NSW GOVERNMENT Health

Vol. 24(1) • 2013
ISSN 1034 7674

NSW PUBLIC HEALTH BULLETIN

Tuberculosis in NSW

Tuberculosis, public health and gathering new evidence to guide control efforts

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More than 100 years after the discovery of the tubercle bacillus by Robert Koch, tuberculosis (TB) remains one of the most important public health challenges worldwide. Despite significant achievements in communicable disease control in the last century, the World Health Organization (WHO) estimates that in 2011 there were 8.7 million incident cases of TB and 1.4 million TB-related deaths, as well as an additional 430 000 deaths as a result of TB and human immunodeficiency virus (HIV) co-infection.[1] In Australia, the incidence of TB has fluctuated at around 6.0 per 100 000 population for the last 15 years, with more than 85% of cases occurring in people born overseas.[2] This special issue of the *NSW Public Health Bulletin* reviews the current epidemiology of TB in New South Wales (NSW), showcases the experiences of clinicians in managing difficult TB cases, highlights the public health challenges involved in TB control, and adds new evidence to aid future action towards the elimination of TB in Australia.

The first paper, from the NSW TB Control Program, describes the epidemiology of TB in the state. Lowbridge, Christensen and McAnulty review TB notifications over the past two decades and explain why, despite high rates of treatment success, this disease remains a continued strategic priority for disease control. They focus our attention on two key themes: TB transmission within sub-groups of the NSW population, and the potential threat of evolving TB epidemics in neighbouring countries. These two themes are reinforced and expanded upon by other papers in the issue.

Gilbert and Sintchenko outline new opportunities in deciphering TB transmission chains presented by the radically improved resolution of subtyping and whole-genome sequencing of *Mycobacterium tuberculosis*. It is important to raise public health professionals' awareness about recent advances in pathogen genome characterisation as these methods are becoming available at state public health laboratories and allow inference about the direction of transmission between cases and the prediction of undiagnosed cases.[3]

Britton, Perez-Velez and Marais offer an update on the clinical management of TB in children. They demonstrate that rates of paediatric TB in Australia are comparable to other developed countries, with minimal local transmission and routine post-exposure prophylaxis.

The case studies present emerging issues in TB management and control. Michail summarises recommendations about monitoring for adverse events following anti-TB therapy. Banner shares the lessons she and her colleagues learnt following a contact tracing exercise within a school environment. Fisher, Cook and Marks estimate the costs of contact screening in a neonatal intensive care unit following the incidental exposure of neonates to a health care worker diagnosed with respiratory TB. Vogelnest, a senior veterinarian, presents TB as an emerging zoonotic disease and highlights the need for occupational health programs and screening programs for susceptible species. These reports illustrate the increasing complexity of TB patient management and public health investigations.

Two papers aim to improve our understanding of effective contact investigations, especially in hard-to-reach populations. They add to the body of knowledge about how to prioritise contacts on the basis of the infectiousness of the

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10.1071/NB12124

index case, intensity of exposure and susceptibility of contacts. Dobler discusses the findings from a retrospective review of TB contact investigations in NSW. This study demonstrated that only 9% of contacts with positive skin tests received treatment for latent TB infection and advocated for more consistent decision-making and testing strategies for latent TB management. Devlin and Passmore highlight the challenges faced by public health professionals in managing ongoing outbreaks in high-risk communities. Their paper provides important details on the transmission of TB in Aboriginal communities in northern NSW, perhaps the only example of an ongoing local TB outbreak in the state.

The final paper reminds us about the critical importance of TB control interventions in high-incidence countries. Shaw explains Australia's role in promoting and supporting TB control within the Western Pacific Region. This region has been responsible for almost a quarter of the world's TB cases and its challenges of drug-resistance and co-infection with HIV make a strong case for improved engagement from Australia. The author details opportunities for our country to contribute to the *Regional Strategy to Stop TB in the Western Pacific*[4] and to the local TB control capacity building in the region.

The editorial team hopes that this issue of the *NSW Public Health Bulletin* will assist both public health professionals and clinicians involved in the management and control of TB and will be of interest to everyone who is passionate about local and international efforts in TB control.

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Notice

This issue of the *Bulletin* marks the beginning of quarterly publication.

Erratum

Typhoid and paratyphoid fever in Western Sydney Local Health District, NSW, January–June 2011 (N S W Public Health Bull 2012; 23(7–8): 148–152).

The paper by Blackstock, Sheppeard, Paterson and Ralph erroneously used the term 'serotype' in some instances where the term 'phage type' should have been used, for example in the sentence "Three *S.* Typhi isolates acquired at large social gatherings in Samoa had the same serotype and susceptibility profiles…" The sentence should have read: "Three *S.* Typhi isolates acquired at large social gatherings in Samoa had the same phage type and susceptibility profiles…" In addition, differences from the locally endemic strain would need to have been shown to "suggest a potential outbreak".

The authors would also like to clarify that, while the results reported in this paper were provided by the NSW Enteric Reference Laboratory, Institute for Clinical Pathology and Medical Research, Westmead Hospital, the phage typing was in fact performed at the Microbiological Diagnostic Unit – Public Health Laboratory, The University of Melbourne.

The *Bulletin* apologises for any confusion resulting from these errors.

Tuberculosis in NSW, 2009–2011

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Abstract: Aim: To describe the epidemiology of tuberculosis in NSW between 2009 and 2011 and compare with previous years. **Methods:** Data from all cases of tuberculosis notified in NSW during this period were extracted from the Notifiable Conditions Information Management System. Descriptive analyses of notification data were undertaken. Incidence rates were calculated per 100 000 population. **Results:** Between 2009 and 2011, there were 1548 cases of tuberculosis notified in NSW, translating to an average annual notification rate of 7.2 per 100 000 population for this period. A total of 89% ($n = 1371$) of notified cases were overseas-born, and 1.6% ($n = 24$) of cases were recorded as Aboriginal persons. The most common site of infection was the lung (60% of cases). Of notified cases, 68% were reported as having been tested for HIV, of which 3% ($n = 28$) of cases had HIV/tuberculosis co-infection. There were 20 cases of multidrug-resistant tuberculosis, including one case of extensively drug-resistant tuberculosis. **Conclusion:** The notification rate of tuberculosis in NSW has remained relatively stable over the past two decades, though small incremental increases since 2003 are evident. Endemic transmission of tuberculosis within sub-groups of the NSW population, as well as the ongoing high endemnicity for tuberculosis in neighbouring countries, highlight the importance of tuberculosis control as a continued strategic priority for disease control in NSW.

Tuberculosis (TB) remains a disease of global public health significance. The World Health Organization (WHO) estimates that in 2011 there were 8.7 million incident cases of TB and 1.4 million TB-related deaths, as well as an additional 430 000 deaths as a result of TB and human immunodeficiency virus (HIV) co-infection.[1] In Australia the incidence of TB is low: in 2010 it was reported by WHO to be 6.1 cases per 100 000 population. Mortality from TB, excluding HIV-positive cases, was less than one TB-related death per 100 000 population in Australia in 2010.[1]

Despite Australia's low incidence, TB control remains a challenge as the epidemiology of this disease must be considered in a global context given the frequency of international travel and migration from high-incidence countries.[2] The incidence and prevalence of TB in many of Australia's international neighbours remains high. Twenty-two countries account for 80% of the global burden of TB; nine of these countries are within the South-East Asian and Western Pacific Regions. These two regions also account for approximately 18% of multidrug-resistant TB (MDR-TB) cases.[1]

Given the global context of TB epidemiology, elimination of disease within any given country is not considered feasible. The key goals and strategies of the New South Wales (NSW) TB Control Program therefore focus on case finding, early diagnoses and effective treatment in order to minimise and eliminate local transmission.[3] NSW has a strong surveillance system in place, whereby all patients diagnosed with TB are notified to a public health unit or chest clinic in accordance with the NSW *Public Health Act 2010*. Case details are then entered into a central registry, the Notifiable Conditions Information Management System.

The aim of this report is to describe the epidemiology of TB in NSW between 2009 and 2011 by examining the demographic and clinical characteristics, and risk factors for infection, of notified cases. We report on the public health follow-up of cases and the extent of contact tracing activities undertaken by public health and clinical services. We also compare incidence data with data from previous years. Understanding the epidemiology of TB in NSW is critical for informing and evaluating disease control strategies.

Methods

Data sources

TB notification data were extracted from the Notifiable Conditions Information Management System. Data were included in the study when the year of diagnosis was between 2009 and 2011 (inclusive). Population data including NSW mid-year population estimates, estimated populations by country of birth and population estimates by Local Health District (LHD) were obtained from the

Australian Bureau of Statistics (ABS) via the Secure Analytics for Population Health Research and Intelligence system. Results for the 2009–2011 period were compared with the two most recently published NSW TB EpiReviews for the periods 2008 and 2003–2007.[2,4]

Definitions

For the purpose of this report TB was defined as active infection with *Mycobacterium tuberculosis*. Cases of latent TB are not included. Pulmonary TB was defined as disease occurring within the patient's lung, excluding the pleura. Extrapulmonary TB was defined as disease affecting any other region of the body including the pleura. A case of TB was defined as 'new' when there was no record of previous TB treatment of more than 1 month duration.

TB notification data were analysed by year of diagnosis. Each case of TB is assigned a year of diagnosis, which is the year in which the majority of clinical and public health action, including diagnosis, treatment, isolation and contact tracing, occurred.

High-risk countries were defined as per the WHO definition of countries in which the incidence of TB is greater than or equal to 60 cases per 100 000 population per year.[5]

Cases were defined as having MDR-TB when their isolates demonstrated resistance to at least isoniazid and rifampicin. Extensively drug-resistant TB (XDR-TB) was defined as cases in which isolates demonstrated resistance to isoniazid and rifampicin, as well as additional resistance to any fluoroquinolone, and to at least one injectable second-line drug (capreomycin, kanamycin or amikacin).[6]

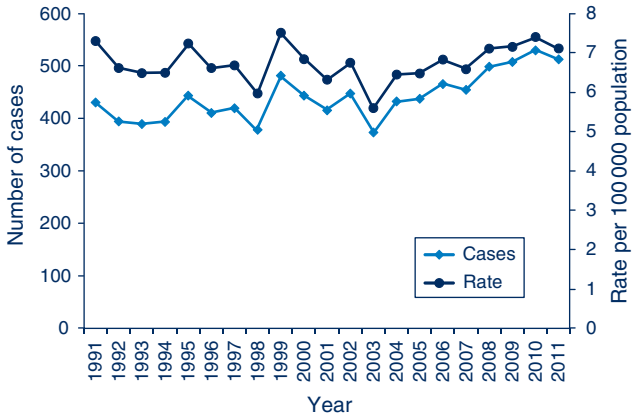

Figure 1. Annual number and rate per 100 000 population of notified tuberculosis cases, NSW, 1991–2011

Source: Notifiable Conditions Information Management System and Secure Analytics for Population Health Research and Intelligence, NSW Ministry of Health (2009–2011), Roberts-Witteveen et al (2008), O'Connor et al (1991–2007).

Table 1. Demographic characteristics, number and rate per 100 000 of notified tuberculosis cases, NSW, 2009–2011

		2009		2010		2011	
		n	Rate	*n*	Rate	*n*	Rate
Sex	Male	282	8.0	301	8.5	287	8.0
	Female	224	6.3	224	6.2	225	6.2
	Unknown	1	–	4	–	0	–
Age	0–4	2	0.4	8	1.7	4	0.8
	5–14	12	1.3	10	1.1	7	0.8
	15–24	90	9.2	101	10.3	87	8.9
	25–34	157	15.7	163	16.4	152	15.3
	35–44	64	6.4	59	5.9	73	7.2
	45–54	67	6.9	63	6.5	56	5.7
	55–64	43	5.3	44	5.4	52	6.2
	65+	72	7.3	81	8.0	81	7.8
Country of birth and Indigenous status	Australian-born	53	1.0	65	1.3	59	n/a
	– Aboriginal or Torres Strait Islander[a]	5	3.1	11	6.8	8	4.8
	– Non-Indigenous	48	1.0	54	1.1	48	n/a
	Overseas-born	454	22.9	464	23.2	453	n/a

n/a = Population estimates not available
[a]Three cases in 2011 had unknown Indigenous status.
Source: Notifiable Conditions Information Management System and Secure Analytics for Population Health Research and Intelligence, NSW Ministry of Health.

Statistical analyses

Descriptive analyses of notification data were undertaken. Cases were categorised as overseas-born, non-Indigenous Australian-born, or Aboriginal and/or Torres Strait Islander Australian-born. Overseas-born cases were categorised into regions of birth using ABS standards.[7] Incidence rates per 100 000 population were calculated for the whole of NSW using select fields from demographic, clinical, risk factor and contact management data categories. Incidence rates for TB by LHD of residence were calculated and mapped. Data were analysed using SAS® Enterprise Guide® (version 4.3, SAS Institute, Cary, NC, USA).

Results

There were 1548 notifications of TB received in NSW between 2009 and 2011 inclusive (507–529 notifications per year), equating to an annualised rate of 7.2 cases per 100 000 population for the period (range 7.1–7.4 per 100 000 population). The rate of TB notification in NSW has remained relatively stable over the past two decades (Figure 1) however there have been small incremental increases since 2003.

Demographic characteristics

Males accounted for 56% of tuberculosis cases diagnosed between 2009 and 2011. The mean age of cases was 41 years (range: 6 months–94 years). Adults aged 25–34 years accounted for the largest proportion (30%) of cases (Table 1). There were 24 cases of TB in Aboriginal persons (1.6% of all cases) in NSW between 2009 and 2011, equating to a crude incidence rate of 4.9 cases per 100 000 population per year. The highest annual crude rate of infection in Aboriginal persons was 6.8 cases per 100 000 population ($n = 11$) in 2010. The rate of infection in non-Indigenous Australian-born persons in 2010 was 1.0 per 100 000 population (9.5% of cases). In 2009, Aboriginal persons were three times more likely to be notified with TB than non-Indigenous Australian-born persons (Incident Rate Ratio (IRR) 3.3, 95% CI: 1.3–8.2), increasing to six times more likely in 2010 (IRR 6.3, 95% CI: 3.3–12.0). Of Aboriginal or Torres Strait Islander persons notified with TB between 2009 and 2011, 50% were residents of the Northern NSW or Mid North Coast LHDs.

The majority of cases of TB between 2009 and 2011 (85%) resided within the Sydney metropolitan area, giving an annualised incidence rate of 11.2 per 100 000 population

Table 2. Number and rate per 100 000 of notified tuberculosis cases by Local Health District, NSW, 2009–2011

	2009		2010		2011		Total	
	n	Rate	*n*	Rate	*n*	Rate	*n*	Rate
Regional and rural	**39**	**1.8**	**46**	**2.1**	**49**	**2.2**	**134**	**2.1**
Murrumbidgee	7	2.4	6	2.1	14	4.8	27	3.1
Far West	<3	3.1	0	0.0	<3	3.2	<3	2.1
Mid North Coast	3	1.4	9	4.3	5	2.3	17	2.7
Southern NSW	6	3.0	3	1.5	4	2.0	13	2.2
Hunter New England	15	1.7	15	1.7	17	1.9	47	1.8
Western NSW	0	0.0	4	1.5	5	1.9	9	1.1
Northern NSW	7	2.4	9	3.0	3	1.0	19	2.1
Outer metro	**25**	**2.4**	**32**	**3.1**	**30**	**2.9**	**87**	**2.8**
Illawarra Shoalhaven	12	3.1	13	3.4	14	3.6	39	3.4
Nepean Blue Mountains	10	2.9	14	4.1	12	3.5	36	3.5
Central Coast	3	1.0	5	1.6	4	1.3	12	1.3
Inner metro	**442**	**11.4**	**450**	**11.5**	**427**	**10.8**	**1319**	**11.2**
Western Sydney	127	15.6	111	13.5	127	15.3	365	14.8
Sydney	91	16.2	84	14.7	88	15.2	263	15.4
South Western Sydney	98	11.4	91	10.5	83	9.4	272	10.4
South Eastern Sydney	68	8.2	101	12.1	68	8.1	237	9.5
Northern Sydney	58	7.0	63	7.6	61	7.3	182	7.3
Other								
Justice Health	0	n/a	0	n/a	5	n/a	5	n/a
Overseas	<3	n/a	<3	n/a	<3	n/a	3	n/a

n/a: Population estimates not available
Small cell counts have been suppressed for privacy and confidentiality reasons.
Source: Notifiable Conditions Information Management System and Secure Analytics for Population Health Research and Intelligence, NSW Ministry of Health.

per year. The rate of infection in outer metropolitan, and regional and rural areas was 2.8 and 2.1 cases per 100 000 population respectively (Table 2). Within the Sydney metropolitan area, Sydney LHD and Western Sydney LHD had the highest overall rates and accounted for 41% of all TB notifications in NSW between 2009 and 2011. Of the regional and rural LHDs, Murrumbidgee had the highest rate (3.1 cases per 100 000 population per year).

Country of birth

The incidence rate of TB in overseas-born persons in 2010 was 23.2 per 100 000 population, compared to 1.3 cases per 100 000 population for Australian-born persons. Population estimates by country of birth were not available for 2011. Between 2009 and 2011, 89% ($n = 1371$) of cases were overseas-born. Of overseas-born cases, 45% ($n = 613$) were born in South-East Asia and 39% ($n = 534$) were born in the Western Pacific Region.

Site of infection

Between 2009 and 2011, pulmonary only disease (defined as site of infection including the lung but excluding the pleura) accounted for 50% ($n = 780$) of TB cases (Table 3). Extrapulmonary disease accounted for 40% ($n = 623$) and cases with both pulmonary and extrapulmonary disease accounted for 9% of cases ($n = 145$). Lymph nodes were the second most common site of infection after the lung and were recorded as a site of infection in 25% of all cases and 51% of cases with extrapulmonary involvement.

