoodNet epidemiologists in all Australian states and territories. The data in this report are provisional and subject to change.

During the 2nd quarter of 2013, OzFoodNet sites reported 426 outbreaks of enteric illness, including those transmitted by contaminated food. Outbreaks of gastroenteritis are often not reported to health agencies or the reports may be delayed, meaning that these figures under-represent the true burden of enteric disease outbreaks. In total, these outbreaks affected 7,891 people, of whom 448 were hospitalised. There were 23 deaths reported during these outbreaks. The majority of outbreaks (74%, n=315) were due to person-to-person transmission (Table 1), with 53% (166/315) of these occurring in residential aged care facilities.

Foodborne and suspected foodborne disease outbreaks

There were 30 outbreaks during this quarter where consumption of contaminated food was suspected or confirmed as being the primary mode of transmission (Table 2). These outbreaks affected 1,089 people and resulted in 55 hospitalisations. There was 1 death reported during these outbreaks. This compares with 34 outbreaks in the 1st quarter of 2013[1] and a 5-year mean of 31 outbreaks for the 2nd quarter between 2008 and 2012. A limitation of the outbreak data provided by OzFoodNet sites for this report was the potential for variation in the categorisation of the features of outbreaks depending on circumstances and investigator interpretation. Changes in the number of foodborne outbreaks should be interpreted with caution due to the small number each quarter.

Salmonella Typhimurium was identified as the aetiological agent in 9 (30%) foodborne or suspected foodborne outbreaks during this quarter. The aetiological agent in the remaining outbreaks included 2 (6.5%) each due to norovirus and *Listeria monocytogenes* and 1 (3%) each due to *Campylobacter*, hepatitis A, *S.* Infantis, *S.* Zanzibar, histamine fish poisoning and a suspected bacterial toxin. In 10 outbreaks (33%), the aetiological agent was unknown.

Twelve outbreaks (40% of foodborne or suspected foodborne outbreaks) reported in this quarter were associated with food prepared in restaurants (Table 3).

To investigate these outbreaks, sites conducted 2 cohort studies, 3 case control studies and collected descriptive case series data for 17 investigations, while for 8 outbreaks no individual patient data were collected. The evidence used to implicate food vehicles included analytical evidence in 1 outbreak, microbiological evidence in 6 outbreaks and both analytical and microbiological in 2 outbreaks. Descriptive evidence alone was obtained for 21 outbreak investigations.

Table 1: Outbreaks and clusters of gastrointestinal illness reported by OzFoodNet, 1 April to 30 June 2013, by mode of transmission

Transmission mode	Number of outbreaks and clusters	Per cent of total
Foodborne and suspected foodborne	30	7
Waterborne and suspected waterborne	18	4.2
Person-to-person	315	73.9
Unknown (*Salmonella* cluster)	12	2.8
Unknown (Other pathogen cluster)	5	1.2
Unknown	46	10.8

* Percentages do not add up due to rounding.

Table 2: Outbreaks of foodborne or suspected foodborne disease reported by OzFoodNet sites, 1 April to 30 June 2013 (n=30)

State or territory	Month*	Setting prepared	Agent responsible	Number affected	Hospitalised	Evidence	Responsible vehicles
MJO	Apr	Primary produce	Norovirus	525	1	M	Oysters
ACT	May	Restaurant	Suspected bacterial toxin(s)	125	0	AM	Curried prawns, Caesar salad
ACT	May	Restaurant	*Salmonella* Typhimurium PT 170/108, MLVA profile 03-09-07-13-523	161	17	AM	Potato salad containing raw egg mayonnaise
ACT	May	Takeaway	Suspected bacterial toxin	3	0	D	Chicken kebab
NSW	Apr	Commercial caterer	Unknown	10	0	D	Unknown
NSW	Apr	Commercially manufactured	*Listeria monocytogenes* PFGE 4A:4:1, ST 1/2b, 3b, 7, BT 223, MLVA profile 04-17-16-05-03-11-14-00-16	3	3	M	Profiteroles
NSW	Apr	Private residence	*S.* Typhimurium PT 135a MLVA profile 03-13-11-9-523	3	3	D	Unknown
NSW	Apr	Restaurant	*S.* Typhimurium PT 135 MLVA profile 03-17-9-12-523	16	3	D	Unknown
NSW	Apr	Restaurant	Unknown	3	0	D	Chicken burger
NSW	Apr	Restaurant	Unknown	4	0	D	Beef and Guinness pie
NSW	Apr	Restaurant	Unknown	6	0	D	Unknown
NSW	Apr	Restaurant	Unknown	15	0	D	Unknown
NSW	Apr	Unknown	*S.* Zanzibar	5	4	D	Unknown
NSW	Jun	Private residence	*S.* Typhimurium PT 9 MLVA profile 03-23-23-11-523	17	5	D	Béarnaise sauce
NSW	Jun	Private residence	Unknown	3	0	D	Unknown
NSW	Jun	Restaurant	Unknown	5	0	D	Unknown
NSW	Jun	Restaurant	Unknown	5	0	D	Unknown
NT	May	Fair/festival/mobile service	*S.* Typhimurium PT 170/108	5	1	D	Gravy
SA	Jun	School	Campylobacter	6	0	D	Honey soy chicken wings
Vic.	Apr	Bakery	*S.* Typhimurium PT 170/108	21	1	M	Cake
Vic.	Apr	Private residence	*S.* Typhimurium PT 64	3	1	D	Frittata
Vic.	May	Military	Norovirus	85	0	A	Unknown
Vic.	May	Restaurant	Histamine	3	0	D	Tuna
Vic.	May	Restaurant	*S.* Typhimurium PT 44	36	7	M	Tartare sauce/aioli (raw eggs)
Vic.	May	Restaurant	Unknown	3	0	D	Suspected foie gras parfait
Vic.	Jun	Private residence	*S.* Typhimurium PT 9	2	0	M	Raw egg mayonnaise
Vic.	Jun	Private residence	Unknown	3	1	D	Aioli with raw eggs

Table 2 continued: Outbreaks of foodborne or suspected foodborne disease reported by OzFoodNet sites, 1 April to 30 June 2013 (n=30)

State or territory	Month*	Setting prepared	Agent responsible	Number affected	Hospitalised	Evidence	Responsible vehicles
WA	Apr	Takeaway	*S.* Infantis	6	1	M	Multiple foods
WA	May	Commercially manufactured	*L. monocytogenes*	3	3	D	Pre-prepared frozen meals
WA	May	Private residence	Hepatitis A	4	4	D	Kava
Total				1,089	55		

*	Month of outbreak is the month of onset of first case or month of notification/investigation of the outbreak.
A	Analytical epidemiological association between illness and 1 or more foods.
BT	Binary type.
D	Descriptive evidence implicating the suspected vehicle or suggesting foodborne transmission.
M	Microbiological confirmation of agent in the suspected vehicle and cases.
MJO	Multi-jurisdictional outbreak
MLVA	Multi-locus variable number tandem repeat analysis.
PFGE	Pulsed-field gel electrophoresis.
PT	Phage type.
ST	Serotype.

The following jurisdictional summaries describe key outbreaks and public health actions that occurred during the quarter.

Table 3: Outbreaks of foodborne or suspected foodborne disease reported by OzFoodNet, 1 April to 30 June 2013, by food preparation setting

Food preparation setting	Outbreaks
Restaurant	12
Private residence	7
Commercially manufactured	2
Takeaway	2
Bakery	1
Commercial caterer	1
Fair/festival/mobile service	1
Military	1
Primary produce	1
School	1
Unknown	1
Total	30

Australian Capital Territory

There were 3 reported outbreaks of foodborne or suspected foodborne illness during the quarter. The aetiological agents were identified as *S.* Typhimurium phage type (PT) 170/108* multi-locus variable number tandem repeat analysis (MLVA) profile† 03-09-07-13-523 in 1 outbreak and suspected bacterial toxins in the other 2 outbreaks.

Description of key outbreaks

An outbreak was detected in May following multiple emergency department presentations for gastroenteritis. A local restaurant was confirmed as the source of exposure. A case control study was undertaken with 161 case and 32 control interviews being conducted. There were 79 laboratory-confirmed *Salmonella* infections and 17 hospitalisations. The case control study showed a number of different food vehicles to have a significant association with illness but only potato salad with a raw egg mayonnaise remained significantly associated with illness after multivariate analysis (adjusted odds ratio [OR] 7.79, 95% confidence interval [CI] 2.2-27.6, *P*=0.001). *S.* Typhimurium PT 170/108, MLVA profile 03-09-07-13-523 was isolated from raw egg mayonnaise recovered from the premises.

A second outbreak was identified through complaints from members of the public following a buffet luncheon. A paper describing this outbreak is published in this issue of *Communicable Diseases Intelligence.*[2] A cohort analysis study was undertaken with 225/303 (74%) attendees being interviewed. Some 56% (125/225) reported illness, with 2 stools being collected but both tested negative for bacteria, virus and parasites. Multivariate analysis showed illness to be significantly associated with consuming curried prawns and Caesar salad. An environmental inspection highlighted issues relating to food storage practices, a lack of hand washing facilities, and a need for substantial cleaning and repairs to the kitchen, with cross contamination and temperature abuse likely contributors to the outbreak. Samples of the prawns and Caesar salad were not available for laboratory testing; however staphylococcal enterotoxin and *Bacillus cereus* diarrhoeal enterotoxin were detected in samples of roast chicken and parboiled chat potatoes. The suspected cause of the outbreak was a bacterial toxin(s).