Case identification and laboratory confirmation

Of cases between 2009 and 2011, 76% were laboratory confirmed. Laboratory confirmation was made by isolation of *M. tuberculosis* by culture in 72% ($n = 1111$) of cases and by polymerase chain reaction alone in 4% ($n = 61$) of cases. In the remaining 24% of cases, diagnosis was made on clinical grounds with or without laboratory-

Table 3. Clinical and diagnostic characteristics of notified tuberculosis cases, NSW, 2009–2011

		2009		2010		2011		Total	
		n	%	*n*	%	*n*	%	*n*	%
Site of infection	Pulmonary only	223	44	284	54	273	53	780	50
	Pulmonary and other site	62	12	51	10	32	6	145	9
	Extrapulmonary only	222	44	194	37	207	40	623	40
	- Lymphatic	147	29	122	23	122	24	391	25
	- Pleural	32	6	39	7	44	9	115	7
	- Connective tissue	35	7	14	3	17	3	66	4
	- Kidney/genito-urinary	20	4	14	3	8	2	42	3
	- Miliary	11	2	7	1	5	1	23	1
	- Brain/central nervous system	14	3	16	3	6	1	36	2
	- Gastrointestinal	21	4	12	2	20	4	53	3
	- Other	38	7	37	7	37	7	112	7
Case classification	New active case	478	94	500	95	474	93	1452	94
	Previously treated in Australia	12	2	9	2	12	2	33	2
	Previously treated overseas	14	3	18	3	19	4	51	3
	Classification unknown	3	1	2	0	7	1	12	1
Laboratory confirmation	Laboratory confirmed (total)	390	77	399	75	383	75	1172	76
	- Culture positive	364	72	385	73	362	71	1111	72
	- PCR positive only	26	5	14	3	21	4	61	4
	Clinical diagnosis only	117	23	130	25	129	25	376	24
Pulmonary cases	Culture positive[a]	185	65	214	64	176	58	575	62
(% of pulmonary cases)	Culture negative[a]	94	33	105	31	113	37	312	34
	Culture not reported[a]	6	2	16	5	16	5	38	4
	Smear positive[a]	88	31	112	33	74	24	274	30
	Smear negative[a]	191	67	207	62	215	70	613	66
	Smear not reported[a]	6	2	16	5	16	5	38	4
HIV	Tested	317	63	375	71	359	70	1051	68
	Positive (% is of those tested for HIV)	8	3	9	2	11	3	28	3

PCR: polymerase chain reaction
[a]Includes only respiratory culture/smear results.
Source: Notifiable Conditions Information Management System and Secure Analytics for Population Health Research and Intelligence, NSW Ministry of Health.

suggestive evidence. Of pulmonary cases, 62% ($n = 575$) had *M. tuberculosis* isolated from a respiratory sample; 30% ($n = 274$) of pulmonary cases were direct sputum smear-positive.

Of cases where the nature of identification was reported ($n = 1529$), the majority (78%) were identified through investigation of symptomatic disease. This was followed by screening for TB (13%); that is, post-migration screening, then contact tracing (6%).

Case classification

Case classification remained stable over the 3-year period from 2009 to 2011, with new active cases making up 94% of all reported cases (Table 3). Previously treated cases made up the remainder, with 3% of cases having received partial or complete treatment overseas and 2% having received partial or complete treatment in Australia.

HIV co-infection

The proportion of cases that were tested for HIV has increased since 2009, with 68% of cases being tested overall for this period. Of those tested for HIV, 28 cases had HIV co-infection (3%) (Table 3). Of HIV co-infected cases, 74% were male and all were aged between 20 and 59 years. Five (18%) were Australian-born, while the remaining cases were born primarily in South and South-East Asian and African countries.

Clinical outcomes

Known clinical outcome was recorded for 1033 cases in 2009 and 2010 (Table 4). A total of 87% ($n = 904$) of cases were successfully treated, consisting of 84% ($n = 869$) who completed treatment and 3% ($n = 35$) who were considered cured (culture positive prior to treatment and culture negative after completion of treatment). There were five TB-related deaths reported, all in 2009. Twenty-three cases (2%) defaulted from treatment; the remainder were either transferred overseas, died of a non-TB related cause, or were continuing on treatment at the time of analysis.

Drug resistance

Between 2009 and 2011 there were 20 cases of MDR-TB reported (including one case with XDR-TB). All but two cases of MDR-TB were overseas-born, including seven born in the Western Pacific Region and eight born in South-East Asia. Of the two Australian-born MDR-TB cases, one had travelled to a high-risk country for more than 3 months, while the other had travelled to several high-risk countries on multiple occasions but never for more than 3 months.

The proportion of cases with mono-resistance to rifampicin has remained stable at 1–2% of cases. However, the proportion of cases with mono-resistance to isoniazid has decreased from 9.3% of cases in 2009 to 5.3% of cases in 2011. This trend was found to be statistically significant when tested using the Chi-square test for trend ($\chi^2 = 5.8, P = 0.02$). However, when a longer period is observed (2007–2011) there is no statistically significant trend.

Risk factors

The most commonly identified risk factor for TB in notified cases between 2009 and 2011 was being born in a high-risk country, with 80% of all cases reporting this risk factor. Past residence of more than 3 months in a high-risk country was reported by 47% of all cases. Other reported risk factors are presented in Table 5.

There was variation in the reported risk factors between Australian- and overseas-born cases. In Australian-born cases, the most frequently reported risk factor was past residence of more than 3 months in a high-risk country (28% of Australian-born cases), followed by having a household member or close contact with TB (25% of Australian-born cases). Of overseas-born cases, 90% were born in a high-risk country and 50% had resided in a high-risk country for more than 3 months. Amongst cases born in a high-risk country, the median length of stay in Australia prior to onset of disease was 4 years (Inter-quartile Range 2–12 years).

Contact tracing

A total of 7338 contacts of TB cases were identified between 2009 and 2011. Of these, 6027 (82%) received contact screening. Of contacts screened, 48 (1%) were determined to have active TB disease. A further 186 (3%)

Table 4. Outcomes of clinical management of notified tuberculosis cases, NSW, 2009–2010

	2009		2010	
	n	%	*n*	%
Treatment success[a]	440	87	464	88
- Completed treatment	424	84	445	84
- Cured[b]	16	3	19	4
Defaulted	15	3	8	2
Treatment failure[c]	0	0	0	0
Treatment interrupted[d]	0	0	0	0
Transferred overseas	24	5	29	5
Died of tuberculosis	5	1	0	0
Died of other or unknown cause	21	4	14	3
Still undergoing treatment	0	0	13	2
Outcome unknown	2	0	1	0
Total number of cases	507	100	529	100

[a]Defined as either completed treatment or cured.
[b]Bacteriologically confirmed cure of smear or culture positive pulmonary cases.
[c]Treatment completed but case not cured.
[d]Treatment interrupted for 2 months or more, but completed.
Source: Notifiable Conditions Information Management System and Secure Analytics for Population Health Research and Intelligence, NSW Ministry of Health.

Table 5. Risk factors for tuberculosis (TB) among notified cases, by country of birth, NSW, 2009–2011

	Australian-born		Overseas-born		All cases	
	n	%	*n*	%	*n*	%
Child (Australian-born) of parent(s) born in a high-risk country[a]	21	11.9	n/a	n/a	21	1.4
Born in a high-risk country[b]	n/a	n/a	1234	90.0	1234	79.7
Past residence (≥3 months) in a high-risk country	49	27.7	685	50.0	734	47.4
Household member or close contact with TB	45	25.4	161	11.7	206	13.3
Immunosuppressive therapy or condition	28	15.8	128	9.3	156	10.1
Currently or ever employed in the health care industry	12	6.8	102	7.4	114	7.4
Previously diagnosed with TB	12	6.8	73	5.3	85	5.5
Risk not able to be determined or not assessed	32	18.1	51	3.7	83	5.4
Chest X-ray suggestive of old untreated TB	2	1.1	12	0.9	14	0.9
Ever employed in a residential institution	0	0.0	7	0.5	7	0.5
Currently or ever residing in a homeless shelter	4	2.3	6	0.4	10	0.6
Currently or ever residing in a residential institution	2	1.1	6	0.4	8	0.5
Ever resided in a correctional facility	4	2.3	3	0.2	7	0.5
Other risk factor	19	10.7	57	4.2	76	4.9

n/a: not applicable
[a]Refers to children aged under 15 years who were born in Australia but whose parent or parents were born in a high-risk country.
[b]As determined by the clinician assessing the patient.
Source: Notifiable Conditions Information Management System and Secure Analytics for Population Health Research and Intelligence, NSW Ministry of Health.

Table 6. Outcomes of contact tracing of notified tuberculosis (TB) cases, in NSW, 2009–2011

	2009		2010		2011		Total	
	n	%	*n*	%	*n*	%	*n*	%
Contacts identified	2527		2427		2384		7338	
Contacts screened[a]	2083	82	1840	76	2104	88	6027	82
Contacts with active TB[b]	10	0	25	1	13	1	48	1
Contacts TST positive on initial screen[b]	652	31	704	38	631	30	1987	33
Contacts TST positive with risk factors for exposure/BCG[b]	565	27	750	41	596	28	1911	32
Contacts with TST conversion[b]	70	3	57	3	59	3	186	3
Contacts on preventive therapy[b]	127	6	186	10	99	5	412	7

BCG: Bacille Calmette-Guérin vaccine
TST: tuberculin skin test
[a]Percentage of all contacts identified.
[b]Percentage of all contacts screened.
Source: Notifiable Conditions Information Management System and Secure Analytics for Population Health Research and Intelligence, NSW Ministry of Health.

contacts screened had a tuberculin skin test (TST) conversion. On initial TST screening, 33% of contacts who received screening were TST positive. Of contacts screened, 412 (7%) received prophylactic treatment. Further breakdown of contact screening data by year is presented in Table 6.

Discussion

Between 2003 and 2011 there was a small but steady increase in the number of notifications of TB in NSW. This increase is consistent with recent national trends[8] and is an indicator of the need for continued TB control measures. As the majority of TB notifications in NSW are in persons who were born in or have lived in a country with a high incidence of TB, the epidemiology of TB notifications in NSW can be expected to broadly reflect global TB trends. The notification rate for TB continues to remain highest in the Sydney metropolitan area, particularly within Sydney's inner city and western suburbs. This has previously been suggested to be a reflection of migrant settlement patterns within NSW.[2] Between 2009 and 2011

there were 24 cases of TB reported in Aboriginal people in NSW; this is double the number of cases reported for the 3 years prior (2006–2008).[2]

Drug resistance is one of the most significant emerging issues in TB control globally.[1] In NSW the proportion of MDR-TB cases continues to remain low (1.3%). This is lower than the national proportion of cases with MDR-TB in 2008 (2.4%).[9] WHO estimates that 3.7% of new TB cases globally are MDR-TB.[1] Despite the low proportion of cases with MDR-TB in NSW, the number of MDR-TB cases notified appears to be increasing. Between 2009 and 2011 the average annual number of MDR-TB cases was 6.7 per year, an increase from 3.8 cases per year between 2003 and 2007.[4] Due to the small numbers of MDR-TB cases, it is difficult to be certain whether this is a true increase or natural variation.

The proportion of cases tested for HIV co-infection has increased from 54% of cases in 2008 to 70% of cases in 2011.[2] Despite this increase NSW remains behind the national level of 81% of cases tested for HIV in 2009.[8] Further work is needed to reach the national performance indicator of 100% of TB cases assessed for HIV. Despite increased testing, the proportion of cases with HIV co-infection remains low (3%). This is consistent with the proportion of HIV co-infected TB cases nationally.[8]

Conclusion

The effectiveness of TB control services in NSW is evidenced by low mortality from TB, the high proportion of cases successfully treated, minimal local transmission of TB and extensive screening of contacts. Incremental increases in the overall notification rate of TB in the last 8 years, an increase in the average annual number of MDR-TB cases and ongoing local transmission within sub-groups of the population highlight the need for continued vigilance in TB control.

Acknowledgments

The authors wish to acknowledge staff from the network of Chest Clinics and Public Health Units in NSW who collected the data. We also acknowledge Dr Vitali Sintchenko, Peter Jelfs and staff of the NSW Mycobacterium Reference Laboratory at the Institute for Clinical Pathology and Medical Research, Westmead Hospital.

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The use of mycobacterial interspersed repetitive unit typing and whole genome sequencing to inform tuberculosis prevention and control activities

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Abstract: Molecular strain typing of *Mycobacterium tuberculosis* has been possible for only about 20 years; it has significantly improved our understanding of the evolution and epidemiology of *Mycobacterium tuberculosis* and tuberculosis disease. Mycobacterial interspersed repetitive unit typing, based on 24 variable number tandem repeat unit loci, is highly discriminatory, relatively easy to perform and interpret and is currently the most widely used molecular typing system for tuberculosis surveillance. Nevertheless, clusters identified by mycobacterial interspersed repetitive unit typing sometimes cannot be confirmed or adequately defined by contact tracing and additional methods are needed. Recently, whole genome sequencing has been used to identify single nucleotide polymorphisms and other mutations, between genotypically indistinguishable isolates from the same cluster, to more accurately trace transmission pathways. Rapidly increasing speed and quality and reduced costs will soon make large scale whole genome sequencing feasible, combined with the use of sophisticated bioinformatics tools, for epidemiological surveillance of tuberculosis.

Unlike many other bacterial pathogens, different strains of *Mycobacterium tuberculosis* complex cannot be easily distinguished by the use of phenotypic methods. It was not until the 1990s, when *M. tuberculosis* complex molecular typing methods were developed, that it became possible to accurately identify tuberculosis (TB) transmission and study the origins and global distribution of *M. tuberculosis* complex genotypes. *M. tuberculosis* complex is a clonal species, in which horizontal transmission (recombination) of genetic material is rare. Genetic variation results from: (a) point mutations or single nucleotide polymorphisms (SNPs); (b) small DNA insertions or deletions, often mediated by mobile genetic elements, such as insertion sequences (IS); (c) larger DNA deletions, resulting in regions of difference (RDs) between strains, major enough to determine subspecies within the *M. tuberculosis* complex; and (d) variation in numbers of repeat sequences at various genomic loci. All of these are potential genotyping targets.

The appropriate choice of targets depends on the purpose of genotyping. For example, monitoring TB transmission requires targets that change rapidly enough to distinguish epidemiologically unrelated strains (such as IS or repeat sequences), but may not provide accurate information about lineage, whereas studies of long-term epidemiological trends and lineages require more stable targets reflecting rare genetic events (such as SNPs or RDs) that can trace the origins and global spread of different strains.

The rationale for molecular typing depends on the setting. In low-incidence settings it is often used, routinely, to identify case clusters (and, potentially, their sources) that are not apparent by conventional contact tracing. Routine typing can also identify laboratory contamination and false-positive culture results and, so, prevent unnecessary treatment. In high-prevalence settings, molecular typing is more likely to be performed, selectively, to investigate the evolution and transmission of *M. tuberculosis* to inform and improve TB control programs.

Strain typing methods

One of the first genotyping methods described was IS*6110* restriction fragment length polymorphism (RFLP) typing which, until recently, was the most discriminatory method available.[1] IS*6110* is found only in the *M. tuberculosis* complex, usually in multiple copies; the number of copies and the sizes of restriction fragments that contain them distinguish different strains, except those with few, or sometimes no, IS*6110* copies. The method involves cutting DNA with a restriction enzyme, identifying fragments

10.1071/NB12106

containing IS*6110* with a labelled molecular probe and separating them on a gel to produce a strain-specific banding pattern. Its disadvantages are that it requires prolonged incubation of isolates to produce a large enough quantity of DNA and the banding patterns can be difficult to interpret and reproduce. However, it has been used successfully, for many years, to provide insights into *M. tuberculosis* transmission, distinguish reactivation from reinfection, and identify laboratory cross-contamination.[2]

Spoligotyping detects the presence or absence of 43 non-repetitive spacer oligonucleotides, which are variably interspersed between short chromosomal repeats at the direct repeat locus of the *M. tuberculosis* genome.[3,4] The direct repeat locus is amplified by polymerase chain reaction (PCR) and the product is hybridized to a series of probes on a strip to identify the presence of spacer sequences. It requires relatively little DNA and can be used on early cultures or clinical specimens.[3] The results are objective and reproducible but it is less discriminatory than IS*6110*-RFLP and so less suitable for transmission studies. However, it differentiates *M. tuberculosis* strains into broad families that generally correspond with geographic areas[5] and, sometimes, with characteristics such as virulence, transmissibility and resistance.[6]

Recently, mycobacterial interspersed repetitive unit (MIRU) typing has largely overtaken both IS*6110* and spoligotyping, although they are sometimes used together. MIRUs are tandem repeat sequences, dispersed among intergenic regions of the *M. tuberculosis* genome, which vary between *M. tuberculosis* strains according to the number of repeats at each locus. They are one of a group of variable number tandem repeat (VNTR) sequences, which are the basis of multilocus VNTR analysis (MLVA), a common bacterial genotyping method.

M. tuberculosis MIRU-VNTR typing, originally based on 12 loci,[7] is rapid, objective and reproducible. It was rapidly adopted as the basis for large-scale, high-throughput *M. tuberculosis* genotyping[8–10] but, even in combination with spoligotyping, was less discriminatory than IS*6110* fingerprinting, especially for isolates of the widespread Beijing spoligotypes.[11] Because of the potential for false clusters, identified by MIRU-12 and spoligotyping, IS*6110*-RFLP typing of clustered isolates was often needed to more accurately define outbreaks,[12] especially if there were no obvious epidemiological links between cases.

Subsequently, a more discriminatory set of 24-MIRU-VNTR loci, including the original 12, was identified. MIRU-24 typing of more than 800 geographically diverse isolates, representing all major lineages, identified 40% more genotypes and demonstrated a fourfold lower rate of clustering than MIRU-12 typing.[13] Even a smaller subset of 15 loci, with the highest evolutionary rates, was as discriminatory as IS*6110*-RFLP typing. Thus, MIRU-15 typing was proposed as a new standard for routine use and MIRU-24 as a high-resolution alternative for phylogenetic studies.[11,13] Others have confirmed the higher discriminatory power of MIRU-24, compared with MIRU-12.[14]

MIRU-24 typing

MIRU-24 (or -15) is now the new 'gold standard' for routine *M. tuberculosis* typing. To facilitate global epidemiological studies, a web-based database (http://www.miru-vntrplus.org/) has been established, based on a collection of 186 reference strains, representing the primary *M. tuberculosis* complex lineages.[15,16] The database includes geographic origin, drug susceptibility profile and comprehensive genetic lineage information, including the MIRU-24, SNP and RD profiles, spoligotype and IS*6110*-RFLP fingerprint of each strain. MIRU-24 analysis reliably predicted the correct lineage of greater than 99% of nearly 700 external strains.[15,16] The database allows users to compare strains with the reference set, search for similar strains and map geographic information. An expanding genotype nomenclature (MLVA MtbC15-9 type) has been implemented to facilitate comparison between laboratories.[16]

MIRU typing can be performed either by separate PCRs for each locus and measurement of amplicon sizes by gel electrophoresis or by several multiplex PCRs, using fluorescently labeled primers, and determination of amplicon sizes by capillary electrophoresis in a DNA analyser. The number of tandem repeats (of known length) at each locus is calculated from the amplicon size and results are expressed as a numerical code corresponding to the numbers of repeats at each locus, which is the strain 'fingerprint'.

In a recent international proficiency study[17] of MIRU-24 typing, a panel of 30 DNA extracts, from 20 well-characterised *M. tuberculosis* strains, was tested in 37 laboratories. There was wide variation in reproducibility of results between laboratories (average 60%); it was better (88%) when commercial kits were used than when in-house-adapted methods using capillary (70%) or gel (50%) electrophoresis were used. However, many in-house-adapted methods achieved greater than 80% reproducibility, suggesting that, with care, they can be used reliably.[17] The study demonstrated potential pitfalls of comparing genotypes between laboratories and the importance of quality assurance programs.

The New South Wales (NSW) Mycobacterium Reference Laboratory has used IS*6110*-RFLP and spoligotyping since 2004, MIRU-12 since 2005 and MIRU-24 since 2010, to confirm suspected transmission between epidemiologically-related TB cases,[18] investigate outbreaks,[12] differentiate TB reactivation from reinfection,[19] identify otherwise unsuspected case clusters or laboratory contamination and estimate rates of recent transmission.[10] The most common spoligotypes in NSW belong to the

Table 1. Comparison of *Mycobacterium tuberculosis* clustering rates in recent studies of tuberculosis transmission

Locations (references)	Canada[14]	Switzerland[22]	China[21]	NSW, Australia[10]	(unpubl.)
Dates (years)	2003–08 (5)	2000–08 (9)	2007–10 (3.5)	2004–06 (3)	2009–11 (3)
Typing method	MIRU-12	MIRU-24	MIRU-24	MIRU-12	MIRU-24
Number of isolates	650	520	267	855	633
Clustering	75%	17.3%	42%	33.7%	24.8%
Average cluster size	10.0	2.6	3.0	6.5	2.6
RRT	0.71	0.11	Not reported	0.25	0.16
Beijing lineage	2%	12%	89%	24%	25%
EAI lineage	5%	10%	Not reported	12%	15%

EAI: East African Indian
MIRU: mycobacterial interspersed repetitive unit
RRT: rate of recent transmission; defined as the number of identical (clustered) isolates minus the number of clusters (accepting a single source case for each cluster), divided by the total number of isolates.

Beijing family (more than one-quarter of all isolates examined), which was first described in China and neighbouring countries in 1995, and has since been reported in many parts of the world, especially Asia and the former Soviet states. We have tracked an expanding cluster of cases, due to a strain with a unique MIRU-24 profile, among Aboriginal communities in the NSW North Coast region, which has involved at least 30 cases since 2000 (unpublished data; see also Devlin and Passmore[20]). Table 1 compares our MIRU-typing results with those of several studies showing rates of recent transmission (RRT) using this method.[14,21,22] It is worth noting that a low RRT reflects the degree of success of the local TB control program.

Despite the improved discriminatory power of MIRU-24 typing, apparent clusters cannot always be confirmed, even by the most detailed contact tracing, suggesting some false clustering, especially in settings with high rates of transmission of closely related *M. tuberculosis* strains. In China, a high proportion of cases are caused by the so-called 'modern' Beijing lineage. Isolates belonging to this lineage have only one or two IS*6110* copies and, generally, similar MIRU-24 patterns. False clustering of MIRU patterns occurs due to homoplasy or convergent evolution (independent mutations resulting in the same genotypes among isolates with different ancestry). This can mean, for example, that reinfection with a similar strain could be misinterpreted as reactivation of infection due to treatment failure. In future, problems like this could be resolved by whole genome sequencing, or inclusion of additional targets in typing methods. For example, SNPs have been identified, which can reliably differentiate these otherwise homogeneous 'modern' Beijing strains, with the same or very similar, MIRU-24 types, into several lineages. In a recent study, the combination of MIRU-15 typing plus PCR amplification and sequence typing of three hypervariable regions and eight SNPs overcame false clustering; it was therefore proposed for second-line typing of clustered isolates in settings of high prevalence of Beijing strains.[21]

Whole genome sequencing

The ultimate strain typing system is whole genome sequencing which, until recently, seemed fanciful because of the cost, time taken and requirement for sophisticated bioinformatics tools for sequence analysis. However, recent advances in sequencing technology have dramatically reduced the cost and turnaround time and improved the quality of sequence data and several recent investigations have demonstrated its potential.

Whole genome sequencing was used in the Netherlands to investigate a well-characterised *M. tuberculosis* transmission chain (confirmed by genotyping and contact tracing) involving five patients aged over 12 years, for which no source had been identified.[23] Four SNPs, a tandem-repeat polymorphism and an IS*6110* transposition were identified between the first and last isolates of this cluster. The remaining isolates were screened for these six polymorphisms and five were found in isolates from one patient, an alcoholic who had been non-compliant with treatment. It was hypothesised that molecular evolution of *M. tuberculosis in vivo* may be driven by environmental factors such as intermittent antibiotic use leading to successive bursts of multiplication, or by genomic stress due to alcohol abuse. Identifying factors that stimulate mutational bursts could have major implications for TB management.[23] In a Canadian study,[24] whole genome sequencing of 32 isolates from a large 3-year community outbreak and four unrelated historical isolates, all with identical MIRU-24 and IS*6110*-RFLP types, was combined with social network analysis based on patient interviews, to determine the origin and transmission dynamics of the outbreak. Analysis of more than 200 SNPs revealed two genetically distinct lineages, both represented among historical isolates, indicating that they had separated before the outbreak started.

Additional, targeted social network and epidemiological analyses identified three co-primary case-patients who had been symptomatic for prolonged periods before diagnosis. The outbreak coincided with an increase in crack cocaine use in the community.[24] Whole genome sequencing implicated socio-environmental factors, not identified by conventional genotyping and contact tracing, in triggering simultaneous expansion of two pre-existing *M. tuberculosis* lineages that were subsequently sustained within a high-risk social network.

The exponential fall in cost and increased speed and quality of whole genome sequencing will continue.[25] Only the availability of appropriate tools to analyse and interpret the results will limit its use. It has the potential to rapidly track *M. tuberculosis* transmission and microevolution and identify virulent and antibiotic resistant strains. When combined with appropriate clinical data this will improve our understanding of disease risks and how to prevent it; allow more timely and individually targeted therapy; and identify new vaccine, antibiotic and diagnostic targets.

Conclusion

In the relatively short period since molecular strain typing of *M. tuberculosis* has been available and widely used, it has considerably increased our understanding of the evolution and modes of transmission of this ubiquitous and important pathogen. It has demonstrated that transmission can occur as a result of apparently casual, transient contact by leading to more detailed investigation of possible common sources of exposure of apparently unrelated individuals who share the same infecting strain. It has allowed comparison of rates of clustering between different population groups and communities, which reflects and can lead to improvement in the efficacy of TB control programs. Finally, it has provided new insights into the evolution of *M. tuberculosis* over long periods of time and widely distant geographic regions and also during the course of a single case cluster. As methods have improved from the highly discriminatory but slow and technically demanding IS*6110* RFLP to the simpler, but equally discriminatory MIRU-24, genotyping has become more accessible, which means that our understanding of *M. tuberculosis* evolution and epidemiology has correspondingly increased. Whole genome sequencing promises to provide further insights and even more discriminatory and informative strain typing.

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Diagnosis, treatment and prevention of tuberculosis in children

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Abstract: In Australia, tuberculosis notification rates have plateaued at a low level and disease is highly concentrated in immigrant communities where children may be affected. Many clinicians regard tuberculosis as an adult disease, hence it is rarely considered in the differential diagnosis of sick children. This paper provides a brief overview of the natural history of the disease in children to demonstrate the importance of taking a careful tuberculosis exposure history. It also provides guidance regarding the diagnosis, treatment and prevention of tuberculosis in children. The management of paediatric cases is not difficult if important differences with adult disease are carefully considered; these differences are discussed in detail.

Tuberculosis (TB) remains a major, but often unrecognised, cause of disease and death among women and children in TB endemic areas.[1] Cases are highly concentrated in areas affected by poverty, social disruption, human immunodeficiency virus (HIV) infection and drug-resistant TB,[2,3] with increased international travel and immigration posing major challenges to the control of TB. In Australia, TB incidence rates are among the lowest in the world at 5–6 per 100 000 population per year.[4] However, rates are highly variable and up to 10 times higher in certain sub-groups of the population. More than 85% of cases occur in immigrant populations and represent imported infection, with the top five countries of origin being India, Viet Nam, the Philippines, China and Indonesia, where high rates of drug-resistant TB have been recorded.[2,4] Evidence of local transmission is limited and restricted to particular disease clusters.[5] New South Wales (NSW) reports the highest absolute number of TB cases within Australia.[4,6] In 2008, children aged under 15 years constituted less than 5% of the disease burden (18/498),[6] similar to other developed countries with minimal internal transmission and routine provision of post-exposure prophylaxis to young and vulnerable children.[7,8] Despite low numbers of children with TB, Australian clinicians need to consider TB as part of the differential diagnosis, as cases are observed at regular intervals.[9–13] This brief overview focuses on recent advances in diagnosis and on issues related to the clinical care of children with TB.

Natural history of disease

The pre-chemotherapy literature provides detailed natural history of disease descriptions which guide risk assessment and management.[14,15] An observation is that most children (>90%) who progress to TB disease do so within the first 12 months after primary infection; this is referred to as the 'window of risk'. Another observation is the pronounced bi-modal risk profile: very young children (aged less than 2 years) experience the greatest risk; a nadir occurs at around 5–10 years of age and then an increase is seen with the onset of puberty. This coincides with a radical shift in the disease spectrum. In young children, lymph node disease with or without airway compression predominates, due to exuberant lymph node responses and small pliable airways. Disseminated disease is also more common due to immature T-cell responses and poor disease containment. The sudden switch to adult-type TB that occurs around puberty, first in girls and then in boys, remains an enigma, but may shed light on key variables underlying individual vulnerability.[16] It is important to remember that adolescent children with adult-type disease are highly infectious.[17] Table 1 summarises some important differences between TB in adults and children.

Diagnosis

Children are usually evaluated for TB as a result of immigrant screening, contact investigation or following presentation with symptoms or signs suggestive of TB disease. It is important to distinguish these different entry points since they influence the diagnostic work-up and interpretation of results (Figure 1). *Mycobacterium tuberculosis* infection detected during immigrant screening probably reflects remote past infection with reduced risk of disease progression, unless it is a young child or immunocompromised individual. *M. tuberculosis* infection detected during contact investigation is likely to be recent, implying a higher risk of disease progression, although this remains highly age-dependent. In this population, isolated radiographic findings in asymptomatic

Table 1. Tuberculosis (TB): differences between adults and children

Aspect	Adults[a]	Children[a]
Epidemiology/ awareness	Massive global disease burden that is well quantified; excellent awareness	Massive global disease burden that is poorly quantified; minimal awareness
Health policy	Main focus of national TB control programs (NTPs)	Rarely recognised as a priority by NTPs
Pathogenesis of lung lesions	Usually adult-type lung disease (previously referred to as post-primary TB)	Usually intra-thoracic lymph node disease (previously referred to as primary TB)
Bacterial load/ transmission/ infection control	Multibacillary	Paucibacillary
	High infection risk after close contact	Low infection risk, but may be infectious if extensive lung involvement with/without cavities; epidemiologic marker of transmission
Drug resistance	Difficult to differentiate acquired from transmitted (primary) drug resistance	Nearly always transmitted (primary) drug resistance indicating recent transmission
Exposure history	Important, but often neglected[b]	Essential
Risk of progression to disease	Relatively low risk of progression to disease following TB exposure/ infection	Highly variable risk of progression to disease following TB exposure/infection – greatest in the very young and/or immunocompromised
Preventive therapy	Limited value, except in immunocompromised adults	Definite value in young (aged <5 years) and/or immunocompromised children
Imaging studies	Chest X-rays (CXRs) not routinely required, unless sputum negative	CXRs (with both frontal and lateral views, of good quality, and competently read) are the most informative study
Disease classification	Pulmonary vs extrapulmonary distinction	Intra-thoracic lymph node disease best classified as pulmonary TB
	Post-primary TB is a confusing concept[c]	Diverse spectrum of pathology that requires accurate classification
Microbiological studies	Easy to collect adequate respiratory specimen and confirm presence of mycobacteria	Difficult to collect adequate respiratory specimens (young children cannot expectorate); smear microscopy has very low yield; cultures and nucleic acid amplication tests have low-to-moderate yield depending on disease severity
Treatment	With at least four drugs	With three or four drugs depending on likely organism load and severity of disease
Prognosis	Excellent outcomes achievable with timely and appropriate treatment	Excellent outcomes achievable with timely and appropriate treatment; potentially grave outcome with delayed diagnosis

Adjusted by the authors from their previous work.[14]
[a]Typical characteristics in the absence of HIV-infection and/or severely compromised immunity.
[b]Taking a careful contact history is often neglected for adults, but has particular relevance for the identification of drug-resistant TB suspects.
[c]The old distinction between primary and post-primary TB obscures the fact that adult-type (post-primary; secondary) TB frequently results from recent re-infection and may also occur within months of documented primary infection (particularly in adolescents).

children are problematic, since transient elements of the Ghon/primary complex are frequently visualised and not necessarily indicative of active disease. Observational studies and current World Health Organization guidance suggest that symptom-based screening is adequate, at least in older children, and the complete absence of current symptoms is sufficient to rule out TB disease in this group.[18,19] Table 2 provides an overview of investigations to establish a diagnosis of TB in children.

Clinical evaluation

Children rarely present with near pathognomonic signs of TB such as a TB gibbus; most clinical manifestations are non-specific. In fact, one of the remarkable features of intra-thoracic TB is the frequent absence of physical signs despite the presence of persistent non-remitting symptoms. Furthermore, despite minimal clinical findings, the clinician may be surprised by the radiographic extent of disease. The pathophysiological explanation for this discrepancy is not clear but may reflect the fact that TB often causes a vasculitis (as observed with TB meningitis) in addition to parenchymal involvement. This implies that both oxygen exchange and blood supply are reduced in affected parts of the lung, limiting the resultant ventilation:perfusion mismatch which may explain the frequent absence of acute respiratory distress despite extensive lung involvement.

A detailed history should explore the likelihood of recent (during the past 12 months) TB exposure and allow accurate symptom characterisation. This is important

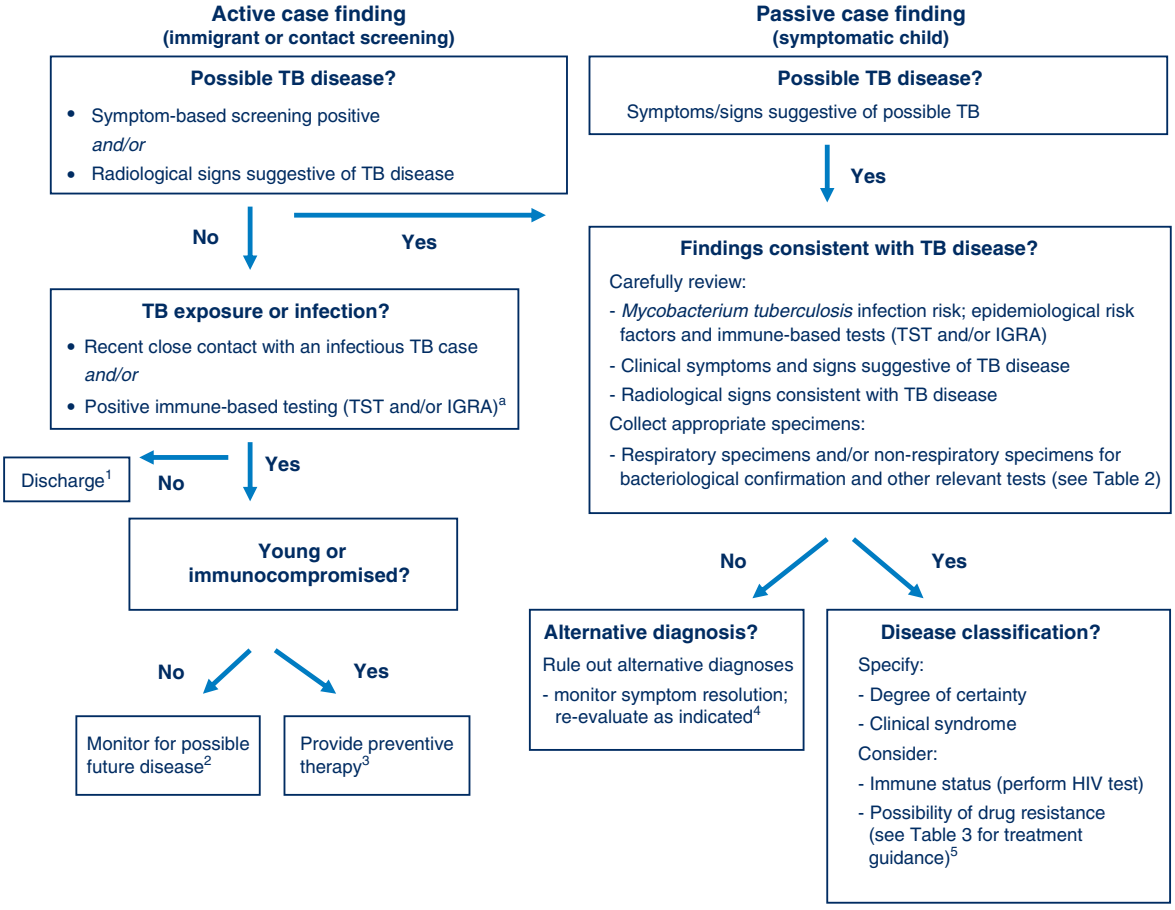

Figure 1. Algorithm for diagnosis and classification of tuberculosis (TB) in children.
Adjusted by the authors from their previous work.[14]

HIV: human immunodeficiency virus; TST: tuberculin skin test; IGRA: interferon-gamma release assay.
[a]Neither of the immune-based tests (TST/IGRA) can 'rule out' TB disease with confidence and conversion may be delayed for 2–3 months after documented exposure. All children aged <5 years and any child with current symptoms should receive a chest X-ray.
Diagnostic labels
[1]No TB exposure or infection.
[2]TB exposure/infection with low risk of progression to disease.
[3]TB exposure/infection with high risk of progression to disease.
[4]Not TB disease.
[5]TB disease.