New South Wales

There were 13 reported outbreaks of foodborne or suspected foodborne illness during the quarter. The aetiological agents were identified in five of these outbreaks: three due to *S.* Typhimurium and one each due to *S.* Zanzibar and *Listeria monocytogenes*.

Description of key outbreak

An outbreak of *L. monocytogenes* infection was detected following the notification of 3 cases within 8 days. All 3 cases were inpatients in hospitals within the same local health district during their incubation period. The specimens were indistinguishable by binary type (BT) 223, serotype (ST) 1/2b, 3b, 7, pulsed-field gel electrophoresis (PFGE) type 4A:4:1 and MLVA profile 04-17-16-05-03-11-14-00-16, indicating a common source. A public health investigation determined that the 3 cases had all consumed profiteroles from the same external commercial supplier on the same day. Multiple environmental swabs from the supplier's premises tested positive for *L. monocytogenes*, which were indistinguishable from that found in the cases. There was 1 death associated with this outbreak.

* Classification of this organism differs between laboratories, with the Microbiological Diagnostic Unit using PT 170 to classify this type of *S.* Typhimurium and the Institute of Medical and Veterinary Science using PT 108 due to a difference in the interpretation of a phenotypic characteristic.

† MLVA profiles are reported using the Australian coding convention agreed at a MLVA typing harmonisation meeting in Sydney in November 2011.

An outbreak of gastrointestinal illness that was associated with a large multi-jurisdictional outbreak of norovirus is discussed under the multi-jurisdictional investigations section of this report.

Northern Territory

There was 1 reported outbreak of foodborne or suspected foodborne illness affecting 5 people during the quarter. The aetiological agent was identified as *S.* Typhimurium PT 170/108.

Description of key outbreak

An outbreak of gastroenteritis affecting 5 people was detected after routine follow up of sporadic cases of salmonellosis. All 5 cases had eaten a meal of meat or chips and gravy at a market stall 2 to 3 days prior to onset of symptoms. All 5 cases tested positive for *S.* Typhimurium PT 170/108. An environmental health inspection of cooking facilities and processes identified inadequate temperature control and monitoring as a likely contributing factor to contamination.

Queensland

There were no reported outbreaks of foodborne or suspected foodborne illness during the quarter. However, an outbreak of gastrointestinal illness that was associated with a large multi-jurisdictional outbreak of norovirus is discussed under the multi-jurisdictional investigations section of this report.

South Australia

There was 1 reported outbreak of foodborne or suspected foodborne illness during the quarter. The aetiological agent was identified as *Campylobacter*.

Description of key outbreak

A cluster of gastrointestinal illness was identified at a boarding school. Six people experienced gastrointestinal illness and two were confirmed with campylobacteriosis. Interviews were conducted and several common meals were identified. An environmental investigation identified a faulty oven that was not sufficiently cooking food on the bottom shelf. There were reports of undercooked honey soy chicken wings being returned to the kitchen. All 6 people ate the chicken wings meal and became ill 2 to 4 days later.

Tasmania

There were no reported outbreaks of foodborne or suspected foodborne illness during the quarter. However, an outbreak of gastrointestinal illness that was associated with a large multi-jurisdictional outbreak of norovirus is discussed under the multi-jurisdictional investigations section of this report.

Victoria

There were 8 reported outbreaks of foodborne or suspected foodborne illness during the quarter. The aetiological agents were identified in six of these outbreaks: four were due to *S.* Typhimurium and one each due to norovirus and histamine.

Description of key outbreaks

An outbreak of gastroenteritis affecting several family members who had attended an engagement party was notified by a doctor from a Melbourne metropolitan hospital. The party was held at a restaurant and an engagement cake made at a bakery was brought to the restaurant by the family. There were 60 guests at the party and 29 were interviewed. Twenty-one guests became ill after the party and *S.* Typhimurium PT 170/108 was isolated from the faecal specimens of 5 cases as well as a sample of leftover engagement cake. It is suspected that the cake was originally contaminated at the bakery where whipped cream decoration on the cake may have been cross contaminated through inadequately sanitised mixing equipment. Inadequate temperature control of the cake after purchase would have permitted bacterial growth.

An outbreak was identified after a doctor notified a case with salmonellosis and commented that several other members from a group of 20, who had dined at a hotel restaurant together, were ill. An additional notification of a patient, who dined at the same restaurant, was received on the same day from another doctor. Interviews were conducted with the initial group of 20 and the single notified case. Active case finding was also conducted through a booking list provided by the restaurant and through notified cases of *Salmonella* residing in the geographical area surrounding the restaurant. A total of 36 cases were identified in restaurant patrons and 16 of these cases had *S.* Typhimurium PT 44 isolated from a faecal specimen. *S.* Typhimurium PT 44 was isolated from a sample of tartare sauce made with raw eggs that were collected from the restaurant 6 days after the last case reported eating there. A review of the process for making the mayonnaise highlighted deficiencies with cleaning and sanitising of blending equipment. *S.* Typhimurium PT 44 was isolated from samples collected by the Department of Environment and Primary Industries during an on-farm investigation.

An outbreak of gastrointestinal illness that was associated with a large multi-jurisdictional outbreak of norovirus is discussed under the multi-jurisdictional investigations section of this report.

Western Australia

There were 3 reported outbreaks of foodborne or suspected foodborne illness during the quarter. The aetiological agents were identified in the outbreaks were *L. monocytogenes*, *S.* Infantis and hepatitis A.

Description of key outbreaks

The Goldfields Public Health Unit investigated 4 cases of hepatitis A that were reported over a short period of time. Investigation found the index case had travelled to Fiji during their incubation period. A paper previously published in *Communicable Diseases Intelligence* describes this outbreak.[3]

While infectious, the index case prepared kava[‡] for a group of friends in the Goldfields area, two of whom subsequently developed hepatitis A. No other common exposure was identified. A child of one of the cases also developed hepatitis A, despite having received a hepatitis A vaccination more than 2 weeks previously. All 4 cases were typed at the Victorian Infectious Diseases Reference Laboratory as hepatitis A genotype IA, with 100% homology.

An outbreak of *L. monocytogenes* infection was detected following notification of 3 elderly people who had all purchased frozen meals from the same home delivery service. Two cases had the same PFGE type, which was indistinguishable from that of a 2011 food isolate from the implicated company. The 3rd case had a different PFGE type. A roast beef meal sample collected during an assessment of the food was positive for *L. monocytogenes* of a different PFGE type to that of the cases. No significant food safety issues were identified during the assessment.

Multi-jurisdictional investigations

Norovirus associated with the consumption of oysters from Tasmania

OzFoodNet commenced a multi-jurisdictional outbreak investigation on 3 April 2013. Tasmanian oysters associated with a gastroenteritis outbreak were confirmed to have been distributed to several other states and suspected cases had been identified in Victoria and New South Wales. A report describing this outbreak was published previously.[4]

There were 525 cases associated with this outbreak. This included 306 cases in Tasmania; 209 in Victoria; eight in New South Wales; and two in Queensland. One case was hospitalised. Of the 10 human samples sent for testing, 8 faecal specimens had norovirus detected and 1 sample also had *Campylobacter* detected.

An environmental survey of the area where the oyster lease is located identified a leaking underwater sewerage pipe as the suspected source of the contamination. The pipe was crimped by the sewerage authority and the leak stopped.

The operator of the oyster lease was advised to withdraw product from retail sale. There was no consumer-level food recall because of business closures over the Easter period and the short shelf life of the product. Urgent media releases were issued and Tasmanian suppliers were instructed to immediately withdraw the remaining product from sale.

Cluster investigations

During the quarter, OzFoodNet sites conducted investigations into 17 clusters of infection for which no common food vehicle or source of infection could be identified. Aetiological agents identified during the investigations included 7 *S.* Typhimurium; 2 Shiga toxin-producing *Escherichia coli* and *S.* Virchow; and 1 each of *Cryptosporidium*; *L. monocytogenes*; *S.* Infantis; *S.* Mbandaka, *S.* Montevideo and *S.* Havana (investigated in a single cluster); *S.* Potsdam and *S.* Stanley.

Comments

The majority of reported outbreaks of gastrointestinal illness in Australia are due to person-to-person transmission, and in this quarter 74% of outbreaks (n=315) were transmitted via this route. The number of foodborne outbreaks this quarter (n=30) compares with the previous quarter (n=34) and is consistent with the 5-year mean (n=31, 2008-2012). Of the 20 foodborne outbreaks for which a source of the outbreak was identified, 6 (33%) were associated with the consumption of raw or minimally cooked egg dishes.

Salmonella species were identified as the aetiological agent in 11 (37%) of the 30 foodborne or suspected foodborne outbreaks during the quarter (Table 2), with 9 outbreaks being due to *S.* Typhimurium. Of

‡ Kava is a traditional Fijian drink consumed during ceremonial and cultural practices and recreational socialising.

the 11 outbreaks where *Salmonella* was implicated as the responsible agent, 5 (45%) were associated with dishes containing raw or minimally cooked eggs.