because poorly-defined symptoms have poor discriminatory power.[20] Common constitutional symptoms include decreased appetite (recent crossing of weight centiles is most informative), fatigue or reduced playfulness, and fever. Despite TB being an infectious disease, fever is often absent, low-grade or intermittent. With lung involvement, children usually present with a persistent non-remitting cough that is unresponsive to standard first-line treatment. Airway compression may manifest as loud (large airway) wheezing that does not respond to bronchodilators. Clinical follow-up is a useful diagnostic tool in children with mild disease manifestations for whom the diagnosis cannot be made with certainty.[20]

Imaging studies

Chest radiography is generally the most informative investigation and should include both frontal and lateral views. Lateral views are important as they improve assessment of the mediastinum and hilar areas. Childhood intra-thoracic TB has a wide range of appearances associated with different disease entities, which justifies careful classification.[21,22] Visible hilar adenopathy with or without airway compression is highly suggestive of TB disease. High-resolution chest computed tomography (CT) provides the most accurate visualisation of intra-thoracic structures,[23] but due to the high cost and associated radiation exposure its use should be limited to complicated cases. CT and/or magnetic resonance imaging (MRI) is the best way to visualise extrapulmonary lesions, especially intra-cranial pathology. MRI is more sensitive for detecting brainstem lesions or early perfusion defects (infarcts) and also provides better evaluation of the spine and soft tissues.[24]

Laboratory studies

Immune-based tests are severely limited by their inability to differentiate *M. tuberculosis* infection from active disease,

Table 2. Summary of investigations to diagnose tuberculosis (TB) in children

Investigation	Uses	Strengths (S) and limitations (L)
Microbiological studies (detection of *Mycobacterium tuberculosis*)		
Microscopy	Diagnosis of TB	**S:** Specificity high; useful in all specimen types; rapid (<1 hour) detection; low cost (fluorescence microscopy most cost effective). **L:** Sensitivity very low, especially in young children; highly operator-dependent; labour intensive; unable to speciate or distinguish viable and dead bacilli.
Growth on special media	– Diagnosis of TB – Species identification	**S:** Specificity high. **L:** Sensitivity low in young children; slow turnaround time.
DNA detection	Drug susceptibility testing	**S:** Specificity high; fully automated platforms; rapid turnaround. **L:** Sensitivity low in young children; cannot distinguish viable from dead bacilli; quality control essential.
Histopathological studies		
Stained tissue samples	Diagnosis of TB	**S:** Allows exclusion of other diagnoses (such as malignancy).
Immune-based studies		
TST IGRAs	Identification of *M. tuberculosis* infection	**L:** Neither test can differentiate *M. tuberculosis* infection from active disease. **L:** TST: affected by BCG vaccination; requires a second visit after 48–72 hours. **S:** IGRAs: unaffected by BCG vaccination; requires a single visit. **L:** Low sensitivity in very young and/or immunocompromised children; indeterminate results problematic.
Imaging		
Radiography CT and MRI Ultrasonography	Diagnosis of TB	Chest radiography (frontal and lateral views) most helpful; CT or MRI useful in uncertain or complicated cases; ultrasonography useful to identify intra-abdominal/retro-peritoneal lymphadenopathy or pleural/pericardial effusions. **L:** Ultrasonography highly operator-dependent.

BCG: Bacille Calmette-Guérin; CT: computed tomography; IGRAs: interferon-gamma release assays; MRI: magnetic resonance imaging; TST: tuberculin skin test.

and neither the purified protein derivative tuberculin skin test (TST) or interferon-gamma release assays (IGRAs) (e.g. QuantiFERON-Gold In Tube®) offer a simple solution.[25] IGRAs do not replace TSTs for the detection of *M. tuberculosis* infection in children and, like TSTs, cannot be used to exclude TB. In certain clinical situations IGRAs may be used in addition to TSTs to improve sensitivity and specificity in the detection of TB infection.[25]

Smear microscopy has poor sensitivity in young children, most of whom are paucibacillary and unable to expectorate; it has been largely superseded by culture and nucleic acid amplification tests (NAATs). In general, culture yields in children are lower than in adults, depending on the severity of disease as well as the quality, quantity and types of specimens collected. Two studies have evaluated the performance of the rapid NAAT-based Xpert® MTB/RIF assay in children, demonstrating similar performance characteristics to adult studies, with excellent specificity and detection of around 70% of culture-positive cases.[26,27]

Collecting adequate respiratory specimens in young children is problematic, but gastric aspirates, induced sputum (with or without laryngopharyngeal suction) and bronchoalveolar lavage (in select patients) offer feasible alternatives. A combination of specimens provides the best yield.[28] Fine-needle aspiration biopsy has excellent utility in children with a peripheral lymph node mass.[29] With tuberculous meningitis, slow clinical onset, cerebrospinal fluid pleocytosis (with total cell count <500) and elevated protein is highly suggestive.[30] Despite the challenges discussed, bacteriological confirmation should always be attempted, although it should not delay treatment initiation in young and vulnerable children. TB can be diagnosed with relative certainty based on a combination of clinical, radiological, laboratory and histopathological (when feasible) findings consistent with TB disease, in association with epidemiological factors and/or immunological evidence of *M. tuberculosis* infection.

Treatment

If a diagnosis of TB disease is established, pragmatic disease classification guides management and facilitates case comparison. From a treatment perspective, likely bacillary load, anatomical location and the possibility of drug resistance are the most important variables to consider. If high bacillary loads are anticipated, the use of multiple drugs during the intensive phase of treatment reduces the risk of acquired drug resistance. Consideration

Table 3. Summary of first-line tuberculosis (TB) drugs and dosage recommendations for children

First-line drugs	Mode and mechanism of action	Main adverse effects[a]	Daily dose mg/kg (range)[b] [maximum dose][c]
Isoniazid	Bactericidal • Inhibits cell wall synthesis • Most potent early bactericidal activity offering the best protection to companion drugs • Contributes mainly by rapidly killing actively metabolising extracellular bacilli; contributes to sterilisation if given for a prolonged period	Hepatitis; peripheral neuropathy	10 (7–15)[d] [300 mg]
Rifampicin	Bactericidal and sterilising • Inhibits ribonucleic acid synthesis • Contributes by killing extracellular and slower growing intracellular bacilli; important contribution to sterilisation	Hepatitis; orange discolouration of secretions; drug-drug interactions	15 (10–20) [600 mg]
Pyrazinamide	Sterilising • Disrupts energy metabolism • Contributes by specifically killing bacilli that persist within the acidic centres of caseating granulomas	Hepatitis; arthralgia	35 (30–40) [2000 mg]
Ethambutol	Bacteriostatic • Inhibits cell wall synthesis • Contributes mainly by offering some additional protection against drug-resistant mutants	Visual disturbance (acuity, colour vision)	20 (15–25) [1200 mg]

Suggested treatment regimens

Disease category	Treatment regimen	Rationale
Uncomplicated intra-thoracic disease	Isoniazid, rifampicin and pyrazinamide (2-month intensive phase) Isoniazid and rifampicin (4/12 continuation phase)	Organism load low, drug penetration good
Extensive lung infiltrates and/or cavities	Add ethambutol during 2-month intensive phase	Organism load high, drug penetration good
Tuberculous meningitis	Add fourth drug, at least during 2-month intensive phase Add steroids for 1 month[e]	Organism load low, drug penetration variable, risk of severe immune-mediated sequelae
Severe airway compression	Three or four drug regimen depending on extent of lung infiltration/cavities Consider adding steroids for 1 month	Organism and drug penetration variable,[f] inflammation may worsen airway compression
Recent exposure/infection No active disease	Preventive therapy Isoniazid (6–9 months) Isoniazid, rifampicin (3 months)	Organism load very low, drug penetration good

Adjusted by the authors from their previous work.[14]
[a]Hypersensitivity reactions and drug rashes may occur with any drug.
[b]Most recent World Health Organization dosage recommendations for children,[37] except where indicated.
[c]Maximum doses from Australian Therapeutic Guidelines.[38]
[d]Range from additional reference.[39]
[e]Recommendations around fourth drug and duration of therapy vary; WHO advise isoniazid, rifampicin, pyrazinamide and ethambutol for 2 months followed by 10 months isoniazid and rifampicin.
[f]Drug penetration into large cold abcesses may be limited, requiring surgical drainage.

should also be given to the possible involvement of 'sanctuary sites' such as the brain and cerebrospinal fluid (CSF), since drugs have highly variable CSF penetration.[31] High and/or rising rates of drug-resistant TB, documented in many countries within the Asia-Pacific region, Eastern Europe and sub-Saharan Africa,[2] make it necessary for clinicians to carefully scrutinise patients who resided in, or travelled through, these countries. The possibility of

drug-resistant TB should be suspected following close contact with a drug-resistant source case; in residents of countries known to have a high prevalence of drug-resistant TB; or following contact with someone who died on TB treatment, is poorly adherent to therapy, or required more than one treatment course.

TB treatment aims to ensure long-term cure without serious adverse effects for the patient. From a public health perspective it is important to terminate transmission and prevent the emergence of drug resistance. Table 3 summarises the mode of action, main adverse effects and recommended dosages of first-line TB drugs, including dosage recommendations for children; sub-optimal drug levels result from using weight-adjusted adult doses.

In the absence of drug resistance, the most likely cause of poor treatment response is non-adherence. If a child presents with a TB recurrence more than 6–12 months after treatment completion and clinical cure, it most likely represents re-infection. Standard first-line treatment would be appropriate (in the absence of risk factors for drug-resistant disease); there is no indication to use an escalated re-treatment regimen. With poor response to adherent therapy, careful re-evaluation of the original diagnosis and assessment for drug resistance is warranted. In NSW, all positive cultures undergo drug susceptibility testing, which provides additional motivation to achieve bacteriological confirmation. With drug-resistant TB, the basic principles of management are unchanged and excellent outcomes can be achieved.[32] All children diagnosed with TB should be tested for HIV infection; management of co-infected children has been recently reviewed.[33]

Prevention

Prevention strategies include vaccination, pre- and post-exposure prophylaxis, treatment of 'latent' infection, and secondary prophylaxis (provided after completion of TB treatment). Bacille Calmette-Guérin (BCG) vaccination reduces the risk of disseminated (miliary) disease and tuberculous meningitis in very young children but protection is incomplete and it offers no consistent protection against adult-type TB.[34] It is not included in routine vaccination schedules in Australia, however, it should be considered when vulnerable children (e.g. aged less than 2 years) are exposed to a high-risk environment, such as visiting a TB endemic country. Research to develop novel vaccines with improved efficacy and safety is ongoing.

Careful risk stratification identifies those at greatest need of preventive therapy following TB exposure. The target population for preventive therapy provision may vary in different settings depending on feasibility and available resources, but all young (aged less than 5 years) and/or immunocompromised children should receive preventive therapy following documented exposure/infection.[19] With good adherence and in the absence of drug resistance, isoniazid monotherapy provides excellent protection following documented exposure/infection. However, parents are often reluctant to provide 'treatment' to an otherwise well child and ensuring good adherence is challenging. Treatment with isoniazid and rifampicin for 3 months has demonstrated equivalent efficacy and improved adherence compared to 9 months of treatment with isoniazid alone, with no increase in adverse events.[35] Twelve doses of weekly rifapentine and isoniazid proved efficacious in a recent adult study,[36] but this regimen cannot yet be recommended in children aged less than 12 years until more safety and efficacy data are available. In HIV-infected children on antiretroviral therapy, drug-drug interactions should be considered with all rifamycin-containing regimens.[33]

Conclusion

Children suffer a huge but under-recognised TB disease burden in endemic countries from which Australia continues to receive immigrants. Multiple challenges remain: to develop more effective vaccines, better diagnostics and shorter treatment regimens. However, it is worth emphasising that most children would be served well by the sensible application of existing tools.

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Tuberculosis: an old world disease providing new world challenges in NSW

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Tuberculosis (TB) is a complex, difficult disease from both public health and clinical perspectives. Problems are the norm, rather than the exception.The NSW TB Control Program consists of a network of highly experienced physicians, nurses, laboratory and public health personnel, working closely to manage this ongoing threat to public health. The following four case studies present issues encountered in managing TB in New South Wales (NSW).

In the first example, Michail draws our attention to the challenges of adverse drug reactions in the management of TB. Early detection, which requires vigilance and judicious monitoring, is critical for reducing the risk of harm. The serious nature of TB, the limited range of effective drugs available and the difficulty in identifying a single causative drug from a multi-drug regimen means that permanent drug cessation or replacement is not a simple option in most cases. Careful consideration is required in deciding if, when and how to re-introduce drugs after suspected adverse drug reactions. While published guidelines offer some assistance, there is enormous variation in the clinical circumstances surrounding each case. Hence, clinical experience and judgment is required. Sometimes the combined experience of several clinicians, gathered by informal consultation or by way of clinical case conferences, is needed to reach decisions on more complex cases. Michail's article highlights the importance of specialised clinical management of TB to optimise patient safety.

Experience, expertise and judgment are all relevant to public health, as well as the clinical management of TB, as highlighted in the two examples by Banner and Fisher et al. In the public arena, TB remains an emotive and poorly understood disease. Fear, anxiety, distrust and suspicion are easily aroused when people are informed they may have had contact with people with TB. On the other hand, failure to detect and treat latent TB infection (LTBI) in contacts of people with TB may result in avoidable cases of TB occuring in those contacts; this may have disastrous consequences if those contacts are young children or infants. Good management is complex and requires balancing the public's right to know with the patient's right to privacy, and the need to protect those at risk with the need to avoid spreading alarm by unnecessary screening. We have imperfect tools for estimating risk in this context and much of the difficulty in managing TB contact investigations arises from the need to make decisions in the presence of substantial uncertainty. For example, the lack of specificity of tests for LTBI means that testing patients at very low risk for LTBI, either by tuberculin skin test or by interferon-gamma release assay, will identify many false positive cases, causing false alarm and, possibly, the initiation of an unnecessary course of treatment. This highlights the importance of carefully selecting those to be screened for LTBI. The episodes reported here draw attention to the importance of pooling our statewide experience in managing complex public health problems in TB care and applying a considered and protocol-driven approach to management.

Vogelnest's report on TB in animals reminds us that, no matter how much we think we know collectively, we should always expect the unexpected in managing TB. While human TB mainly affects humans, other animals can be infected (usually by humans) and can be a source of infection for other animals and humans. Fortunately no cases of active TB in humans have arisen from the recent cases at an Australian zoo.[1]

The outcomes of the NSW TB Control Program have been good for many years. The incidence of the disease is low, deaths are uncommon,[2] local transmission is limited[3] and relapse after treatment is very rare.[4] Despite these positive outcomes the following case studies demonstrate that there is no room for complacency. The complex and unpredictable nature of TB means that we must retain vigilance, programmatic management, and our collective clinical and public health expertise, to ensure that the gains of the last 20 years are consolidated and that further progress is made.

10.1071/NB13007

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Monitoring for adverse events among patients on tuberculosis therapy

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Tuberculosis (TB) continues to be a significant public health problem in New South Wales (NSW) with 512 case notifications in 2011.[1] The NSW Health Policy Directive on the management of people with TB in NSW states:

> *The aim of the NSW Department of Health TB Program is to minimise the burden of TB and to prevent the transmission of TB through early detection and appropriate treatment of people with TB. Patients with suspected TB should be referred for management in an Area Health Service (AHS) TB Prevention and Control Service – Chest Clinic.*[2]

In Australia, patients with diagnosed or clinically suspected TB are treated under the guidance of a specialist with training in TB management. Standard therapy for TB follows international and Australian guidelines and traditionally involves an intensive phase of drug therapy followed by a continuation phase. The majority of treatment – with only rare exceptions – is administered by directly observed therapy (DOT) to aid with compliance and completion of therapy.[2–4] The overall goals of treatment are to cure the patient and to minimise the risk of transmission to others.

Side effects and adverse reactions to anti-TB therapy are not uncommon and can be serious and even life-threatening when they do occur. While various definitions of adverse drug reactions (ADRs) exist a comprehensive definition is:

> *An appreciably harmful or unpleasant reaction, resulting from an intervention related to the use of a medicinal product, which predicts hazard from future administration and warrants prevention or specific treatment, or alteration of the dosage regimen, or withdrawal of the product.*[5]

Most medications used in standard anti-TB regimens were developed decades ago, and standard treatment regimens carry a risk of up to 30% for significant ADRs developing in the intensive phase of treatment.[6] Other studies have reported fewer incidences.[7–9] A significant ADR is one that necessitates interruption of therapy. The most commonly noted include hepatotoxicity and fulminant liver failure, peripheral neuropathy, rash, and visual disturbance, amongst others.[6] Systems aimed at rapid identification of potential ADRs may be able to minimise their impact on morbidity and mortality and improve tolerance and successful completion of anti-TB therapy.

Early identification of ADRs that occur during the course of therapy for TB requires:

- a thorough knowledge of reported adverse reactions associated with specific drugs
- awareness of clinical situations, including co-morbidity and co-administration of other drugs, that increase a given individual's risk[10] (individuals who have HIV co-infection and are on antiretroviral therapy are one important high-risk group)
- careful surveillance for the early manifestations of ADRs (which, in turn, requires vigilance on the part of both patients and health care workers).

Although there are no standard guidelines for surveillance regimens, there is widespread agreement on some elements that are standard practice at the Parramatta Chest Clinic, Sydney, Australia, which provides services for Western Sydney residents, including patients of Westmead and Blacktown Hospitals.

General principles of monitoring

- Appropriate prescriber and health care provider education regarding common and less common side effects of frequently prescribed TB medications.
- Thorough baseline assessment of individual risk, including appropriate blood tests, and review of co-morbidities, medication and lifestyle factors.
- Detailed patient education and pre-treatment counselling, including written information (in the patient's native language where possible) regarding symptoms or signs to monitor, and appropriate health care provider contact details and/or management plan in case of development of symptoms or signs.
- Checklist of symptoms to be completed at interaction between health care provider and patient during therapy administration at DOT visits. The practice of DOT gives a scheduled frequent interaction between the health care provider and the patient that should facilitate frequent symptom review and early identification of any potential problems.
- Periodic TB specialist consultation for symptom review and examination.

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- Appropriate use of repeat blood testing, either scheduled or for further assessment of symptoms.[11]
- Periodic ophthalmic review either through a local Eye Clinic or by appropriately trained TB Clinic staff.

Management of ADRs during therapy for TB requires specialist knowledge. It frequently involves discontinuation of one or all TB medications, as well as supportive management until the ADR has resolved. Decisions on the timely reintroduction of appropriate therapy and the need to increase the duration of therapy to compensate for treatment interruptions are challenges that face treating physicians.

Management of adverse drug reactions

Hepatotoxicity is a particularly concerning and difficult to manage complication of TB therapy. Any one of, or a combination of, isoniazid, rifampicin and pyrazinamide (three of the four first-line drugs) may cause hepatotoxicity.