Acknowledgements

OzFoodNet thanks the investigators in the public health units and state and territory departments of health, as well as public health laboratories, local government environmental health officers and food safety agencies who provided the data used in this report. We would particularly like to thank reference laboratories for conducting sub-typing of *Salmonella*, *Listeria monocytogenes* and other enteric pathogens and for their continuing work and advice during the quarter.

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National Notifiable Diseases Surveillance System, 1 July to 30 September 2014

A summary of diseases currently being reported by each jurisdiction is provided in Table 1. There were 64,307 notifications to the National Notifiable Diseases Surveillance System (NNDSS) with a notification received date between 1 July to 30 September 2014 (Table 2). The notification rate of diseases per 100,000 population for each state or territory is presented in Table 3.

Table 1: Reporting of notifiable diseases by jurisdiction

Disease	Data received from:
Bloodborne diseases	
Hepatitis (NEC)	All jurisdictions
Hepatitis B (newly acquired)	All jurisdictions
Hepatitis B (unspecified)	All jurisdictions
Hepatitis C (newly acquired)	All jurisdictions except Queensland
Hepatitis C (unspecified)	All jurisdictions
Hepatitis D	All jurisdictions
Gastrointestinal diseases	
Botulism	All jurisdictions
Campylobacteriosis	All jurisdictions except New South Wales
Cryptosporidiosis	All jurisdictions
Haemolytic uraemic syndrome	All jurisdictions
Hepatitis A	All jurisdictions
Hepatitis E	All jurisdictions
Listeriosis	All jurisdictions
STEC, VTEC*	All jurisdictions
Salmonellosis	All jurisdictions
Shigellosis	All jurisdictions
Typhoid	All jurisdictions
Quarantinable diseases	
Cholera	All jurisdictions
Highly pathogenic avian influenza in humans	All jurisdictions
Plague	All jurisdictions
Rabies	All jurisdictions
Severe acute respiratory syndrome	All jurisdictions
Smallpox	All jurisdictions
Viral haemorrhagic fever	All jurisdictions
Yellow fever	All jurisdictions
Sexually transmissible infections	
Chlamydial infection	All jurisdictions
Donovanosis	All jurisdictions
Gonococcal infection	All jurisdictions
Syphilis - congenital	All jurisdictions
Syphilis <2 years duration	All jurisdictions
Syphilis >2 years or unspecified duration	All jurisdictions

Table 1 *continued*: Reporting of notifiable diseases by jurisdiction

Disease	Data received from:
Vaccine preventable diseases	
Diphtheria	All jurisdictions
Haemophilus influenzae type b	All jurisdictions
Influenza (laboratory confirmed)	All jurisdictions
Measles	All jurisdictions
Mumps	All jurisdictions
Pertussis	All jurisdictions
Pneumococcal disease (invasive)	All jurisdictions
Poliomyelitis	All jurisdictions
Rubella	All jurisdictions
Rubella - congenital	All jurisdictions
Tetanus	All jurisdictions
Varicella zoster (chickenpox)	All jurisdictions except New South Wales
Varicella zoster (shingles)	All jurisdictions except New South Wales
Varicella zoster (unspecified)	All jurisdictions except New South Wales
Vectorborne diseases	
Arbovirus infection (NEC)	All jurisdictions
Barmah Forest virus infection	All jurisdictions
Dengue virus infection	All jurisdictions
Japanese encephalitis virus infection	All jurisdictions
Kunjin virus infection	All jurisdictions
Malaria	All jurisdictions
Murray Valley encephalitis virus infection	All jurisdictions
Ross River virus infection	All jurisdictions
Zoonoses	
Anthrax	All jurisdictions
Australian bat lyssavirus	All jurisdictions
Brucellosis	All jurisdictions
Leptospirosis	All jurisdictions
Lyssavirus (NEC)	All jurisdictions
Ornithosis	All jurisdictions
Q fever	All jurisdictions
Tularaemia	All jurisdictions
Other bacterial infections	
Legionellosis	All jurisdictions
Leprosy	All jurisdictions
Meningococcal infection	All jurisdictions
Tuberculosis	All jurisdictions

* Infections with Shiga-like toxin (verotoxin) producing *Escherichia coli* (STEC/VTEC).

NEC Not elsewhere classified.

Table 2: Notifications of diseases received by state and territory health authorities, 1 July to 30 September 2014, by date of diagnosis*

Disease	State or territory								Total 3rd quarter 2014	Total 2nd quarter 2014	Total 3rd quarter 2013	Last 5 years mean 3rd quarter	Ratio	Year to date 2014	Last 5 years YTD mean
	ACT	NSW	NT	Qld	SA	Tas	Vic	WA							
Bloodborne diseases															
Hepatitis (NEC)	0	0	0	0	0	0	0	0	0	0	0	0.0	0.0	0	0.0
Hepatitis B (newly acquired)†	0	1	0	11	2	2	11	6	33	46	36	52.4	0.6	135	158.8
Hepatitis B (unspecified)‡	25	636	31	269	92	8	434	201	1,696	1,673	1,880	1,787.8	0.9	4,976	5,160.4
Hepatitis C (newly acquired)†	1	4	0	0	12	4	30	42	93	106	103	101.2	0.9	296	318.4
Hepatitis C (unspecified)‡	37	960	44	703	119	43	525	239	2,670	2,615	2,773	2,700.6	1.0	7,729	7,864.4
Hepatitis D	0	3	0	3	0	0	5	1	12	16	8	8.4	1.4	38	29.6
Gastrointestinal diseases															
Botulism	0	0	0	0	0	0	0	0	0	1	1	0.4	0.0	1	1.4
Campylobacteriosis	105	NN	63	1,551	486	200	1,285	749	4,439	4,731	3,529	3,899.6	1.1	13,865	11,749.8
Cryptosporidiosis	2	56	13	101	28	9	163	41	413	671	420	310.6	1.3	1,936	2,563.8
Haemolytic uraemic syndrome	0	0	0	1	1	0	1	1	4	5	2	2.4	1.7	17	10.2
Hepatitis A	2	16	1	13	0	1	13	5	51	40	45	52.8	1.0	176	183.4
Hepatitis E	0	6	0	2	0	0	1	0	9	22	2	5.8	1.6	41	28.2
Listeriosis	0	3	0	9	3	2	1	0	18	21	15	14.6	1.2	60	59.8
STEC, VTEC§	0	0	0	9	10	0	2	1	22	34	78	31.6	0.7	96	87.6
Salmonellosis	36	656	90	742	254	26	687	258	2,749	4,302	2,252	1,974.0	1.4	12,166	8,659.2
Shigellosis	3	48	23	35	11	1	114	13	248	215	122	114.8	2.2	766	414.0
Typhoid	0	8	0	2	2	0	6	3	21	23	16	19.8	1.1	90	93.8
Quarantinable diseases															
Cholera	0	0	0	0	0	0	0	0	0	1	0	1.2	0.0	2	3.8
Highly pathogenic avian influenza in humans	0	0	0	0	0	0	0	0	0	0	0	0.0	0.0	0	0.0
Plague	0	0	0	0	0	0	0	0	0	0	0	0.0	0.0	0	0.0
Rabies	0	0	0	0	0	0	0	0	0	0	0	0.0	0.0	0	0.0
Severe acute respiratory syndrome	0	0	0	0	0	0	0	0	0	0	0	0.0	0.0	0	0.0
Smallpox	0	0	0	0	0	0	0	0	0	0	0	0.0	0.0	0	0.0
Viral haemorrhagic fever	0	0	0	0	0	0	0	0	0	0	0	0.0	0.0	0	0.0
Yellow fever	0	0	0	0	0	0	0	0	0	0	0	0.0	0.0	0	0.7

Table 2 *continued*: Notifications of diseases received by state and territory health authorities, 1 July to 30 September 2014, by date of diagnosis*

Disease	State or territory								Total 3rd quarter 2014	Total 2nd quarter 2014	Total 3rd quarter 2013	Last 5 years mean 3rd quarter	Ratio	Year to date 2014	Last 5 years YTD mean
	ACT	NSW	NT	Qld	SA	Tas	Vic	WA							
Sexually transmissible infections															
Chlamydial infection[‖,¶]	307	5,571	750	5,110	1,143	427	4,063	2,728	20,099	21,736	20,532	18,938.4	1.1	64,080	57,276.6
Donovanosis	0	0	0	0	0	0	0	0	0	0	0	0.4	0.0	0	0.6
Gonococcal infection[¶]	14	1,223	434	595	150	16	671	537	3,640	4,062	3,624	2,807.0	1.3	11,864	8,901.6
Syphilis – congenital	0	0	4	0	0	0	0	0	4	0	3	1.4	2.9	4	3.6
Syphilis <2 years duration[¶]	5	148	26	106	11	4	153	23	476	479	464	359.0	1.3	1,392	1,081.0
Syphilis >2 years or unspecified duration[‡,¶]	3	112	17	69	28	3	219	14	465	467	473	372.2	1.2	1,402	1,085.8
Vaccine preventable diseases															
Diphtheria	0	0	0	1	0	0	0	0	1	0	0	0.0	0.0	1	1.0
Haemophilus influenzae type b	0	3	0	2	1	0	0	0	6	6	8	5.0	1.2	15	14.6
Influenza (laboratory confirmed)	1,025	18,002	415	13,471	8,616	482	7,324	3,771	53,106	4,641	17,042	23,640.2	2.2	61,523	31,061.8
Measles	6	8	0	8	0	5	18	12	57	73	44	49.0	1.2	304	107.8
Mumps	1	16	0	10	4	2	4	10	47	38	44	37.6	1.3	148	130.6
Pertussis	87	791	33	302	126	11	1,277	467	3,094	2,131	2,990	6,773.0	0.5	7,528	19,771.6
Pneumococcal disease (invasive)	5	185	16	101	62	12	133	72	586	411	554	651.0	0.9	1,208	1,330.2
Poliomyelitis	0	0	0	0	0	0	0	0	0	0	0	0.0	0.0	0	0.0
Rubella	0	2	0	0	1	0	0	0	3	3	11	10.8	0.3	12	32.8
Rubella – congenital	0	0	0	0	0	0	0	0	0	0	0	0.2	0.0	0	0.4
Tetanus	0	0	0	0	0	0	0	0	0	0	0	0.6	0.0	1	3.0
Varicella zoster (chickenpox)	6	NN	34	121	81	11	162	122	537	483	606	581.4	0.9	1,506	1,388.8
Varicella zoster (shingles)	28	NN	65	7	466	62	305	360	1,293	1,359	1,147	917.0	1.4	4,047	2,844.0
Varicella zoster (unspecified)	58	NN	3	1,389	68	38	903	275	2,734	2,582	2,671	2,030.4	1.3	8,006	5,823.2
Vectorborne diseases															
Arbovirus infection (NEC)	0	0	0	2	0	0	0	0	2	10	8	4.2	0.5	26	10.4
Barmah Forest virus infection	0	23	5	45	0	0	5	11	89	216	796	370.8	0.2	635	1,722.4
Dengue virus infection	1	57	13	36	14	3	4	84	212	430	508	247.8	0.9	1,289	1,095.4
Japanese encephalitis virus infection	0	0	0	0	1	0	0	0	1	0	2	0.4	2.5	1	1.0
Kunjin virus infection**	0	0	0	0	0	0	0	0	0	1	0	0.0	0.0	1	1.0
Malaria	4	19	4	19	1	2	22	9	80	82	108	113.0	0.7	252	319.8
Murray Valley encephalitis virus infection**	0	0	0	0	0	0	0	0	0	0	1	0.2	0.0	0	4.2
Ross River virus infection	0	136	74	403	15	0	39	207	874	1,340	679	584.8	1.5	3,803	3,950.8

Table 2 *continued*: Notifications of diseases received by state and territory health authorities, 1 July to 30 September 2014, by date of diagnosis

Disease	State or territory								Total 3rd quarter 2014	Total 2nd quarter 2014	Total 3rd quarter 2013	Last 5 years mean 3rd quarter	Ratio	Year to date 2014	Last 5 years YTD mean
	ACT	NSW	NT	Qld	SA	Tas	Vic	WA							
Zoonoses															
Anthrax	0	0	0	0	0	0	0	0	0	0	0	0.0	0.0	0	0.2
Australian bat lyssavirus	0	0	0	0	0	0	0	0	0	0	0	0.0	0.0	0	0.2
Brucellosis	0	1	1	0	0	0	2	0	4	3	1	7.0	0.6	13	19.8
Leptospirosis	0	3	0	6	1	1	4	1	16	30	20	19.4	0.8	73	117.2
Lyssavirus (NEC)	0	0	0	0	0	0	0	0	0	0	0	0.0	0.0	0	0.0
Ornithosis	0	1	0	1	0	0	4	0	6	6	9	14.4	0.4	23	42.8
Q fever	0	41	0	54	1	0	5	3	104	116	118	88.0	1.2	345	279.4
Tularaemia	0	0	0	0	0	0	0	0	0	0	0	0.0	0.0	0	0.3
Other bacterial infections															
Legionellosis	0	11	2	28	9	4	21	30	105	111	174	96.0	1.1	304	275.2
Leprosy	0	0	0	0	0	0	0	0	0	4	4	2.6	0.0	7	6.6
Meningococcal infection††	1	7	1	14	15	2	13	4	57	41	49	73.8	0.8	123	172.0
Tuberculosis	8	134	8	46	9	3	98	45	351	308	335	349.6	1.0	969	948.2
Total	1,770	28,891	2,170	25,397	11,843	1,384	18,727	10,345	100,527	55,691	64,307			213,295	

* The date of diagnosis is the onset date or where the date of onset was not known, the earliest of the specimen collection date, the notification date, or the notification receive date. For hepatitis B (unspecified), hepatitis C (unspecified), leprosy, syphilis (> 2 years or unspecified duration) and tuberculosis, the public health unit notification receive date was used.

† Newly acquired hepatitis includes cases where the infection was determined to be acquired within 24 months prior to diagnosis. Queensland reports hepatitis C newly acquired under hepatitis unspecified.

‡ Unspecified hepatitis and syphilis includes cases where the duration of infection could not be determined or is greater than 24 months.

§ Infection with Shiga toxin/verotoxin-producing *Escherichia coli.*

|| Includes *Chlamydia trachomatis* identified from cervical, rectal, urine, urethral and throat samples, except for South Australia, which reports only cervical, urine and urethral specimens. From 1 July 2013 case definition changed to exclude all ocular infections.

¶ The national case definitions for chlamydial, gonococcal and syphilis diagnoses include infections that may be acquired through a non-sexual mode (especially in children – e.g. perinatal infections, epidemic gonococcal conjunctivitis).

** In the Australian Capital Territory, Murray Valley encephalitis virus infection and Kunjin virus infection are combined under Murray Valley encephalitis virus infection.

†† Only invasive meningococcal disease is nationally notifiable. However, New South Wales and the Australian Capital Territory also report conjunctival cases.

NN Not notifiable

NEC Not elsewhere classified

Totals comprise data from all states and territories. Cumulative figures are subject to retrospective revision so there may be discrepancies between the number of new notifications and the increment in the cumulative figure from the previous period.

Table 3: Notification rates of diseases, 1 July to 30 September 2014, by state or territory. (Annualised rate per 100,000 population)*,†

Disease	State or territory								Aust
	ACT	NSW	NT	Qld	SA	Tas	Vic	WA	
Bloodborne diseases									
Hepatitis (NEC)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Hepatitis B (newly acquired)‡	0.0	0.1	0.0	0.9	0.5	1.6	0.8	1.0	0.6
Hepatitis B (unspecified)§	26.2	34.3	51.4	23.1	22.0	6.2	30.2	31.9	29.3
Hepatitis C (newly acquired)‡	1.0	0.2	0.0	0.0	2.9	3.1	2.1	6.7	1.6
Hepatitis C (unspecified)§	38.8	51.8	73.0	60.4	28.5	33.5	36.6	37.9	46.2
Hepatitis D	0.0	0.2	0.0	0.3	0.0	0.0	0.3	0.2	0.2
Gastrointestinal diseases									
Botulism	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Campylobacteriosis	110.1	NN	104.5	133.3	116.4	155.9	89.6	118.9	112.9
Cryptosporidiosis	2.1	3.0	21.6	8.7	6.7	7.0	11.4	6.5	7.1
Haemolytic uraemic syndrome	0.0	0.0	0.0	0.1	0.2	0.0	0.1	0.2	0.1
Hepatitis A	2.1	0.9	1.7	1.1	0.0	0.8	0.9	0.8	0.9
Hepatitis E	0.0	0.3	0.0	0.2	0.0	0.0	0.1	0.0	0.2
Listeriosis	0.0	0.2	0.0	0.8	0.7	1.6	0.1	0.0	0.3
STEC,VTEC‖	0.0	0.0	0.0	0.8	2.4	0.0	0.1	0.2	0.4
Salmonellosis	37.7	35.4	149.3	63.8	60.8	20.3	47.9	40.9	47.5
Shigellosis	3.1	2.6	38.1	3.0	2.6	0.8	7.9	2.1	4.3
Typhoid fever	0.0	0.4	0.0	0.2	0.5	0.0	0.4	0.5	0.4
Quarantinable diseases									
Cholera	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Human pathogenic avian influenza in humans	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Plague	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Rabies	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Severe acute respiratory syndrome	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Smallpox	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Viral haemorrhagic fever	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Yellow fever	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Sexually transmitted infections									
Chlamydial infection¶,**	321.9	300.7	1,243.8	439.1	273.7	332.9	283.2	432.9	347.5
Donovanosis	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Gonococcal infection**	14.7	66.0	719.7	51.1	35.9	12.5	46.8	85.2	62.9
Syphilis – congenital	0.0	0.0	6.6	0.0	0.0	0.0	0.0	0.0	0.1
Syphilis <2 years duration**	5.2	8.0	43.1	9.1	2.6	3.1	10.7	3.6	8.2
Syphilis >2 years or unspecified duration§,**	3.1	6.0	28.2	5.9	6.7	2.3	15.3	2.2	8.0
Vaccine preventable diseases									
Diphtheria	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0
Haemophilus influenzae type b	0.0	0.2	0.0	0.2	0.2	0.0	0.0	0.0	0.1
Influenza (laboratory confirmed)	1,074.8	971.8	688.2	1,157.5	2,062.9	375.7	510.5	598.4	918.2
Measles	6.3	0.4	0.0	0.7	0.0	3.9	1.3	1.9	1.0
Mumps	1.0	0.9	0.0	0.9	1.0	1.6	0.3	1.6	0.8
Pertussis	91.2	42.7	54.7	26.0	30.2	8.6	89.0	74.1	53.5
Pneumococcal disease (invasive)	5.2	10.0	26.5	8.7	14.8	9.4	9.3	11.4	10.1
Poliomyelitis	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Rubella	0.0	0.1	0.0	0.0	0.2	0.0	0.0	0.0	0.1
Rubella – congenital	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Tetanus	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Table 3 *continued*: Notification rates of diseases, 1 July to 30 September 2014, by state or territory. (Annualised rate per 100,000 population)*,†