Hepatotoxicity may be identified as a result of presentation with abnormal symptoms and/or signs (anorexia, nausea, vomiting, abdominal discomfort, right upper quadrant tenderness or jaundice) or by routine surveillance blood tests. Management practice at the Parramatta Chest Clinic varies between the following two scenarios:[12–14]

- Asymptomatic patients with an increase in serum transaminases from baseline – if the increase in transaminases is <5-fold over normal baseline value, continue the current regimen, monitor for development of symptoms of liver dysfunction, and continue to periodically check liver function tests (minimum recommended frequency at least weekly). If the transaminases increase >5-fold over normal baseline normal value, cease all medications
- Symptomatic patients – withhold all drugs and measure liver function and coagulation status immediately. If transaminases are elevated >3-fold over normal baseline values, continue to withhold all drugs until symptoms resolve and transaminases decrease to <2-fold above normal, then re-introduce medications under specialist guidance.

For other severe ADRs, the following practices are used at the Parramatta Chest Clinic:

- full assessment of the patient by a member of the Chest Clinic or Respiratory Department medical/nursing staff as soon as possible, including comprehensive examination and blood testing
- immediate cessation of all anti-TB drugs
- review of other non-TB medications that may be contributing, or medications requiring dose adjustment in liver failure (if the drug reaction has caused hepatotoxicity)
- supportive care as required
- consideration of admission to hospital if indicated.

Once a patient has recovered from the drug reaction, reintroduction of therapy is undertaken under the guidance of a TB specialist.

Conclusion

TB remains a significant public health problem in NSW. With rapid identification of active cases and appropriate therapy under the guidance of a team well trained in the management of TB patients, successful therapy with minimisation of risk of adverse reactions can be achieved. Thorough knowledge of potential symptoms and signs of drug reactions, as well as frequent nurse and physician-initiated surveillance, are key.

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Tuberculosis contact tracing within a school environment: lessons for the future

Pam Banner

NSW Tuberculosis Program

Contact tracing plays a large role in the everyday work of chest clinics in NSW. It is a routine procedure that follows the 'concentric circle' method of screening. When a chest clinic becomes aware of a confirmed case of tuberculosis (TB), the inner ring of the circle (which comprises those with the highest risk of infection, including family and others in close contact with the index case) are screened first. If infection is detected in this group, screening proceeds to the medium-risk group and then, if necessary, to low-risk contacts, until no new infections are found. When explained, this method is usually readily understood and accepted by contacts. However, screening can become disrupted when contacts and others become fearful.

This paper highlights the case of a complex school screening which involved both screening all rings of the concentric circle (i.e. high, medium and low-risk contacts) and screening outside the circle (i.e. non-contacts).

In 2007 an overseas-born casual infants/primary school teacher in NSW was diagnosed with infectious cavitary TB disease by sputum smear, culture and chest X-ray. She had originally been diagnosed with pneumonia and was on sick leave for 1 month. One hour into the second day of her return to work, she had a massive haemoptysis (coughing up of blood) and was hospitalised.

Her household contacts were an overseas-born husband who was tuberculin skin test (TST) positive with a clear chest X-ray, and an Australian-born child who was TST negative. No other contacts were provided to the TB Coordinator at the Chest Clinic. Because of the teacher's smear and chest X-ray results, the TB Coordinator consulted with the then NSW Department of Health and local Public Health Unit (local units which work to identify, prevent and minimise public health risks to the community). Following this consultation, it was agreed to notify the school.

The school executive identified 160 children and staff the teacher had the closest contact with; they were included in the high-risk, first screening circle. A letter to parents, TB information, and a screening consent form were sent home with the identified children. The TB Coordinator gave an information session to staff, which was open to any concerned parents. It was decided that case management and screening would be performed at the school.

Initial screening identified one teacher and one child as infected. However, at follow-up screening of this group a few months later, 14 students, five teachers and the teacher's child returned positive TSTs. All had clear chest X-rays and were offered preventive treatment through the Chest Clinic.

The Public Health Unit Director and TB Coordinator attended further meetings at the school. An information evening for parents was discussed but, at this time, the school executive declined. A further 40 medium-risk (second circle) students and teachers were then identified and screened, with another two students found to be infected.

As children began preventive treatment a rumour spread that there was an outbreak of TB at the school. Parents arriving at school were approached by media reporters. Screening was demanded by some parents whose children had never been in any of the teacher's classes.

An expert panel was convened to discuss the issue. Decisions were made to screen a low-risk group of a further 60 students and staff (the third circle); hold a parent information evening; release a statement to the media; send a letter to all local general practitioners (GPs) to inform them of the situation; and hold a meeting for GPs. Screening of this low-risk group found only one child infected. Eighteen non-contacts outside the circles were also screened at the request of parents, with no infected children found.

The TB Coordinator, along with representatives from the school, Public Health Unit and media representatives from the Local Health District (LHD), held a successful information evening for parents. It was stressed that there were no new cases of TB, was no ongoing risk of infection, those infected cannot spread TB to others and that 90% of people infected never develop disease.

From the 260 contacts screened, seven teachers, 18 students and the teacher's child were infected. This represented 12% of the high-risk group, 5.5% of the medium-risk group and 1.5% of the low-risk group. To date, no contacts have developed active disease.

10.1071/NB12096

As a result of the screening exercise, there were valuable lessons learnt that can guide future school contact tracing exercises. It is recommended that after an initial teleconference with all relevant personnel (in this case, the TB Coordinator, Public Health Unit Director and school principal), the Public Health Unit Director (or equivalent) should write a briefing note for the relevant Health Department Director (in this case, the Chief Health Officer) and the head of the local health service (in this case, the Chief Executive of the LHD) including a summary of the key issues and recommendations. The media departments in both the LHD and the Health Department should also be alerted and updated.

The school principal, in conjunction with the local TB Coordinator, should hold an information session for all teachers at the school. This session should reinforce confidentiality issues and provide education on possible screening results. The school principal should send a letter and TB factsheet to parents of all children in the entire year(s) affected, even if only a small portion is to be screened. Also consider sending a letter to all parents in the school if the school is small. Education Department regional officers and school occupational health and safety regional officers should be informed by the school of the screening, and given a TB factsheet and an individualised screening plan for the event.

Advice should be given to the school executive to hold an open parent information evening before screening commences. The screening consent form should also request the details of the child's GP so he or she can be informed of the screening plan.

This example highlights the importance of implementing an agreed screening plan to effectively manage large screenings; this will ensure consistency of processes and information given and provide a central point of communication for all involved.

Costs of a contact screening activity in a neonatal intensive care unit

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In March 2011, a medical officer working in a metropolitan New South Wales (NSW) neonatal intensive care unit (NICU) was diagnosed with active pulmonary tuberculosis (TB). He had immigrated to Australia from a high-incidence country 2 years earlier with negative pre-immigration screening. Occupational TB screening prior to commencing employment at the hospital, conducted in line with NSW Health policy,[1] was also negative. The man was screened again, also in line with the NSW Health policy, after he displayed TB symptoms (i.e. a 6-month history of non-productive cough and weight loss), and was smear-positive on induced sputum. *Mycobacterium tuberculosis* was confirmed on polymerase chain reaction, fully sensitive to standard anti-TB therapy.

The index case worked full-time in the NICU during his infectious period from December 2010 to March 2011. As neonates are at higher risk than older children or adults of developing severe and potentially fatal disease soon after infection with TB, it was decided to immediately offer screening to all exposed neonates and others who were potentially exposed rather than implementing a staged response.[2,3] The outcome of this investigation is being reported elsewhere.[4] Here we describe the costs of the investigation.

Contact investigation

All 125 neonates, 165 of their relatives and 122 health care workers identified from medical records and departmental rosters as having had contact with the index case during his infectious period were offered screening (Table 1).

Ninety-six neonates were followed up at the hospital, 15 were followed up in other Local Health Districts, nine had died of unrelated causes and five failed to attend. Exposed neonates received a tuberculin skin test (TST) at 3 months corrected age; TSTs have been shown to be unreliable prior to this age.[5–7] Neonates who were too young to be screened were commenced on isoniazid prophylaxis until they reached 3 months corrected age.

Relatives and health care workers were offered TST screening at the Chest Clinic. A reaction of ≥10 mm (or ≥15 mm with a Bacille Calmette-Guérin (BCG) scar) was defined as a positive TST.

Data on exposure and outcomes were collected from clinical records and departmental rosters. None of the 100 neonates screened (89 in the hospital and 11 in other Local Health Districts) had positive TSTs.[4] Fifty-one of 152 (34%) relatives and nine of 120 (8%) health care workers screened had positive TSTs.[4] All subsequently had negative chest X-rays, sputum cultures and/or interferon-gamma release assays (IGRAs). All positive TSTs were associated with origin from a high-incidence country and/or previous BCG vaccination. No adult contacts were treated for TB infection or disease.

Resources used

The time spent on this investigation by nurses, doctors and pharmacists was obtained from rosters and interviews with staff. Salaries were calculated using 2011 NSW Health awards.[8–10] Travel costs were estimated using National Roads and Motorists' Association costs for a medium-sized vehicle.[11] The costs of laboratory tests and radiology were obtained from the Medicare Benefits Schedule (items 58503 and 69327), and hospital radiology and pathology departments.[12] The hospital pharmacy provided information on the cost of isoniazid. The cost of consumables was calculated from clinic invoices. Car parking and postage costs were obtained from the investigation cost centre. All costs presented are therefore estimates (Table 2).

Neonates were screened by Chest Clinic registered nurses. Neonates on isoniazid were also monitored in medical review clinics. Chest Clinic and infection control clinical nurse consultants also attended the neonatal clinics. The time nurses spent on neonatal screening cost $24 489.[8] Chest Clinic registered nurses also conducted the relative and health care worker screening at a cost of $14 913.[8]

Neonatologists and paediatricians reviewed the neonates at the screening and medical review clinics at a cost of $19 059.[9] Respiratory physicians interviewed and counselled the families of exposed neonates at the initial screening clinics at a cost of $9148.[9]

The estimated 910 km travelled for screening home visits and medication delivery cost approximately $682.[11]

Table 1. South Western Sydney Local Health District neonatal intensive care unit tuberculosis contact investigation: exposed contact demographics and screening outcomes, 2011

	Neonates	Relatives	Health care workers
Number exposed	125	165	122
Mean age at start of investigation	2.1 weeks corrected (95% CI: 1.0–3.1)	32.5 years (95% CI: 31.0–33.4)	40.1 years (95% CI: 38.0–42.1)
Gender			
Male	70 (56%)	72 (44%)	12 (10%)
Female	55 (44%)	93 (56%)	110 (90%)
Born overseas	0 (0%)	72 (44%)	54 (44%)
Previous BCG	0 (0%)	23 (14%)	65 (53%)
Previous known TB	0 (0%)	2 (1%)	0 (0%)
Received isoniazid prophylaxis	*Hospital clinic*: 66/89 (74%)	0 (0%)	0 (0%)
Positive TST during investigation	*Hospital clinic*: 0/89 (0%) *Out of area*: 0/11 (0%)	51/152 (34%)	9/120 (8%)

BCG: Bacille Calmette-Guérin; CI: confidence interval; TST: tuberculin skin test.

Table 2. Estimated costs of the neonatal intensive care unit tuberculosis contact investigation for the contacts screened in the South Western Sydney Local Health District, 2011

Category	Estimated cost
Nurses' time *(99 days of chest clinic RN time, 11 days of chest clinic CNC time, 10 days of infection control CNC time, 2 weeks of neonatology RN time)*	$39 402
Doctors' time *(25 days of neonatologist and paediatrician time, 12 days of respiratory physician time)*	$28 207
Investigation coordination *(23 weeks of CNC time)*	$40 970
Home visits *(Travel costs over 910 km and nursing time of 10 RN hours and 12 CNC hours)*	$1653
Screening tests *(220 CXRs, 487 TSTs, 10 IGRAs, 2 x 3 sputum smear/cultures)*	$12 450
Isoniazid prophylaxis *(4425 days of isoniazid solution and 69 hours of pharmacist time)*	$2658
Other *(consumables, car parking, postage)*	$3090
Total estimated cost	**$128 430**

NB: Costs associated with screening neonates living in other Local Health Districts are not included in this estimate.
CNC: clinical nurse consultant; CXR: chest X-ray; IGRA: interferon-gamma release assay; RN: registered nurse; TST: tuberculin skin test.

Nurses' time spent conducting home visits cost an additional $971.[8] A clinical nurse consultant was appointed to coordinate the investigation over 23 weeks at a cost of $40 970.[8] Screening tests conducted included chest X-rays (220 performed for a total of $10 373), TSTs (487 performed for $1406), IGRAs (10 performed for $500) and sputum smears/cultures (two contacts with three specimens each for $171).[12]

The 66 neonates commenced on prophylaxis received a total of 4425 isoniazid treatment days. At an average dose of 50 mg/day the isoniazid solution cost $167, with no additional cost passed onto the families. Manufacturing and dispensing the isoniazid solution took the hospital pharmacists approximately 69 hours, at a cost of $2491.[10]

Additional costs included consumables ($1034), parking for families ($1826) and postage for letters sent to families and health care providers (approximately $230).

There are few neonatal nosocomial TB exposure investigations in the published literature, and little evidence on their cost.[2,5,13–16] We estimate the total cost to the hospital of this screening investigation was $128 430. This may underestimate the true cost as some items could not be quantified, including the cost of screening the 15 neonates and their relatives who attended other facilities for screening, the cost to families of travel to the clinics and pharmacy, and the investigation hotline. The time spent by hospital executives, the media unit, the NSW Ministry of Health and Public Health Unit staff is also not included in this estimate.

Indirect costs that are difficult to quantify include the cost of a parent's time away from work and usual duties. The opportunity cost to other departments of scarce health care resources including health care worker time, clinic space and tests used for the investigation is significant but difficult to quantify.

The potentially substantial costs of screening investigations are not always included within health service budgets. This episode highlights the importance of including funds for screening within the public health or prevention components of budgets to accommodate such events.

Intangible costs including the anxiety and stress caused to families from the potential infection of their neonate, as well as to exposed health care workers and relatives, are considerable but not readily expressed in dollar terms.

Conclusion

There is a paucity of evidence around neonatal nosocomial TB exposure events, making it difficult to plan an appropriate response. In the absence of information it is difficult to justify not taking a precautionary approach when neonates are involved, but alternative approaches could be considered. Rather than screening all contacts as in this investigation, after careful risk assessment screening could initially be restricted to those with the highest exposure and extended to those at lower risk only if cases are detected. If no evidence of transmission was detected in the most highly-exposed contacts, further unnecessary screening of contacts at lower risk would be prevented, resulting in potential cost savings.

No evidence of transmission was detected in this and previous similar investigations; the risk of nosocomial transmission in the NICU setting appears to be low.[2–7,13–17] This may add confidence that a staged approach for future TB screening activities in neonatal settings can be a safe and cost-effective alternative to initially screening all potentially exposed neonates.

Acknowledgments

The authors wish to acknowledge the hard work of staff from the South Western Sydney Local Health District Chest Clinic, NICU, Departments of Paediatrics and Community Paediatrics, and the Sydney and South Western Sydney Public Health Unit during the investigation.

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Tuberculosis: an emerging zoonosis

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Tuberculosis (TB) caused by *Mycobacterium tuberculosis* is primarily a disease of humans who are considered the primary reservoir host for this pathogen. It is an ancient disease, with descriptions dating back thousands of years. It is currently estimated that one-third of the global human population is infected,[1] and TB accounts for millions of deaths annually.

Mycobacterium tuberculosis in animals

Humans have had a very close association with animals for millennia, utilising them for food, labour, transport, clothing, companionship, disability assistance, recreation, sport, religious and cultural icons, security, entertainment and research and in rescue, rehabilitation and conservation efforts. It is inevitable then that as a result of this close association, transmission of pathogens from humans to animals and *vice versa* will occur. *M. tuberculosis* infections have been reported in a wide range of animal species including: elephants,[2–6] non-human primates,[3,5,7] rhinoceroses,[6] tapir,[7] various non-domestic ungulates,[6,7] seals,[3,5] various non-domestic carnivores,[5] dogs,[8,9] cats,[9] guinea pigs,[10] rabbits,[10] cattle[11] and birds.[3,5,12] Susceptibility to infection with *M. tuberculosis* varies significantly between animal taxonomic groups, with species such as old world monkeys, lesser apes, elephants, hamsters and guinea pigs being highly susceptible; great apes, new world monkeys, canids, seals, tapir, rhinoceroses, pigs, rats and mice are moderately susceptible; and prosimians, felids, equids, ungulates, rabbits, birds and reptiles have low susceptibility.[3] The susceptibility for many species is unknown. Animals are generally considered to acquire infection from humans with active TB, however animal-to-animal transmission also occurs, including between different species.[6]

Historically, zoonotic TB has been associated with *M. bovis*, however the incidence has declined significantly with the control and eradication of *M. bovis* in many countries and the advent of the pasteurisation of milk.[13] It is now emerging that animals are a potential source of *M. tuberculosis* infection for humans, and it is becoming an important occupational and public health concern. Although the relative incidence is low, there are now several reports of transmission of *M. tuberculosis* from animals to humans.[5,6,9,14–17] In the majority of these cases infection occurred in humans that had a close and/or prolonged association with the infected animal/s, most commonly through occupational exposure.

Risk factors for animal-to-human transmission

Many of the risk factors identified for contracting TB from a human with active TB are equally applicable to acquiring infection from an animal. These include: the number of bacilli being actively shed; total time of exposure; droplet size; persistence of aerosols through insufficient ventilation; and immune status.[13] Additional risks associated with working with animals include: proximity to an infected animal; aerosol-generating practices (such as the use of high pressure hosing when cleaning); conducting clinical veterinary procedures such as trunk washes in elephants; conducting necropsies on an infected animal; being an elephant trainer/keeper; and inconsistent or improper use of N95 masks when working with known or potentially infected animals.[6] Generally, however, it is concluded that humans must be in close proximity to, and have more than incidental contact with, an infected animal to be at risk of infection.[13,14]

Case studies of animal-to-human transmission

A number of recent case studies provide examples of zoonotic *M. tuberculosis* infections. One report documents the infection of veterinary personnel during the clinical and pathological examination of a dog with unexpected disseminated TB. Contact investigation among the owners and veterinary personnel indicated that the index dog did not infect humans during its lifetime. However, all three pathologists performing the necropsy on the dog later returned positive results. Infection was most likely due to inhalation of aerosols created by using an electric saw to open the brain cavity.[9]

Tuberculosis caused by *M. tuberculosis* is emerging as an important disease of Asian elephants (*Elephas maximus*).[2–6] There have been numerous reports of transmission of *M. tuberculosis* from elephants to humans.[5,6,14–17] TB was diagnosed in two Asian elephants, three Rocky Mountain goats (*Oreamnos americanus*) and one black rhinoceros (*Diceros bicornis*) in the Los Angeles Zoo. Tuberculin skin test conversions were associated with working with the elephants and attending an elephant necropsy.[6] Five employees working at an elephant refuge in Tennessee had tuberculin skin test conversions linked to the presence of an infected elephant at the refuge. Risk of conversion was increased for elephant caregivers and administrative personnel working

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in the barn housing the elephant or in offices connected to the barn. Indirect exposure to aerosolised organisms and delayed and inadequate infection control practices likely contributed to transmission.[16] After the death of three elephants at an exotic animal farm in Illinois due to TB and the diagnosis in a fourth live elephant, 22 caregivers at the farm were screened for TB; 11 caregivers had positive tuberculin skin test reactions, one of whom was diagnosed with active TB. Genotyping demonstrated that the isolates from the four elephants and the caregiver with active TB were the same.[15] After the diagnosis of TB in an Asian elephant and a chimpanzee (*Pan troglodytes*) in an Australian zoo, over 145 staff and volunteers were screened and completed a detailed questionnaire to assess exposure risk. There was no evidence of risk to people who did not work with the elephants.[18,19]

Conclusion

People should be aware of the risk of contracting TB from animals where there is a risk of animal exposure to *M. tuberculosis*, particularly with susceptible species and in regions of the world where the incidence of TB in the human population is high. Animal industries and professions (e.g. zoological institutions, the veterinary profession and wildlife rescue and rehabilitation centres) should have occupational health programs that include personnel education, adequate infection control practices, appropriate use of personal protective equipment, TB screening programs for susceptible species, regular screening of employees working with these species and pre-employment screening to establish baseline exposure for TB.

Acknowledgment

I would like to thank Nicola Stephens, Manager, Communicable Disease Epidemiology and Surveillance Section, Health Protection Branch, Department of Health, Victoria (work completed while at Communicable Diseases Branch, Health Protection NSW) for her assistance with the preparation of this paper.

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What do we know about the outcomes of tuberculosis contact investigations in NSW?

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Abstract: A recently conducted study on tuberculosis contact investigations in six Sydney tuberculosis clinics – that together managed 59% of all tuberculosis cases in NSW from January 2000 to December 2009 – found that the prevalence of tuberculosis among contacts was comparable to other low-incidence settings. However, only 9% of contacts with latent tuberculosis infection received treatment. This paper explores the results of the study, evaluating potential missed opportunities to prevent tuberculosis among contacts, and discussing the mechanisms in decision making about treatment of latent tuberculosis infection. In particular, the paper focuses on the challenges of tuberculin skin test interpretation among contacts who have received Bacille Calmette-Guérin vaccination and who were born in countries where tuberculosis is endemic.

Screening of contacts of people with active tuberculosis (TB) is a cornerstone of TB control in low-incidence countries such as Australia.[1] Contact tracing aims to identify contacts with active TB or latent tuberculosis infection (LTBI) and to provide adequate treatment and follow-up. Active TB is evaluated by taking a history of clinical symptoms, performing a chest X-ray, and examining sputum samples if the chest X-ray is abnormal. A diagnosis of LTBI is based on a positive tuberculin skin test (TST), taking into account the pre-test probability of a contact having LTBI when interpreting the TST result. Contacts with a previously positive TST do not usually undergo a repeat TST, but the risk of having sustained a new infection from the current index case – depending on the infectiousness of the index case and duration and intensity of exposure of the contact – will be assessed by the reviewing physician. High-risk contacts will be offered LTBI treatment, and the remainder of the contacts will be followed-up with repeat chest X-rays for a minimum of 2 years.

In New South Wales (NSW), TB contact screening (including TSTs and preventive TB treatment) is guided by NSW Health policy directives.[2–4] This paper will discuss the findings of a recently conducted study examining the risk of active TB among 14 371 contacts of people with TB in NSW.[5]

Ethics apporval was obtained from the NSW Population and Health Services Research Ethics Committee (HREC/10/CIPHS/58).

Active TB among contacts

The study population of this retrospective cohort study comprised all persons who were screened as contacts of people with TB between January 2000 and December 2009 at TB clinics within the former Sydney West and Sydney South West Area Health Services. The six TB clinics within these two former Area Health Services together managed 59% of all TB cases in NSW during the study period. Cases of active TB among the study population were identified by linking a database containing details for all identified contacts (the Clinical Surveillance System) and the NSW Notifiable Diseases Database, which includes the TB registry and was used for the collection of notifiable disease case information in NSW until the implementation of the Notifiable Conditions Information Management System in 2010.

Of all contacts who were seen as part of TB contact investigations, 1.9% were diagnosed with active TB either at the time of the first screening or during follow-up. The prevalence of TB among contacts at the time of the initial screening (within 3 months after the first health-care contact) was 1.5% and thus consistent with the prevalence of active TB among contacts in other low-incidence settings.[6] This relatively high yield for active TB at the time of initial screening (78% of contacts with active TB) compared to the lower yield during the subsequent follow-up period (22% of contacts with active TB were diagnosed during a mean follow-up period of 4.6 years) highlights the importance of ensuring at least one initial health-care screening visit for every contact at risk of having been infected.

Latent TB infection: lost opportunities to prevent TB among contacts?

In this study, 35% of all contacts with at least one TST performed had a TST $\geq$10 mm at the time of the initial screening visit or during follow-up and thus were identified

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as having LTBI. Applying the threshold for TST recommended in United States (US) guidelines[7] (5 mm) or European guidelines[8] (TST ≥10 mm in non-Bacille Calmette-Guérin (BCG)-vaccinated or BCG vaccinated <12 months of age; TST ≥15 mm in BCG-vaccinated >12 months of age) would have resulted in higher and lower estimated prevalence, respectively.

Only 9% of contacts with a positive TST in this study received treatment for LTBI. Do these findings imply that we are missing opportunities to prevent TB among contacts in NSW? Is comprehensive coverage of preventive treatment in contacts with evidence of LTBI what we should strive for? To answer these questions we need to take a closer look at those contacts that developed TB.

Of 273 contacts with active TB, 212 already had the disease at the beginning of contact screening and thus could not have been considered for treatment of LTBI. Of the remaining 61 contacts who developed TB during the follow-up period, details on TST results and/or chest X-rays were available for 45. Of those, 30 (18 of whom were aged less than 35 years) had a TST ≥10 mm at the time of initial screening and did not receive LTBI treatment. Three of these 30 contacts were not given LTBI treatment because their chest X-ray was abnormal (including one contact aged less than 35 years), and active TB could not be excluded with certainty; they were followed up with a chest X-ray. Interestingly, 25 of the 27 contacts with a TST ≥10 mm and a normal chest X-ray who did not receive LTBI treatment were born overseas; the majority of these 25 contacts had received BCG vaccination.

Historically, US guidelines have recommended excluding from LTBI treatment persons aged 35 years and over with a positive TST but no other risk factors for TB.[9] This recommendation followed a study that showed an association between age and increased risk of (potentially fatal) isoniazid-induced hepatitis.[10] Subsequent US guidelines focus on screening and treatment of LTBI in high-risk populations only; the age cut-off no longer applies as this recommendation was directed at persons at low risk.[1] The NSW policy directive on preventive therapy still applies an age cut-off of 35 years in considerations about who should be offered LTBI treatment.[3]

Given current NSW guidelines, at least the 17 contacts under the age of 35 years with a TST ≥10 mm and a normal chest X-ray at initial screening should have been considered for LTBI treatment. Sixteen of these contacts were born overseas and had received BCG vaccination. The findings highlight the challenge of TST interpretation in contacts who have received BCG vaccination and who were born in countries where TB is endemic; these contacts are likely to have been infected with TB previously. The decision to treat LTBI is a complex one in which the risk of progression to active TB (and associated morbidity and mortality) must be weighed against the risk of an adverse event from LTBI treatment. As the perceived potential risk of progression to active TB depends, amongst other things, on the likelihood of a false-positive TST (particularly in BCG-vaccinated contacts) and the likelihood of recent (compared to past) infection, this may explain a reluctance to offer treatment of LTBI to overseas-born contacts who have been BCG-vaccinated. Facing these uncertainties, it seems that the majority of chest clinic physicians in the study followed the principle '*primum nil nocere*/first, do no harm' by avoiding the risk of adverse events from LTBI treatment.

The role of interferon-gamma release assays in contact tracing

TSTs have poor specificity in BCG-vaccinated individuals due to cross-reactivity with the antigens in the BCG vaccine. Interferon-gamma release assays (IGRAs), which have a much lower potential for false-positive results due to cross-reactivity, have been proposed as an alternative to the TST. However, IGRAs are currently not routinely used in NSW as an alternative or supplemental test in contact tracing.[2] The reluctance to integrate IGRAs routinely as a diagnostic procedure in contact tracing is likely related to the fact that until recently there was little evidence that a positive IGRA result is a predictor of the risk of developing active TB. However, in recent years this association has been shown in several studies. Two meta-analyses published in 2012 examined the predictive value of IGRAs for progression to active TB: one concluded that the predictive value of IGRAs for development of TB is similar to the TST;[11] the other found that IGRAs have a higher positive and negative predictive value for progression to active TB, especially in high-risk groups.[12] In other countries with a low incidence of TB, such as the United Kingdom and the US, IGRAs have been introduced into guidelines on contact tracing.[13,14] In these countries, IGRAs are used to verify a positive TST[13] or as an alternative to the TST.[14] The Australian National Position Statement on the role of IGRAs in the detection of LTBI, published in March 2012, also acknowledges the role of IGRAs as a supplementary test to confirm LTBI in low-risk individuals with a positive TST in the context of contact tracing.[15] Due to the recently gained knowledge on the predictive value of IGRAs for active TB, which seems to be at least equivalent to the TST, and the higher specificity of IGRAs in BCG-vaccinated individuals, consideration should be given to integrating IGRAs, in addition to TSTs, into contact investigations in NSW.

LTBI in overseas-born contacts

The other challenge in TST interpretation (other than previous BCG vaccination) in contacts born in countries where TB is endemic is the uncertainty about the time of infection. LTBI treatment for recent infection is more

beneficial than treatment for infection in the past, as the risk of progressing from LTBI to active TB disease is greatest in the 2 years following infection.[16] If there is clear evidence of TB transmission from the index case, for example when an Australian-born child contact has a positive TST, this supports the assumption that recent infection could have occurred in all close contacts. However, if all household contacts of an index case were born in countries with a high TB incidence, it is difficult to establish whether recent transmission has occurred. It is likely that the reviewing physician takes uncertainty about the time of infection into account. This could explain the finding that overseas-born contacts with a positive TST often do not receive LTBI treatment. There is, however, evidence that treatment of LTBI in overseas-born close (household) contacts is cost-effective[17,18] and worthwhile in terms of quality-adjusted life years.[17] Indeed, further analysis of the NSW TB contact study shows that overseas-born contacts had a higher risk of developing active TB than Australian-born contacts (after adjustment for age, gender, TST size and whether preventive treatment was given) with odds ratios of 3.35 (95% CI 1.84–6.10), 3.64 (95% CI 2.48–5.35) and 5.79 (95% CI 4.08–8.21) in overseas-born contacts from countries with a TB incidence of <10, 10–99 and ≥ 100 per 100 000 population respectively (unpublished data). A more proactive approach to LTBI treatment in overseas-born high-risk contacts in NSW therefore seems indicated.

Effectiveness of LTBI treatment

In the NSW TB contact study, an estimated 3942 additional contacts with a TST ≥ 10 mm would have to have received LTBI treatment to prevent 38 cases of TB that occurred after initial screening among contacts with a TST ≥ 10 mm; that is assuming 100% uptake, adherence, completion and effectiveness (unpublished data). However, in clinical practice, patient adherence to LTBI treatment is often a limiting factor in treatment effectiveness. Previous studies suggest low completion rates, ranging from 19% (for isoniazid for 9 months) to 82% (for isoniazid for 6 months), with a completion rate of 75% for 6 months of isoniazid described at a major Sydney chest clinic.[19] A Cochrane review of randomised controlled trials found an overall effect estimate of 60% for treatment of LTBI (taking into account patient adherence to treatment).[20] While concerns about the overall effectiveness of LTBI treatment may be a reason for the reluctance of physicians to offer LTBI treatment, it is important to remember that randomised controlled trials have demonstrated that isoniazid has a 90% efficacy in preventing TB in infected contacts (and other individuals with LTBI) when taken properly.[21]

Conclusion

The prevalence of active TB among contacts in NSW is comparable to other settings with a low incidence of TB. Less than 10% of contacts with a TST ≥ 10 mm in the NSW TB contact study received prophylactic treatment. Some missed opportunities to prevent TB have been identified, especially among young overseas-born high-risk contacts. Future challenges for TB contact tracing in NSW include achieving consistency in decision-making about LTBI treatment while taking individual patient factors into account, and defining the role of IGRAs in contact investigations.

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Ongoing transmission of tuberculosis in Aboriginal communities in NSW

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Abstract: This report describes the ongoing transmission of tuberculosis in Aboriginal communities in NSW. From October 2000 to July 2012 there were 30 linked cases of tuberculosis diagnosed in Aboriginal people – 22 in the North Coast area of NSW, with a further three cases in Sydney and five in southern Queensland. It is likely that a range of factors have contributed to this ongoing transmission, including delayed diagnosis, the extensive social connections within the communities affected, and the highly mobile living arrangements of many of those affected. Cases have continued to emerge despite implementation of tuberculosis control measures in line with state and international protocols. Tuberculosis control staff are working in partnership with Aboriginal communities to identify and implement appropriate tuberculosis control strategies.

Tuberculosis (TB) is an important public health issue and a leading cause of death worldwide.[1] The public health burden of TB is substantial, even in developed countries with comprehensive TB control programs. In Australia, the incidence of TB is low (6.0 cases per 100 000 population in 2009), with the majority of cases occurring in migrants from countries with a high incidence of TB.[2] For Aboriginal Australians, the incidence of TB has been declining since 2002 but remains over five times higher than for Australian-born non-Aboriginal people (4.8 versus 0.9 per 100 000 population).[2] The persistence of TB in Aboriginal people has been attributed to poor living conditions and malnutrition compounded by chronic diseases and alcohol use.[3–5] The aim of this paper is to describe the epidemiology of a cluster of TB cases with ongoing transmission amongst Aboriginal people in New South Wales (NSW), and the public health response.

Methods

This paper presents results up to July 2012, however new cases continue to be identified and the public health response is ongoing.

TB is a notifiable disease under the NSW *Public Health Act 2010*. The data presented in this paper have been collected as a part of routine TB control procedures implemented in accordance with the Act. The data were obtained from the NSW Notifiable Conditions Information Management System, a statewide database of disease notifications held by NSW Health. Standard TB case definitions are used.[6] Clustered cases are defined as: *MIRU-linked cases* – laboratory-confirmed TB cases with the mycobacterial interspersed repetitive unit (MIRU) pattern 23′3425153322; and *epidemiologically-linked cases* – clinical TB cases with no TB organism identified but with epidemiological links to a MIRU cluster case. Incidence rates per 100 000 population were calculated using the Australian Bureau of Statistics estimated mid-year NSW populations for 2000–2012, obtained from NSW Health's Secure Analytics for Population Health Research and Intelligence.

Results

Identification of cases in the cluster

A total of 30 linked cases of TB were identified in the period October 2000–July 2012 (Figure 1). Twenty-six of the 30 cases shared the MIRU pattern for this cluster. The remaining four were clinically diagnosed cases that had strong epidemiological links to the cluster (e.g. child household contacts of cases). One person developed TB twice and was counted twice in the cluster. This person had household contact with several cases following successful completion of directly observed treatment and so was considered a case of reinfection. Most cases ($n = 22$) were diagnosed on the NSW North Coast (the area covered by the Northern NSW and Mid North Coast Local Health Districts), with a further three cases in Sydney and five in Queensland. The MIRU pattern for this cluster is found almost exclusively in Aboriginal people. Only one non-Aboriginal person in Australia has been identified as having had this MIRU pattern since 2000: an elderly overseas-born woman in Victoria. This woman had no identifiable epidemiological link to the cluster cases, and was therefore excluded from the cluster.

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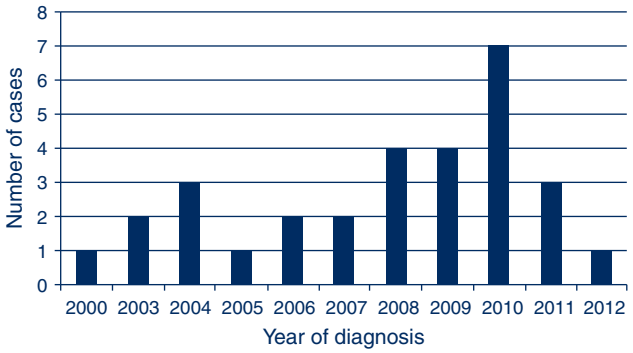

Figure 1. Tuberculosis cases by year of diagnosis, NSW/QLD cluster, October 2000–July 2012 ($n = 30$).
Source: Notifiable Conditions Information Management System, NSW Ministry of Health.

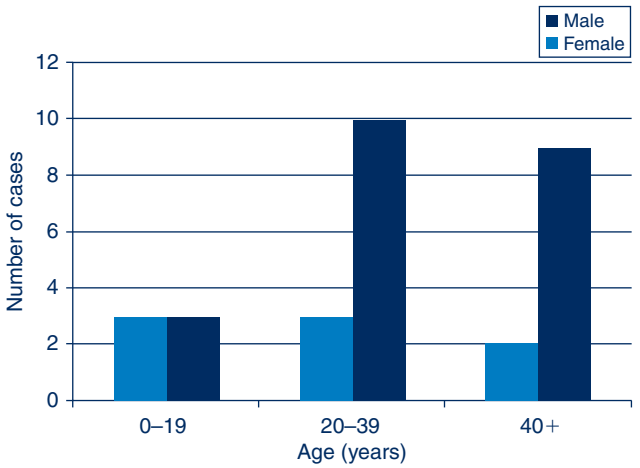

Figure 2. Age and gender distribution of tuberculosis cases, NSW/QLD cluster, October 2000–July 2012.
Source: Notifiable Conditions Information Management System, NSW Ministry of Health.