Disease	State or territory								Aust
	ACT	NSW	NT	Qld	SA	Tas	Vic	WA	
Vaccine preventable diseases, *cont'd*									
Varicella zoster (chickenpox)	6.3	NN	56.4	10.4	19.4	8.6	11.3	19.4	13.7
Varicella zoster (shingles)	29.4	NN	107.8	0.6	111.6	48.3	21.3	57.1	32.9
Varicella zoster (unspecified)	60.8	NN	5.0	119.4	16.3	29.6	62.9	43.6	69.5
Vectorborne diseases									
Arbovirus infection (NEC)	0.0	0.0	0.0	0.2	0.0	0.0	0.0	0.0	0.0
Barmah Forest virus infection	0.0	1.2	8.3	3.9	0.0	0.0	0.3	1.7	1.5
Dengue virus infection	1.0	3.1	21.6	3.1	3.4	2.3	0.3	13.3	3.7
Japanese encephalitis virus infection	0.0	0.0	0.0	0.0	0.2	0.0	0.0	0.0	0.0
Kunjin virus infection[††]	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Malaria	4.2	1.0	6.6	1.6	0.2	1.6	1.5	1.4	1.4
Murray Valley encephalitis virus infection[††]	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Ross River virus infection	0.0	7.3	122.7	34.6	3.6	0.0	2.7	32.8	15.1
Zoonoses									
Anthrax	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Australia bat lyssavirus	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Brucellosis	0.0	0.1	1.7	0.0	0.0	0.0	0.1	0.0	0.1
Leptospirosis	0.0	0.2	0.0	0.5	0.2	0.8	0.3	0.2	0.3
Lyssavirus (NEC)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Ornithosis	0.0	0.1	0.0	0.1	0.0	0.0	0.3	0.0	0.1
Q fever	0.0	2.2	0.0	4.6	0.2	0.0	0.3	0.5	1.8
Tularaemia	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Other bacterial diseases									
Legionellosis	0.0	0.6	3.3	2.4	2.2	3.1	1.5	4.8	1.8
Leprosy	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Meningococcal infection[‡‡]	1.0	0.4	1.7	1.2	3.6	1.6	0.9	0.6	1.0
Tuberculosis	8.4	7.2	13.3	4.0	2.2	2.3	6.8	7.1	6.1

* The date of diagnosis is the onset date or where the date of onset was not known, the earliest of the specimen collection date, the notification date, or the notification receive date. For hepatitis B (unspecified), hepatitis C (unspecified), leprosy, syphilis (>2 years or unspecified duration) and tuberculosis, the public health unit notification receive date was used.

† Rate per 100,000 of population. Annualisation Factor was 4.0

‡ Newly acquired hepatitis includes cases where the infection was determined to be acquired within 24 months prior to diagnosis. Queensland reports hepatitis C newly acquired under hepatitis C unspecified.

§ Unspecified hepatitis and syphilis includes cases where the duration of infection could not be determined or is greater than 24 months.

|| Infection with Shiga toxin/verotoxin-producing *Escherichia coli*.

¶ Includes *Chlamydia trachomatis* identified from cervical, rectal, urine, urethral and throat samples, except for South Australia, which reports only cervical, urine and urethral specimens. From 1 July 2013 case definition changed to exclude all ocular infections.

** The national case definitions for chlamydial, gonococcal and syphilis diagnoses include infections that may be acquired through a non-sexual mode (especially in children – e.g. perinatal infections, epidemic gonococcal conjunctivitis).

†† In the Australian Capital Territory, Murray Valley encephalitis virus infection and Kunjin virus infection are combined under Murray Valley encephalitis virus infection.

‡‡ Only invasive meningococcal disease is nationally notifiable. However, New South Wales and the Australian Capital Territory also report conjunctival cases.

NEC Not elsewhere classified.

NN Not notifiable.

Australian Gonococcal Surveillance Programme, 1 April to 30 June 2014

Monica M Lahra for the Australian Gonococcal Surveillance Programme

Introduction

The Australian National Neisseria Network (NNN) comprises reference laboratories in each state and territory that report data on sensitivity to an agreed group of antimicrobial agents for the Australian Gonococcal Surveillance Programme (AGSP). The antibiotics are penicillin, ceftriaxone, azithromycin and ciprofloxacin, which are current or potential agents used for the treatment of gonorrhoea. Azithromycin testing has been recently introduced by all states and territories as it is part of a dual therapy regimen with ceftriaxone recommended for the treatment of gonorrhoea in the majority of Australia. Because of the substantial geographic differences in susceptibility patterns in Australia, regional as well as aggregated data are presented. In certain remote regions of the Northern Territory and Western Australia gonococcal antimicrobial resistance rates are low and an oral treatment regimen comprising amoxycillin, probenecid and azithromycin is recommended for the treatment of gonorrhoea. When in vitro resistance to a recommended agent is demonstrated in 5% or more of isolates from a general population, it is usual to remove that agent from the list of recommended treatments.[1] The AGSP has a program-specific quality assurance process. The AGSP data are presented quarterly in tabulated form, as well as in the AGSP annual report, which includes additional data on other antibiotics. For more information see *Commun Dis Intell* 2014;38(1):E94–E95.

Results

A summary of the proportion of isolates with decreased susceptibility to ceftriaxone, and the proportion resistant to penicillin, ciprofloxacin and azithromycin are shown in Table 1.

Penicillin

Penicillin resistant *Neisseria gonorrhoeae* are defined as those isolates with a minimum inhibitory concentration (MIC) to penicillin equal to or greater than 1.0 mg/L. Penicillin resistance includes penicillinase producing *N. gonorrhoeae* (PPNG), and *N. gonorrhoeae* that have chromosomally mediated resistance to penicillin. In certain areas, classified as remote in the Northern Territory and Western Australia, a treatment regimen based on oral amoxycillin, probenecid and azithromycin is used. Low numbers of cultures are collected in these remote regions due to the distance specimens must travel to a laboratory, and thus by necessity use nucleic acid amplification testing (NAAT). In remote Western

Table 1: Gonococcal isolates showing decreased susceptibility to ceftriaxone and resistance to ciprofloxacin, azithromycin and penicillin, Australia, 1 April to 30 June 2014, by state or territory

State or territory	Number of isolates tested	Decreased susceptibility				Resistance			
		Ceftriaxone		Ciprofloxacin		Azithromycin		Penicillin	
		n	%	n	%	n	%	n	%
Australian Capital Territory	15	0	0.0	8	53.0	0	0.0	2	13.0
New South Wales	370	16	4.3	189	51.0	3	0.8	174	47.0
Queensland	172	2	1.0	58	34.0	5	3.0	40	23.0
South Australia	49	1	2.0	23	47.0	0	0.0	3	6.1
Tasmania	4	1	25.0	2	50.0	0	0.0	1	25.0
Victoria	339	37	10.9	135	40.0	7	2.1	69	20.0
Northern Territory/Urban and Rural	17	0	0.0	3	18.0	0	0.0	2	12.0
Northern Territory/Remote	34	0	0.0	2	5.9	0	0.0	3	8.8
Western Australia/Urban and Rural	86	6	7.0	27	31.0	4	4.8	22	26.0
Western Australia/Remote	31	0	0.0	2	6.5	0	0.0	1	3.2
Australia	1,117	63	5.6	449	40.0	19	1.7	317	28.0

Australia the introduction of a targeted NAAT, developed by the NNN to detect PPNG, is in use to enhance surveillance.[2,3]

Ciprofloxacin

Ciprofloxacin resistance includes isolates with an MIC to ciprofloxacin equal to or greater than 0.06 mg/L.

Azithromycin

Azithromycin resistance is defined as a MIC to azithromycin equal to or greater than 1.0 mg/L. In 2013, 4 gonococcal strains with azithromycin high level resistance were reported from Victoria and Queensland.[4] There were no isolates reported in Australia with high level resistance (azithromycin MIC value >256 mg/L) in this quarter, 2014.

Ceftriaxone

Ceftriaxone MIC values in the range 0.06–0.125 mg/L have been reported in the category decreased susceptibility since 2005.

In the 1st quarter of 2014 there was a decrease in the proportion of *N. gonorrhoeae* isolates with decreased susceptibility to ceftriaxone, when compared with the same quarter in 2013; and the annual data for 2013.[4] There were predominantly from New South Wales and Victoria. When compared to the 1st quarter of 2013, there was a decrease from 6.8% to 5.6% in the proportion of *N. gonorrhoeae* isolates with decreased susceptibility to ceftriaxone nationally; however this proportion is more than double that reported in the 2nd quarters of 2011 and 2012 (2.7%–3.5%).