The presence of a cluster became evident when several cases of TB were diagnosed through contact tracing in response to an Aboriginal person diagnosed with pulmonary smear-positive TB on the NSW North Coast in 2003. This person was estimated to have been infectious for 4 months prior to diagnosis, and assisted with the contact tracing by disclosing a wide network of family and friends. In 2004, an Aboriginal person in Queensland who was newly diagnosed with TB and a North Coast Aboriginal person who had been diagnosed with TB in 2000 were found to share the same MIRU pattern as the initial case.

MIRU-linked cases continued to emerge despite implementation of TB control measures in line with state and international protocols[6,7] and additional community-based screening where possible. Some cases were known contacts of previous cases, however the geographic spread of the disease broadened and the epidemiological links for some cases were not immediately evident.

In 2006 an Aboriginal person diagnosed with MIRU-linked TB in Sydney reported travelling to the North Coast periodically however no epidemiological links with the North Coast cases could be identified. Two further MIRU-linked cases were diagnosed in Sydney: one person diagnosed in 2009 who reported "knowing" the first Sydney case and who had a history of travel to the North Coast; and one person diagnosed in 2012 with no identified connections to the North Coast or any cluster cases. A Queensland person diagnosed with TB in 2006 was MIRU-linked to the cluster. It was subsequently discovered that this person moved in the same social circles as a North Coast person diagnosed in 2005, at the time the North Coast person was infectious. A household sub-cluster with three additional cases emerged around this Queensland case.

The diagnosis in 2010 of a further five adults with TB on the North Coast revealed significant information about the connections between the North Coast cases, their contacts, and their mobility practices and patterns. The North Coast cases diagnosed in 2010 had epidemiological connections with multiple cases in this TB cluster.

Characteristics of the cluster

Twenty-two of the 30 cases (73%) were male; the average age of cases was 33.2 years (Standard Deviation = 15.8) (Figure 2). Most cases ($n = 22$, 73%) presented with pulmonary smear-positive TB; the remainder presented with pulmonary smear-negative TB and extrapulmonary TB. Cases reported having symptoms of TB for an average of 5 months prior to seeking medical attention or being identified through contact tracing (range 1–13 months). Eight cases (27%) were identified through contact tracing. Four of the 30 cases (13%) were children, all of whom had household contact with an adult with pulmonary TB. This particular MIRU pattern is susceptible to first-line TB antibiotics, and all cases completed treatment. There have been no known deaths due to TB in this cluster.

Since October 2000, there have been 55 notifications of TB in Aboriginal people in NSW, 25 of which (45%) are part of this cluster. The average annual TB notification rate for Aboriginal people in the North Coast area in the period 2000–2011 was 12.1 notifications per 100 000 population. This rate is elevated compared to Aboriginal people in the rest of NSW (1.7 per 100 000 population), and compared to non-Aboriginal people in both the North Coast area (1.6 notifications per 100 000 population) and the rest of NSW (7.2 notifications per 100 000 population). The increased rate of TB in Aboriginal people in the North Coast area is entirely due to this cluster – of the TB notifications in Aboriginal people in the North Coast area since 2000, all but one case has been linked to this cluster.

The epidemiological links between these cases are complex (Figure 3). Rather than a complete 'map' of links

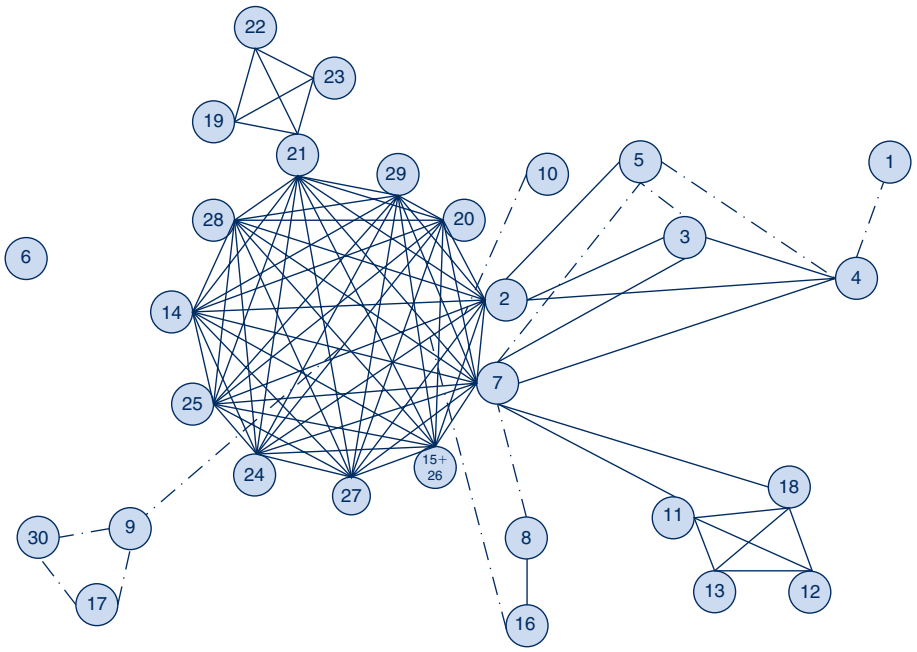

Figure 3. Social networks of tuberculosis cases, NSW/QLD cluster, October 2000–July 2012.

Note: Solid lines denote close social or household contact, dashed lines denote casual or community-level contact.

Source: TB Prevention and Control Team, Northern NSW and Mid North Coast Local Health Districts.

between cases, the connections shown in Figure 3 reflect the depth of information disclosed by each case and/or knowledge amassed by the North Coast TB Prevention and Control Team (Team TB) through its work in the field. The understanding of connections between cases evolves over time, and depends on the cultural competence of Team TB to develop mutually trusting and respectful relationships with individuals and communities. As the cluster continues it becomes increasingly difficult to identify patterns of transmission and infection. The cases have extensive overlapping social networks and many cases lived in overcrowded households and were highly mobile during their long infectious period.

Equity aspects of the cluster

This TB cluster represents a health inequity between Aboriginal and non-Aboriginal Australians in NSW. The history of displacement, disempowerment, grief and loss experienced by Aboriginal people continues to impact on their health and wellbeing and the constellation of social factors that contribute to TB are a reflection of the broader health inequities between Aboriginal and non-Aboriginal people. In this TB cluster, social risk factors include transient homelessness, living in crowded houses, unemployment and incarceration. Most of the adult cases in this cluster have a history of only seeking medical care when injured or extremely unwell, and their TB symptoms may have been masked by other health and wellbeing issues such as drug and alcohol use, smoking and depression. Many of the people with TB in this cluster are the most vulnerable individuals within already marginalised communities. For many, daily life challenges and competing health conditions compound their experience of TB and their ability to seek healthcare.

However, the strengths of the Aboriginal people and communities affected by this cluster must be acknowledged. Team TB recognise examples of individual healing; strong families; individual, family and community action; evidence of adults coping, recovering and flourishing. It is a testament to the strength and resilience of the people who have had active TB, and their family and community support system, that despite these life challenges and the burden of shame and stigma, they have all completed treatment and many have made personal sacrifices to benefit the community.

The North Coast TB Team response to the cluster

To identify contacts of people with TB, Team TB utilise an *intensive household contact tracing*[8] approach. This involves having wide-ranging discussions ("yarning") with the person, family members and others involved with the community to identify social and family networks and places the person visits (e.g. households, congregation areas), then offering screening to the people at these locations. TB screening, including clinical assessment of symptoms, tuberculin skin tests (TSTs) and/or chest X-rays, has been offered widely to the Aboriginal people

in North Coast towns. This is in response to the Aboriginal communities' concern; recognition of the extended social networks and high mobility in Aboriginal communities which result in a high number of close contacts, many of whom can be difficult to identify and/or locate; leads provided through contact tracing; and identification that not all infected people were being reached through contact tracing models. Community-wide screening is also utilised when the community is not aware of the identity of a case as it allows for confidentiality to be maintained. These screening approaches have been developed by Team TB in conjunction with communities and local Aboriginal Health Workers. Early in the public health response to the cluster, 'concentric circle' contact tracing was used in line with NSW guidelines,[6] however retrospective identification of connections between cases and TST data revealed that with this approach people at risk of infection were not always nominated.

Team TB's response to the cluster is guided by the principles of cultural respect, equity and partnership with Aboriginal communities[9] and community engagement is central to the public health response. In particular, Team TB has invested in the development of cultural competence and awareness sharing with the community (i.e. two-way learning). They have consulted with Aboriginal community groups and leaders, a range of government and non-government service providers, and Aboriginal people affected by TB to develop appropriate response strategies. Team TB participates in a range of activities with communities to facilitate shared ownership of solutions to the ongoing transmission of TB. The recruitment of Aboriginal Health Workers into Team TB has strengthened its capacity to develop and implement strategies that are acceptable to all parties, while being feasible within the broader social and cultural context.

Discussion

This paper describes the only reported instance of ongoing transmission of TB in NSW, the public health response to the cluster, and the rationale for this response.

The limitations of routine TB contact tracing approaches have been documented in the international literature[10,11] and are amplified in vulnerable groups such as Aboriginal people.[12] In this cluster, cases were identified using a combination of contact tracing and community-wide screening for Aboriginal people. Novel methods of contact tracing that focus on social networks, locations and behavioural factors have been successfully used to examine TB clusters and outbreaks overseas[13–16] and their application in Australian Aboriginal communities warrants further investigation.

The uptake of treatment for latent TB infection remains a major ongoing challenge in the response to the cluster. More than 1000 TSTs have been provided as part of screening, and all individuals with latent TB infection are offered preventive treatment. Uptake and completion is high in high-risk child contacts, facilitated by directly observed treatment or support and monitoring by TB nurses. However, many infected adults decline treatment for latent TB infection or fail to complete the 6-month course of isoniazid. This highlights the significant ethical tension between individual autonomy and community benefit.

To date, TB prevention and control activities have concentrated on providing access to clinical services through delivery of *primary care* focused on early diagnosis and timely and effective treatment. The ongoing transmission suggests closing the gap in TB rates between Aboriginal and non-Aboriginal Australians involves acknowledging that TB is embedded in a complex system[17] influenced by contemporary and historical social determinants of health. It is time to consider a comprehensive *primary health care* approach that addresses the range of social, environmental and structural factors that contribute to TB and ill-health, and those that contribute to good health.[18] Team TB is committed to operating on social justice principles with practitioners dedicated to enabling individual clients and communities[19] and implementing micro-empowerment strategies (e.g. working with people to build TB management around how and where they live their lives, incorporating social and emotional care into TB management, contributing to community-initiated events and programs for community development, and giving 'voice' to people who have been affected by TB).[20]

Empowerment is a recurrent theme throughout the literature on improving the health and wellbeing of Aboriginal and Torres Strait Islander people. Empowerment is one of the six components of the WHO Stop TB Strategy[21] and is incorporated in many TB control programs internationally.[22] Furthermore, it is a viable public health strategy[23] which can be viewed from two complementary perspectives: empowered communities can control TB and controlling TB can empower communities. It is conceivable that incorporating empowerment into the TB prevention and control model could contribute more to the health of the target group than just the elimination of TB. The challenge is to move from business as usual to develop a deeper understanding of the setting and to explore innovative and novel ways to move from *primary care* towards *primary health care*.

Conclusion

The ongoing transmission of TB amongst Aboriginal Australians in NSW suggests closing the gap in TB rates between Aboriginal and non-Aboriginal Australians involves acknowledging that TB is embedded in a complex system influenced by contemporary and historical social

determinants of health. An effective response depends on working in partnership with Aboriginal communities to develop strategies for TB control that empower communities and act on these social determinants of health.

Acknowledgments

The public health response to this TB cluster is a collaborative effort. The authors acknowledge the contribution of Aboriginal community members, TB nurses, Aboriginal Health Workers, public health unit staff, clinicians, laboratory scientists, and other government and community organisations in responding to this cluster. The authors also acknowledge the expert guidance provided by the TB Cluster Expert Panel, a subcommittee of the NSW TB Advisory Committee.

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Australia's role in promoting and supporting tuberculosis control in the Western Pacific Region

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Abstract: Twenty-one percent of the world's tuberculosis cases are found in the Western Pacific Region. The region has demonstrated a lower rate of decline in incidence than the regions of Africa, the Americas and Europe. Issues around drug resistance, human immunodeficiency virus and diabetes impact on the burden of tuberculosis disease in the Western Pacific Region. Australia has exhibited a low and relatively stable tuberculosis incidence rate but has not progressed toward the desired international goal for tuberculosis elimination (<1 case per million population). The pathogenesis and transmission of tuberculosis make it difficult to achieve elimination within a geographically defined area. These aspects of disease control are amplified by globalisation and Australia's increasing economic and strategic engagement within the Western Pacific Region and South-East Asia. Promoting and supporting tuberculosis control within the Western Pacific Region provides an opportunity for Australia to maintain its low tuberculosis incidence rate and progress toward elimination.

There has been major progress in reducing tuberculosis (TB) incidence and deaths worldwide since the World Health Organization (WHO) declared TB a global emergency in 1993, yet the global situation continues to be described as a TB epidemic.[1]

Significantly for Australia, 60% of the world's TB cases are found in the Asia Pacific, which constitutes the two geographical areas described by WHO as the Western Pacific Region (WPR) (which includes Australia) and the South-East Asia Region (SEAR) (Figure 1). Both regions demonstrated lower rates of decline in TB incidence from 2010 to 2011 than the regions of Africa, the Americas and Europe (2.3%, 2.0%, 3.1%, 3.8%, 8.5% respectively).[1] As demonstrated by national data, the profile of TB in Australia is affected by the burden of TB in these two regions, with approximately 73% of TB cases notified in Australia being born in the WPR (30%) or the SEAR (43%).[1–3] This paper will outline the profile of TB in the WPR, Australia's current role in regional* TB control and the importance of Australia's strategic engagement in the WPR in sustaining an effective local TB control program.

The Western Pacific Region

The WPR (Figure 2) is home to nearly one-third of the world's population (approximately 1.8 billion people). It comprises some 37 countries and is recognised as one of the most diverse of the WHO regions, containing highly developed countries (e.g. Australia, Japan, New Zealand, the Republic of Korea and Singapore), some of the world's least developed countries (e.g. Cambodia, Kiribati, Samoa, Solomon Islands and Vanuatu) and fast growing economies such as China and Viet Nam. Large variations in population size exist between countries of the WPR, with over 1 billion people residing in China and only 52 people living in the Pitcairn Islands. Importantly, the WPR does not include Indonesia, Timor-Leste, India or Bangladesh, which contribute significantly to the burden of TB disease in Australia;[4] these countries are within the SEAR, which is not the subject of this paper.

Tuberculosis control in the WPR

WHO estimates that in 2011 there were approximately 1.7 million incident cases of TB in the WPR.[1] The WPR contains four of the 22 high TB incidence countries that have received particular attention at the global level since 2000: Cambodia, China, the Philippines and Viet Nam account for 17% of TB incident cases worldwide, and almost 93% of the TB incident cases in the WPR.[1] It is estimated that 28% of global multidrug-resistant TB (MDR-TB) cases are within the WPR; China, the Philippines and Viet Nam account for the majority of

*Unless otherwise indicated, the terms 'regional' and 'region' refer to the WPR.

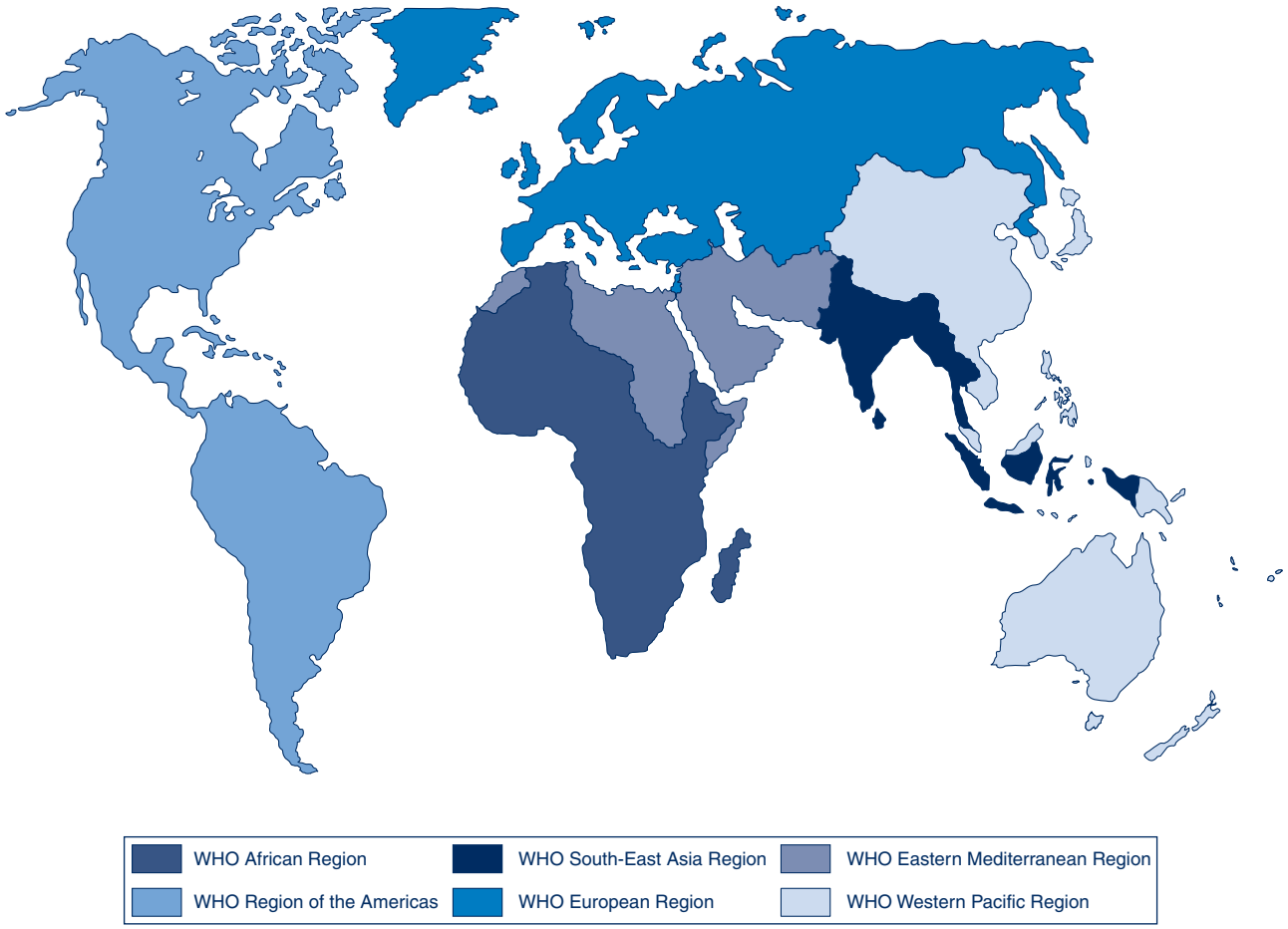

Figure 1. World Health Organization regions.
Source: World Health Organization.

these cases.[3] According to WHO, 84 countries have reported cases of extensively drug-resistant TB (XDR-TB). Within these countries, an average of 9% of MDR-TB cases have XDR-TB.[1] Eight of the 37 (22%) countries of the WPR have reported at least one case of XDR-TB.[5]

Particular challenges for TB control in Australia include its proximity to, and relationship with, Papua New Guinea (PNG), which had a TB incidence rate of 346 cases per 100 000 population in 2011.[1] The Torres Strait Protected Zone is an area within the narrow seaway separating Australia and PNG; scattered throughout are over 100 islands (22 of which are currently inhabited). People from the area are entitled to free movement between Australia and PNG. Past uncertainty as to the role of different agencies in treating people with TB in this area has resulted in a failure to control TB in the Zone and has provided possible avenues for transmission of MDR-TB to Australia. Significantly, transmission of MDR-TB has been recognised among PNG nationals accessing health care in the Torres Strait Islands of Queensland. From 2004 to 2007, 24 cases of MDR-TB were diagnosed among this group, representing a substantial demand on human and financial resources and highlighting the need for effective, collaborative TB control strategies.[2,4,6] While improvements in the care of MDR-TB have made it possible to manage the disease in most cases, it requires special multidisciplinary care by expert groups.[2,4] MDR-TB cases arising in the WPR will continue to have an impact on TB control in Australia in the future. TB services will need to plan to deal with these impacts.