The highest proportions of isolates with decreased susceptibility to ceftriaxone were reported from Victoria, New South Wales and Western Australia. From Victoria there were 37 strains with decreased susceptibility to ceftriaxone and of those, 20 (45%) were multi-drug resistant (MDR); 34 (92%) were from males; and 24 (%) were isolated from extragenital sites (rectal and pharyngeal). From New South Wales, there were 16 strains with decreased susceptibility to ceftriaxone and of those, 10 (62%) were (MDR; 16 (100%) were from males; and 9 (56%) were isolated from extragenital sites (rectal and pharyngeal). From Western Australia there were 6 strains with decreased susceptibility to ceftriaxone and, of those, 5 (83%) were MDR; 6 (100%) were from males; and 3 (50%) were isolated from extragenital sites (rectal and pharyngeal). In contrast, there were no gonococci with decreased susceptibility to ceftriaxone reported from the Australian Capital Territory, the Northern Territory or remote Western Australia and low numbers were reported from Queensland and South Australia. From Tasmania there was 1 strain with decreased susceptibility to ceftriaxone of the 4 strain tested.

The proportion of strains with decreased susceptibility to ceftriaxone is of increasing concern in Australia and overseas, as this is phenotypic of the genotype with the key mutations that are the precursor to ceftriaxone resistance.[5] There were recent reports of ceftriaxone 500 mg treatment failures in patients from Victoria and New South Wales in patients with pharyngeal gonococcal infections. In these patients the infecting gonococcal strains had ceftriaxone MIC values in the range 0.03–0.06 mg/L.[6,7] Until 2014, there had not been an isolate reported in Australia with a ceftriaxone MIC value > 0.125 mg/L.[4] In late December 2013, a MDR gonococcal strain with a ceftriaxone MIC of 0.5 mg/L, the highest ever reported in Australia, was isolated (unpublished data from the NNN). To date, there has been no evidence of spread of this strain in the first 2 quarters of 2014.

The category of ceftriaxone decreased susceptibility as reported by the AGSP includes the MIC values 0.06 and 0.125 mg/L. The right shift in the distribution of ceftriaxone MIC values over recent years (Table 2), is statistically significant with a sustained increase in the proportion of strains with an MIC value of 0.06 mg/L (2011–2012: [$P=0.02$, 95% CI: 1.04–1.62], and 2012–2013 [$P < 0.0001$, 95% CI: 1.70–2.38]). In 2010, the proportion of strains with ceftriaxone decreased susceptibility was higher than that reported in 2011. This proportion has subsequently increased as described. The proportion of strains with a ceftriaxone MIC 0.125 mg/L has also increased from 0.1% in 2010 and 2011, to 0.3% in 2012 and to 0.6% in 2013. These differences were not significant, which may be attributable to the low

Table 2: Percentage of gonococcal isolates with decreased susceptibility to ceftriaxone MIC 0.06–0.125 mg/L, Australia, 2010 to 2013, and 1 April to 30 June 2014, by state or territory

Ceftriaxone MIC mg/L	2010	2011	2012	2013	2014 Q1	2014 Q2
0.06	4.6	3.2	4.1	8.2	6.4	5.4
0.125	0.1	0.1	0.3	0.6	0.4	0.3

number of strains in this MIC category.[4] In the first 2 quarters of 2014, there are lower proportions of strains at both 0.06 and 0.125 mg/L than reported in 2013.

Dual therapy of ceftriaxone plus azithromycin is the recommended treatment for gonorrhoea as a strategy to temper development of more widespread resistance.[8] Patients with infections in extragenital sites, where the isolate has decreased susceptibility to ceftriaxone, are recommended to have test of cure cultures collected. Continued surveillance to monitor *N. gonorrhoeae* with elevated MIC values, coupled with sentinel site surveillance in high risk populations remains critically important to inform therapeutic strategies, to identify incursion of resistant strains and to detect instances of treatment failure.

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Meningococcal surveillance Australia, 1 July to 30 September 2014

Monica M Lahra, Rodney Enriquez for the Australian Meningococcal Surveillance Programme

Introduction

The reference laboratories of the Australian Meningococcal Surveillance Programme (AMSP) report data on the number of cases confirmed by laboratory testing using culture and by non-culture based techniques. Culture positive cases, where *Neisseria meningitidis* is grown from a normally sterile site or skin lesions, and non-culture based diagnoses, derived from results of nucleic acid amplification testing and serological techniques, are defined as invasive meningococcal disease (IMD) according to Public Health Laboratory Network definitions. Data contained in quarterly reports are restricted to a description of the numbers of cases by jurisdiction and serogroup, where known. Some minor corrections to data in the Table may be made in subsequent reports if additional data are received. A full analysis of laboratory confirmed cases of IMD in each calendar year is contained in the AMSP annual report published in *Communicable Diseases Intelligence*.

For more information see *Commun Dis Intell* 2014;38(1):E97.

Results

Laboratory confirmed cases of invasive meningococcal disease for the period 1 July to 30 September 2014 are shown in the Table.

Table: Number of laboratory confirmed cases of invasive meningococcal disease, Australia, 1 July to 30 September 2014, by serogroup and state or territory

State or territory	Year	Serogroup													
		A		B		C		Y		W135		ND		All	
		Q3	YTD	Q3	YTD	Q3	YTD	Q3	YTD	Q3	YTD	Q3	YTD	Q3	YTD
Australian Capital Territory	2014	0	0	0	1	0	0	0	0	0	0	0	0	0	1
	2013	0	0	1	2	0	0	0	1	0	0	0	0	1	3
New South Wales	2014	0	0	4	13	0	0	0	6	0	2	1	2	5	23
	2013	0	0	7	16	0	2	3	4	5	5	1	2	16	29
Northern Territory	2014	0	0	1	3	0	0	0	0	0	0	0	0	1	3
	2013	0	0	1	2	0	0	0	0	0	0	0	0	1	2
Queensland	2014	0	0	9	25	1	1	1	1	2	3	0	2	13	32
	2013	0	0	4	17	1	2	0	1	1	2	0	0	6	22
South Australia	2014	0	0	10	19	0	0	0	0	0	0	0	0	10	19
	2013	0	0	7	16	0	0	0	1	0	1	0	0	7	18
Tasmania	2014	0	0	1	1	0	0	0	0	1	1	0	0	2	2
	2013	0	0	1	2	0	0	0	0	0	0	1	1	2	3
Victoria	2014	0	0	12	21	0	0	0	1	1	3	0	0	13	25
	2013	0	0	8	16	0	1	0	0	1	1	0	1	9	19
Western Australia	2014	0	0	3	9	0	2	1	1	0	1	0	0	4	13
	2013	0	0	3	11	1	2	0	0	0	1	0	0	4	14
Total	2014	0	0	40	92	1	3	2	9	4	10	1	4	48	118
	2013	0	0	32	82	2	7	3	7	7	10	2	4	46	110

Australian Sentinel Practices Research Network, 1 July to 30 September 2013

Monique B-N Chilver, Daniel Blakeley, Nigel P Stocks for the Australian Sentinel Practices Research Network

Introduction

The Australian Sentinel Practices Research Network (ASPREN) is a national surveillance system that is funded by the Australian Government Department of Health, owned and operated by the Royal Australian College of General Practitioners and directed through the Discipline of General Practice at the University of Adelaide.

The network consists of general practitioners who report presentations on a number of defined medical conditions each week. ASPREN was established in 1991 to provide a rapid monitoring scheme for infectious diseases that can alert public health officials of epidemics in their early stages as well as play a role in the evaluation of public health campaigns and research of conditions commonly seen in general practice. Electronic, web-based data collection was established in 2006.

In June 2010, ASPREN's laboratory influenza-like illness (ILI) testing was implemented, allowing for viral testing of 25% of ILI patients for a range of respiratory viruses including influenza A, influenza B and influenza A H1N1(2009).

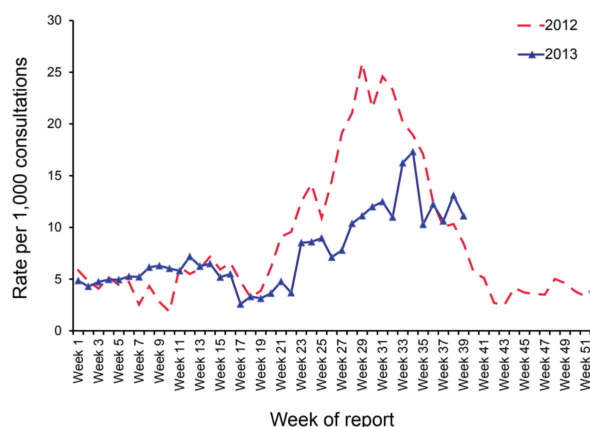
The list of conditions is reviewed annually by the ASPREN management committee. In 2013, 4 conditions are being monitored. They include ILI, gastroenteritis and varicella infections (chickenpox and shingles). Definitions of these conditions are described in Surveillance systems reported in CDI, published in *Commun Dis Intell* 2014;38(1):E96.

Results

Sentinel practices contributing to ASPREN were located in all 8 states and territories in Australia. A total of 278 general practitioners contributed data to ASPREN in the 3rd quarter of 2013. Each week an average of 219 general practitioners provided information to ASPREN at an average of 19,752 (range 14,721–21,245) consultations per week and an average of 351 (range 273–490) notifications per week.

ILI rates reported from 1 July to 30 September 2013 averaged 12 cases per 1,000 consultations (range 8–17 cases per 1,000 consultations). This was lower compared with rates in the same reporting period in 2012, which averaged 18 cases per 1,000 consultations (range 8–26 cases per 1,000 consultations, Figure 1).

Figure 1: Consultation rates for influenza-like illness, ASPREN, 2012 and 1 January to 30 September 2013, by week of report



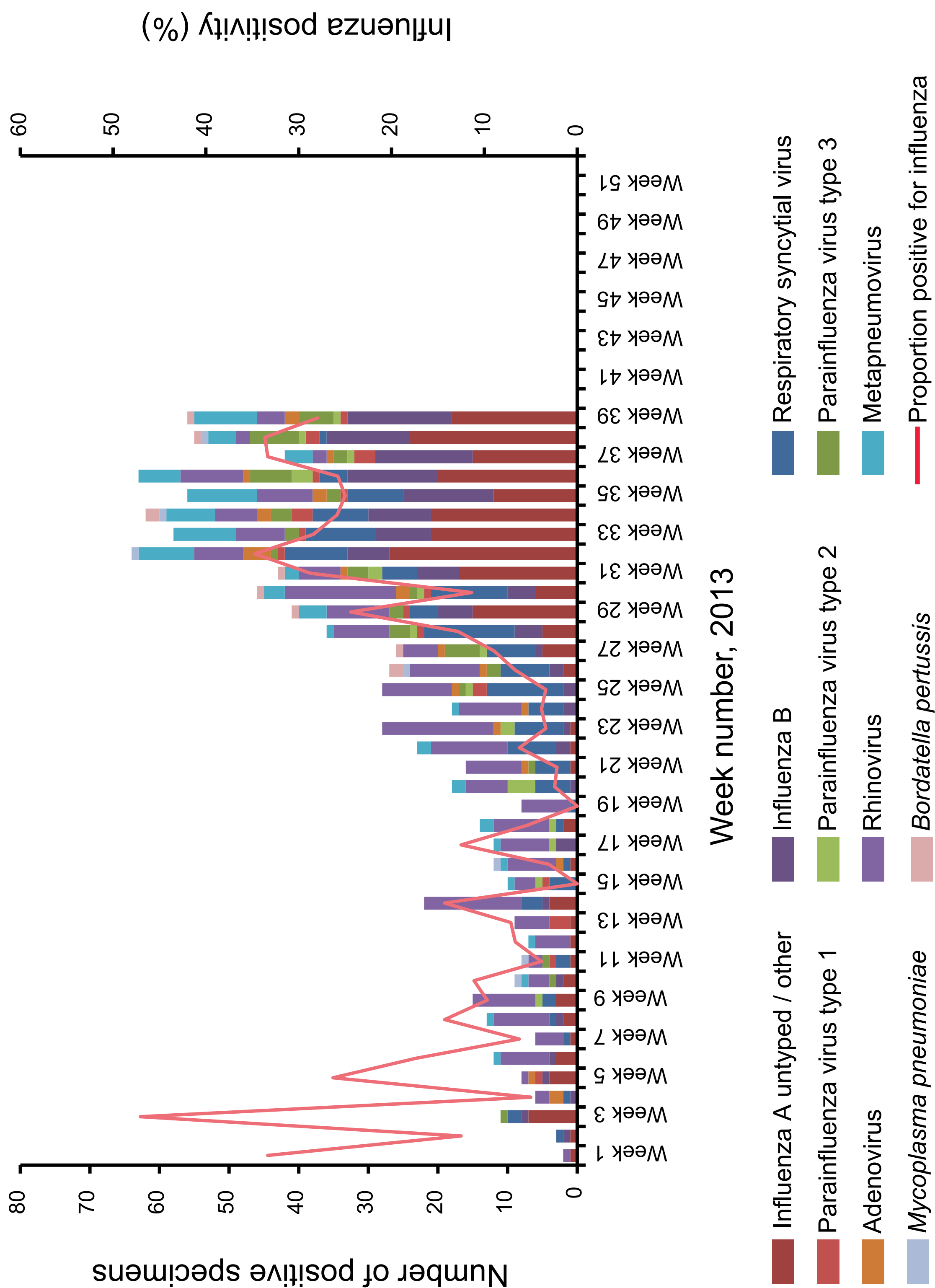
ILI swab testing continued in 2013. The most commonly reported virus during this reporting period was rhinovirus (12.4% of all swabs performed, Figure 2), with the 2nd most common virus being influenza A (untyped) (12% of all swabs performed).

From the beginning of 2013 to the end of week 39, 376 cases of influenza were detected composed of influenza A (untyped) (12% of all swabs performed) and influenza B (6% of all swabs performed) (Figure 2).

During this reporting period, consultation rates for gastroenteritis averaged 5 cases per 1,000 consultations (range 4–6 cases per 1,000, Figure 3). This was higher compared with rates in the same reporting period in 2012 where the average was 4 cases per 1,000 consultations (range 2–5 cases per 1,000).

Varicella infections were reported at a lower rate for the 3rd quarter of 2013 compared with the same period in 2012. From 1 July to 30 September 2013, recorded rates for chickenpox averaged 0.18 cases per 1,000 consultations (range 0.06–0.70 cases per 1,000 consultations, Figure 4).

Figure 2: Influenza-like illness swab testing results, ASPREN, 1 January to 30 September 2013, by week of report



In the 3rd quarter of 2013, reported rates for shingles averaged 0.93 cases per 1,000 consultations (range 0.41–1.85 cases per 1,000 consultations, Figure 5), which was higher compared with the same reporting period in 2012 where the average shingles rate was 0.69 case per 1,000 consultations (range 0.33–0.91 cases per 1,000 consultations).

Figure 3: Consultation rates for gastroenteritis, ASPREN, 2012 and 1 January to 30 September 2013, by week of report

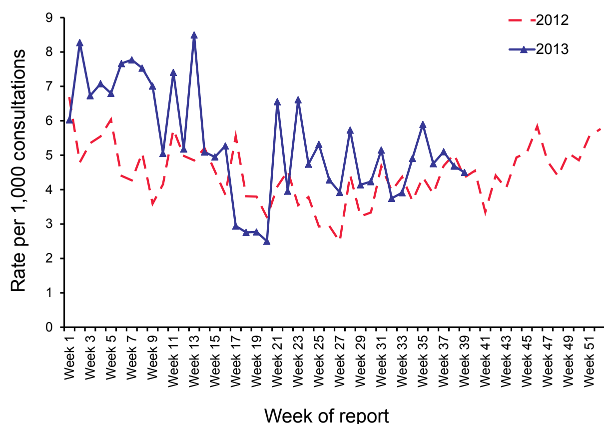


Figure 4: Consultation rates for chickenpox, ASPREN, 2012 and 1 January to 30 September 2013, by week of report

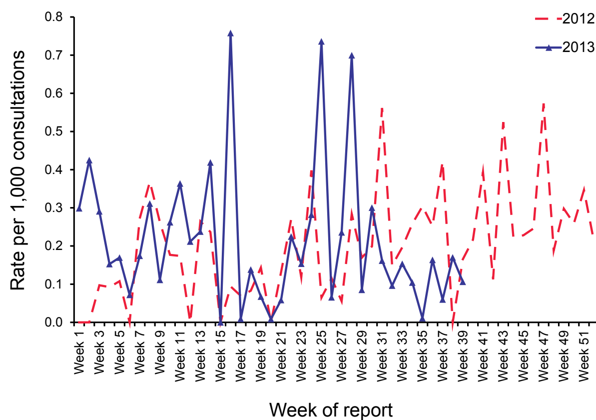
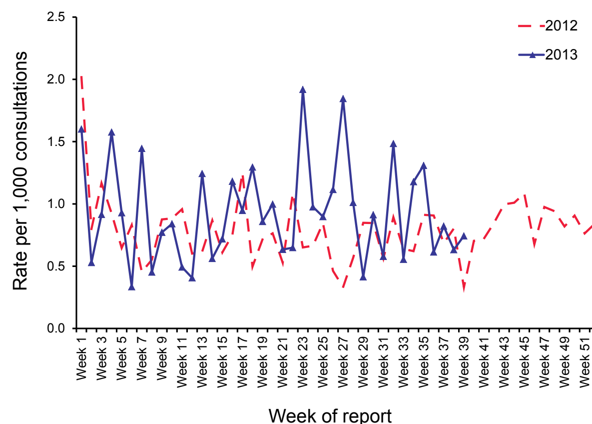


Figure 5: Consultation rates for shingles, ASPREN, 2012 and 1 January to 30 September 2013, by week of report



Policy and guidelines

Essential components of a tuberculosis control program within Australia

The National Tuberculosis Advisory Committee

In Australia, tuberculosis (TB) control is managed, operationally, through state and territory-based programs rather than a single national program as seen in most other countries. The jurisdictional boundaries of these programs are well defined, and communication and cooperation between the programs is effective. The TB control programs in each jurisdiction are quite different and operate as a consequence of the history of their development as well as social, political and demographic circumstances. However, each jurisdiction and the National TB Advisory Committee (NTAC) agree on key components of a TB program. While it is appropriate for the structure and operation of each program to be adapted to best suit the specific local circumstances, these components, and the outcomes that are associated with each, are essential for effective TB control.

The basis for TB programs and the importance of on-going, effective TB control in Australia is described in *The Strategic Plan for Control of Tuberculosis in Australia: 2011–2015*.[1] The purpose of this paper is to define a set of essential components of a jurisdictional TB Control Program in Australia. These components are general to account for differing jurisdictional circumstances. In particular, this paper does not define a program structure, nor specify how the components should be implemented. Ensuring these essential components in jurisdictional programs is a key part of the National TB Program.

The TB programs in each jurisdiction are interdependent, such that an inadequate program in one is likely to impact on TB control in others and also nationally. TB control is maintained nationally, through the interaction and cooperation between jurisdictional programs. This network is most evident in NTAC, but is also dependant on networks that exist between many of the essential components described in this paper, such as between specialist TB nurses, notification data custodians and mycobacterial laboratories. Thus, ensuring a minimum, nationally agreed standard for these components is critical to maintaining national TB control.

Maintenance of a dedicated specialist service

It is important that dedicated services for TB control are maintained. There has been a tendency for TB services to be downsized and divested to larger multi-functional services as the incidence of the disease falls.[2] It has been well documented that this leads to a loss of TB control, especially in the United States of America.[3]

A dedicated service is of particular importance in Australia because of the potential for loss of control amongst an increasing number of visitors and migrants from high incidence countries. Also, in a low incidence setting, such as Australia, expertise and experience in TB control become diluted and lost unless a specialist service maintains them.

It is inadequate to have the components of a TB program present within a larger multi-functional service. Loss of control of TB, both in the individual and the community, is usually insidious and easily missed. Unless maintained by a dedicated unit, a TB program will be neglected.

A dedicated TB service implies:

- a dedicated budget i.e. not shared with other functions;
- government commitment to service provision – this is principally financial, and, in Australia, means state or territory government commitment. It must also recognise that TB management is free of charge and it must not rely on Medicare, as many clients are non-resident;
- specialist personnel; and
- one or more (depending on the population size and distribution) recognised site(s).

Other features of a dedicated TB service should include:

- ease of access – both by communication (other health care providers) and physically (clients);
- sensitive to different cultural and linguistic backgrounds – TB program clients are more often migrants, non-English speaking or Aboriginal and Torres Strait Islander peoples;

- free of charge to the client – including all screening and diagnostic tests, consultation and treatment, irrespective of the residency status of the client. TB is associated with poverty and a financial barrier to service will reduce the effectiveness of control;
- well established links with multiple other relevant service providers, including private and public hospitals and clinicians, community nursing, remote health providers, Aboriginal medical services, the Department of Immigration and Border Protection (DIBP), and non-government agencies involved in migrant screening etc.

Agencies

The roles and functions of a TB program fall broadly under 4 types of activity:

- governance;
- clinical care;
- mycobacterial laboratory; and
- public health activity.

The agencies that undertake these activities may or may not be co-located and managed, but must work together in a close and clearly defined network.

The public health activity is emphasised in this paper because it is at most risk of not being met. Even in a neglected program, clinical care that will diagnose and treat TB is likely to still exist. However, there are many instances in the past of public health activities being neglected and consequent deterioration in TB control. In New York City during the 1970–80s when TB programs were devolved to primary care, specific public health activities of TB clinics were lost and TB rates tripled.[3]

Hub and spokes

Each jurisdictional TB program must have at least one central dedicated site or 'hub'. This centre maintains high level expertise and oversees clinical governance of the program. It is also the centre for co-ordination with other jurisdictions (e.g. for national data collection, transfer of patients between jurisdictions and international contact tracing), and for interdepartmental communication and cooperation. The DIBP in particular, requires a single point of contact for coordination of migrant screening activity.

In a decentralised model there may be many other sites, or 'spokes', undertaking TB program activities, and these may be done by providers that have a broader range of roles. However, the peripheral providers should be monitored by the central site and have the opportunity to refer to this site for assistance as required. In other circumstances, the expertise and resources will not exist for the treatment of TB patients and contact tracing, so the central site must have pre-planned mechanisms of out-reach to rural and remote centres. In addition, the central site needs to maintain some level of expert clinical care e.g. management of complex and multi-drug-resistant (MDR) cases. In this way there is a clear link between the 'coal face' clinical operations and the public health and higher level coordination of the program.

Activity of a tuberculosis control program

The dedicated TB control program must fulfil several key activities, which are also summarised in the National Strategic Plan.[1] While diagnosis and treatment of TB may occur in multiple undedicated sites, ensuring the maintenance of TB program specific activity is usually the role of the central dedicated site ('hub'). These activities are mainly public health activities. They include:

a. TB case management: Active TB is diagnosed and treated in a wide variety of health care settings that are not necessarily dedicated to TB. However, the TB program is responsible for the outcome of **all** TB notifications. While the dedicated TB program may or may not provide direct clinical care to a TB case, it must ensure, as far as possible, that the treatment regimen is appropriate, and the treatment is uninterrupted and satisfactorily completed. This includes direct supervision of treatment (DOT) in cases where it is deemed necessary.

b. Multi-drug-resistant tuberculosis: Case management is of pre-eminent importance in the management of MDR TB, which is both difficult to treat and of high level public health importance. Each jurisdiction should have a committee specifically for the purpose of overseeing the clinical care and public health management of MDR TB cases. The committee should consist of the TB director and program manager and other personnel with TB expertise, and should be an integral component of the central program site ('hub'). All MDR TB cases should be managed by a physician experienced in the treatment of drug resistant TB and, while the treatment decisions are ultimately between this physician and the TB patient, the physician should report regularly to the MDR TB committee.

c. Active surveillance: involves screening high-risk groups for both active TB and latent TB infection (LTBI). Groups of particular importance include:

- contacts of active TB cases;

- migrants – both pre– and post migration screening according to DIBP stipulation, as well as specifically targeted screening e.g. refugees, DIBP detainees;
- health care worker;
- Aboriginal and Torres Strait Islander peoples

  Part of this surveillance is the management of TB risk, including treatment of LTBI and Bacille Calmette-Guérin vaccination, and surveillance of emerging high-risk groups.

d. **Notification database**: Notification and enhanced surveillance data needs to be collected, with the timely provision of these data for national and World Health Organization analysis. These data should also inform decision making in local program development, to ensure maintenance of control.

e. **Policy**: development, implementation and evaluation specific to TB control.

f. **Education**: of both health care providers to maintain expertise and the community in general, particularly with regard to TB risk management. A program must be conscious of maintaining the professional development of its specialist personnel in the context of a low incidence disease, particularly specialist nurses. The program should provide dedicated training in TB skills and accredit personnel that complete the training and are deemed competent.

g. **Research and regional activities**: The program should conduct and promote research into public health, basic science and clinical aspects of TB. Support for Australian TB experts working in high prevalence settings in Australia's region is also an important role of a TB program. This work may be research, capacity building or aid, and can benefit the individual doing the work, the Australian TB program and the recipient TB program.

Components of a tuberculosis control program

Specific personnel and infrastructure are required to fulfil the roles of a TB program:

a. **Director**: a senior doctor or nurse with a high level of training and expertise should be appointed, in a part or full-time capacity, specifically for the leadership of the program. The expertise required is broad-based including clinical, public health, research and teaching. While this individual may, and probably should, be involved in operational activity of the program, this role is strategic rather than managerial (refer to c. Manager). This person should report to a senior level of the relevant department or ministry of health that is responsible for population health.

b. **Governance committee**: should exist for the development of a strategic plan and policies for the program, and to oversee their implementation. This committee may allow for external appraisal of the performance of the program through its membership, and should report on this.

c. **Manager**: An individual should oversee the operation of the program. The individual in charge can be a nurse or doctor, but should have specialist training in both the public health and clinical aspects of TB.

d. **Specialist nurses**: with skills in community and public health nursing, but dedicated to TB case management. They are primarily responsible for the public health roles of the program, specifically drug supply, treatment monitoring, DOT, contact tracing, screening etc.

e. **Trained doctors**: While many specialist physicians will have clinical expertise relevant to TB, a program needs to have doctors with specific training and an on-going interest in TB medicine, both clinical and public health aspects.

f. **Mycobacterial reference laboratory**: TB microbiological tests may be undertaken in multiple different sites, but all should refer back to a single reference laboratory. This facility undertakes higher level diagnostic activities (e.g. positive culture species identification and susceptibility testing), confirms results, maintains a nationally-agreed minimum standard through quality control activities, and collects laboratory data for jurisdictional and national analysis. A strong link must exist between this laboratory and the clinical and public health arms of the TB program. Minimum standards for TB reference laboratories, including the expertise required of the director and scientists that do the work, are given in more detail elsewhere.[4]

g. **Data manager/ epidemiologist**: for the review and analysis of TB notification data and other epidemiological data requirements of the program.

h. **Central site**: a dedicated space for the 'hub' activities described above.

i. Drug supply: A reliable supply of first and second line TB drugs must be maintained, irrespective of the license status of the drugs in Australia.

Program monitoring and evaluation

A TB Control Program should regularly review the effectiveness of the program activity against a set of pre-determined, TB specific, outcomes. This is primarily the work of the Medical Director and senior staff of the central hub, with the assistance of the data manager / epidemiologist. It is, however, done under the review of the Governance Committee. These outcomes should be nationally consistent, and the audit activity should be shared between jurisdictions and other relevant agencies.

Conclusion

Australia has one of the best histories of TB control of any country in the world, and continues to maintain a very low rate of tuberculosis. However, there is potential for the programs that maintain this control to be neglected because the incidence is so low. The components described in this paper are the essential elements of a TB program. If these components are not present, it is likely that TB control in Australia will deteriorate.

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Administration

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