The estimated prevalence of human immunodeficiency virus (HIV) in new TB cases in the WPR was 2.3% in 2010,[3] with countries ranging from less than 1% up to 15%. WHO reports that HIV has the potential to reverse the gains of TB control in several parts of the region, particularly in Cambodia, Malaysia, PNG, Viet Nam and areas of China.[3]

Diabetes is associated with an increased risk of progression to active TB disease. People with diabetes have a three times greater risk of developing TB following exposure, a four times greater risk of relapse post-TB treatment and a five times greater risk of death during TB treatment.[7] In 2011, the estimated prevalence of diabetes in the WPR was 8.5% for the adult population; this is expected to increase to 10.6% by 2030.[8] Within the WPR, Pacific Island countries/territories were reported as having the highest diabetes prevalence rates (15.5%) globally in 2008 and the largest rise in rates of fasting plasma glucose between 1980 and 2008.[9] In Palau, Guam, Federated States of

Figure 2. Countries and areas of the World Health Organization Western Pacific Region.
Source: World Health Organization.

Micronesia, Republic of Marshall Islands, American Samoa and Commonwealth of Northern Mariana Islands (Figure 2), TB programs are reporting 30–75% of their caseload as having co-morbid diabetes.[10] Diabetes is reported to affect 4% of the Australian population, having more than doubled between 1990 and 2008.[11] If diabetes prevalence rates continue to increase in Australia, this will probably influence the incidence of TB. Furthermore, increased numbers of people with co-morbid diabetes will lead to increasingly complex case management and greater challenges for TB services.

The Regional Strategy to Stop Tuberculosis in the Western Pacific (2011–2015)[3] was adopted by the Western Pacific Regional Office (WPRO) of WHO in October 2010 (Box 1). WHO data show that the WPR is on track to meet the United Nations Millennium Development Goals to halve the TB prevalence and mortality rates of the year 2000 by 2015.[1]

TB control strategies are implemented by each country in the WPR through their national TB control programs. Regional networks also exist to support these activities and include not only the WPRO, but also the Union Asia Pacific Region (Union APR) and the Secretariat of the Pacific Community (SPC). These latter networks provide structures through which the WPR can negotiate cooperative activity with neighbouring regions such as the SEAR.

Australia's current role in TB control in the WPR

Australia provides support for TB control in the WPR via a number of government, non-government and international organisations. Strengthening regional partnerships has long been recognised by Australian TB authorities as an important activity and is made explicit within the national strategy for TB control.[2,12] This approach also reflects Australia's current diplomatic approach which is "to connect and create partnerships that build and strengthen the global and regional rules-based order and have the capacity to solve shared global problems".[13] Regional partnerships offer opportunities to advocate for local and regional approaches to TB control, such as adequate resourcing of TB programs; workforce development, education and training; basic and operational research; as well as technical assistance provided through structured programs which service the recipient and provider by offering opportunities to gain and maintain skills. However, strengthening regional TB partnerships has, to date, been primarily a passive and opportunistic response by

Box 1. *Regional Strategy to Stop Tuberculosis (TB) in the Western Pacific (2011–2015)*

Goal

To reduce by half the prevalence of and mortality from all forms of TB by 2015, relative to 2000 levels, in all countries with a high burden of TB by moving towards universal access to diagnosis and treatment of all forms of TB, including smear-negative and multidrug and extensively drug-resistant TB.

Objectives

1. Promoting universal and equitable access to quality TB diagnosis and treatment for all people
2. Strengthening TB laboratory capacity
3. Scaling up the programmatic management of drug-resistant TB
4. Expanding TB/HIV collaborative activities
5. Strengthening TB program management capacity

Source: World Health Organization. Regional Strategy to Stop Tuberculosis in the Western Pacific 2011–2015.

individuals and organisations within Australia to an expressed need, rather than a structured strategic approach to regional disease control.

The Australian Government is committed to the United Nations Millennium Development Goals that aim to maximise the impact of foreign aid to improve the lives of the poor. TB has long been associated with poverty and those people vulnerable to ill health through socio-economic, biological and environmental factors.[14] Foreign aid constitutes 2% ($5.2 billion) of the Federal Budget in 2012–13. Seventy percent of the foreign aid budget in 2015 is to go to the Asia Pacific Region;[15] of this, approximately $1.5 billion will be spent in countries of the WPR. The funded programs support TB control by addressing poverty, improving policing and building stability (PNG, Solomon Islands, Vanuatu, Kiribati, Tuvalu and Nauru); improving access to immunisation, higher education and drinkable water (Kiribati); and improving education and agricultural productivity (Cambodia and Laos).[16] Of the foreign aid budget in 2012–13, $70 million is allocated to the Global Fund to Fight AIDS, Tuberculosis and Malaria.

Specific Australian TB promotion and support in the WPR

The Australian Government has recently endorsed *The strategic plan for control of tuberculosis in Australia: 2011–2015*.[2] While this plan outlines a strategy for TB control in Australia, it incorporates a regional approach to disease control and aligns Australian initiatives with those detailed in the WHO's *Regional Strategy to Stop Tuberculosis in the Western Pacific 2011–2015*.[3]

There are a range of agencies supporting TB control in the WPR. Australia's TB laboratory network, along with those from New Zealand and the United States, provide TB culture and drug susceptibility testing to countries of the WPR, as well as Timor-Leste. These networks also contribute to regional laboratory capacity building through education and training. Research organisations such as the Woolcock Institute of Medical Research, the Centenary Institute, the Burnet Institute, and the Walter and Eliza Hall Institute of Medical Research, as well as various Australian universities, have been investing in TB in the WPR and contributing to increased regional capacity for operational research. International advocacy agencies such as RESULTS (International) Australia actively lobby the Federal Government on regional aid issues, including TB.

Non-government agencies fund TB capacity building projects, such as the partnership between the Australian Respiratory Council (ARC), the Thoracic Society of Australia and New Zealand and the Cambodia Anti-Tuberculosis Association, combating TB in the villages and factories of Phnom Penh.

The ARC is the Australian constituent member of the International Union Against Tuberculosis and Lung Disease (the Union), the international organisation spearheading global efforts against TB throughout the last century. This relationship affords opportunities for regional dialogue on all aspects of TB control, via the Union APR Council and Scientific Committees. The ARC has been supporting regional education and training activities for clinicians, laboratories, nurses and allied health workers since the 1950s, most recently in partnership with the WPRO, SPC, the Pacific Island Health Officers' Association and the United States Centers for Disease Control and Prevention. Australian TB experts are engaged by countries themselves, the WPRO, the Union APR and SPC to provide technical assistance to TB programs and to participate in regional discussions on TB control, such as the biennial Pacific Stop TB meetings and Union APR Regional Conferences.

WHO, the Union APR and the SPC all struggle to meet the technical needs within the region. *The strategic plan for*

control of tuberculosis in Australia: 2011–2015 offers an opportunity for Australia to develop a more deliberate and structured approach to regional engagement for TB control.

TB control in Australia

As a developed nation and an island continent, Australia has enjoyed low indices for burden of TB disease (mortality, incidence, HIV co-infection, MDR-TB and XDR-TB disease).[4] The incidence of TB in Australia has remained low over the last 30 years (5–6 cases per 100 000 population),[4,17] however there has been little progress toward TB elimination (<1 case per million population).[1] Incidence rates for the Australian-born population have decreased while those for the overseas-born population are increasing.[4,17] There has been a continual increase in the number and rate of multidrug-resistant cases since 1995 to a rate of 2.9% of TB cases in 2009 ($n = 31$).[4,17] Almost 95% of MDR-TB cases are in the overseas-born population.[6] Regional success in controlling TB impacts on Australia's success in controlling this disease.[2,4,6] The pathogenesis and transmission of TB make it difficult to achieve elimination within a geographically bound area.[4] Globalisation and increasing economic and strategic engagement within the region amplifies this effect. Australia is dependent on immigration for population growth and economic development.[18] Australia's ability to maintain current indices of TB control and progress toward elimination within this environment requires not only a range of national strategies, but also international strategies which contribute to global efforts to combat the disease. Immigration trends need to be considered in the development of strategies for controlling TB in Australia.

The Australian National TB Program requires the Commonwealth, states and territories to work together. The Commonwealth monitors the incidence and prevalence of TB on a national basis using data from the states and territories. The National TB Advisory Committee provides expert guidance and support to the Commonwealth on issues related to TB control. The states and territories have complementary roles to the Commonwealth, including managing TB services; ensuring close working relationships between public health, laboratories, clinicians and TB services; and conducting research.[12] The TB programs in the states and territories are very differently structured and each have their own models of care for delivering TB services. Faced with increasing health system rationalisation and focus on acute care delivery and non-communicable diseases, Australian TB programs are increasingly reporting concerns regarding their sustainability and program maintenance.[19–22] These concerns relate to the ageing workforce, the provision of training and education, service fragmentation, financial resourcing, sustainable drug supply and access to vaccination for at-risk groups.

Australia's future role in TB control in the WPR

While it has been a considerable achievement to maintain a low TB incidence rate in Australia, progression towards TB elimination, and perhaps ongoing maintenance of current achievements, presents a significant challenge. The maintenance and advancement of TB control in Australia requires: a commitment to TB program funding at national, state and local levels; investment in basic and operational TB research in Australia and the WPR; and financial commitment to support regional collaboration among experts to address local and regional issues and to provide mentoring and technical support to regional partners. Strategic engagement with regional partners provides an opportunity to progress these objectives while also providing opportunities for Australian health workers to increase their knowledge and skills in TB management and to undertake TB research. Advocacy has a role to play in increasing the Australian public's understanding of TB and to mobilise community and public support for enhanced efforts toward TB elimination in Australia and the region.

Conclusion

The profile of TB in the WPR is reflected in the profile of TB in Australia. Australia's role in the WPR includes a range of capacity building, advocacy and research activities. Increased and strategic engagement within the region offers Australia an opportunity to progress towards TB elimination and to contribute to regional and global TB elimination efforts.

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Diagnosis, investigation and management of tuberculosis at an Australian zoo

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Human disease

Tuberculosis (*Mycobacterium tuberculosis*) is the greatest killer in human history, and it continues to be a significant problem today: it is estimated that one in three people in the world are infected with tuberculosis (TB).[1] Although more than 95% of infections occur in developing countries, in an increasingly globalised world with high levels of travel and migration it is important that countries such as Australia (with a relatively low incidence: 6 cases per 100 000 population in 2009) remain vigilant about this disease.[2]

Zoonotic disease

M. tuberculosis infections have been reported in a wide range of animal species.[3] This occurs by *reverse zoonosis*; that is, a human pathogen transmitted to animals. *M. tuberculosis* is emerging as an important disease of elephants. In parts of Asia, where there are high rates of human infection, many elephants are used in religious and cultural ceremonies, for transport, entertainment and tourism and live in close association with humans. Once infected by humans, animal-to-animal transmission can occur.[4]

Tuberculosis at an Australian zoo

In November 2010 a post-partum, clinically healthy Asian elephant cow tested positive on trunk wash culture for *M. tuberculosis* and subsequently underwent a 12-month course of treatment. In September 2011, on a routine health check, a male chimpanzee that had been unwell was found to have advanced active TB and was euthanased. In October 2011, genotyping confirmed the chimpanzee's isolate as identical to that of the elephant.

The animal investigation and management

The frequency of screening of elephants was increased and the remaining 17 chimpanzees were screened. Six chimpanzees had one or more positive TB tests but no evidence of active disease. These chimpanzees were treated prophylactically. Enhanced infection control and biosecurity measures were implemented and all outgoing mammal transactions were suspended. A program of screening and monitoring for the Zoo's entire mammal population commenced. No cases of TB have since been diagnosed in any Zoo mammal or wildlife from within the Zoo grounds.

The NSW Health investigation

After diagnosis of the elephant NSW Health screened, by tuberculin skin test (TST), more than 50 Zoo staff who had been in contact with the elephant. After the elephant and chimpanzee were linked in October 2011, the investigation was extended: an expert panel was convened and the screening population was widened. A total of 138 staff were screened by questionnaire and TST. Management included enhanced infection control measures and communication and education for Zoo staff.

No cases of active disease were found in Zoo staff. There was a paired TST conversion in four of 47 cases who had both pre- and post-exposure TSTs, and close contact with the elephant appeared to be the most likely risk factor in these conversions.

Transmission pathway investigation

There were several hypotheses as to how *M. tuberculosis* may have been transmitted from the elephant to the chimpanzee: aerosol, vector (e.g. bird, rodent, possum), elephant faeces or fomite (any object or substance capable of carrying infectious organisms, for example, soft vegetation such as leaves and branches used as animal food, equipment, clothing, waste disposal bins). The investigation included literature reviews, international consultation, on-site inspections, analysis of prevailing winds, analysis of staff and volunteer screening results and questionnaires. The study was unable to determine a plausible pathway of transmission that was consistent with the known transmission dynamics of *M. tuberculosis*.

This study highlights the value of systematic risk assessment in the management of TB in captive animals.

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Leprosy

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Leprosy is a chronic disease caused by the bacillus *Mycobacterium leprae*, and is closely related to tuberculosis. Leprosy remains a leading infectious cause of disability in the world today; untreated it can lead to progressive and permanent damage in the nerves, skin, limbs and eyes. It is believed to be transmitted primarily from person-to-person via nasal droplets. Although prevalence has reduced dramatically following the introduction of multidrug therapy, there are still approximately 250 000 new cases of leprosy every year, most of which occur in 17 countries including India (accounting for about half of all new cases), Brazil, Ethiopia, China and Indonesia.[1]

Leprosy is a relatively uncommon disease in Australia and New South Wales (NSW), with just 24 notifications in the state over the last 10 years. Most notifications are in migrants from countries where leprosy is endemic, with some locally acquired cases in Aboriginal communities.[2]

Leprosy is categorised according to the Ridley Jopling classification. On one end of the spectrum are patients with tuberculoid disease who have good cell-mediated immunity with few skin lesions and low bacterial load. At the other extreme are patients with lepromatous leprosy who have poor immunity and multiple lesions with high bacterial load. Between these two classifications are the borderline leprosy types, in which the immune response is thought to be unstable.

The World Health Organization (WHO) has introduced a simple classification that uses the number of skin lesions to classify disease as paucibacillary (up to five skin lesions) or multibacillary (more than five skin lesions). Multibacillary leprosy roughly correlates with the lepromatous side of the Ridley Jopling spectrum, and is both more infectious and takes longer to treat than other forms of the disease.[3]

Diagnosis

Diagnosis is based on clinical suspicion of leprosy as a cause of skin lesions, or peripheral nerve thickening or impairment in a person from a leprosy-endemic region. Confirmation is by demonstration of acid-fast bacilli in slit skin smears or biopsies. Other symptoms include numbness or tingling in the hands and feet and swelling of the face or earlobes. Nerve damage can take place before, during or after treatment and may cause long-term disability and disfigurement. Patients can suffer immune-mediated reversal reactions during or after treatment, including spontaneous increase in inflammation in skin and nerve lesions, and erythema nodosum leprosum. Reversal reactions occur in approximately 30% of multibacillary patients and require treatment with corticosteroids for at least 5 months.

Most leprosy cases can be effectively treated with a multidrug regimen for 6 (paucibacillary cases) or 12 (multibacillary cases) months. Patients are considered to be no longer infectious once they start multidrug therapy, and relapse rates are as low as 1% once treatment is complete.[3]

Prevention and control

The Bacille Calmette-Guérin vaccine given to prevent tuberculosis has a protective efficacy against leprosy of between 28 and 60%, and vaccine administration to neonates has contributed to a decrease in leprosy prevalence worldwide.

Leprosy is not highly infectious and the absolute risk of transmission has been estimated at 1% in endemic settings. Risk factors include proximity to a case for a prolonged period, for example through being in the same household. A single dose of rifampicin given to contacts of multibacillary patients has been found to reduce the incidence of leprosy in a 2-year period.[4]

Management of leprosy cases is sometimes complicated by the existing lack of clarity around the use of chemoprophylaxis in non-household contacts, as no definition exists of the amount of time or closeness of contact which places someone at risk. Further studies on the feasibility and cost-effectiveness of administering chemoprophylaxis to non-household contacts are needed.

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10.1071/NB12068

Communicable Diseases Report, NSW, November and December 2012

Communicable Diseases Branch
Health Protection NSW

For updated information, including data and facts on specific diseases, visit www.health.nsw.gov.au and click on **Public Health** and then **Infectious Diseases**. The communicable diseases site is available at: http://www.health.nsw.gov.au/publichealth/infectious/index.asp.

Figure 1 and Tables 1 and 2 show notifications of communicable diseases with onset in November and December 2012 in New South Wales (NSW).

Enteric infections

Outbreaks of suspected foodborne disease

There were seven outbreaks of suspected foodborne disease reported in NSW in the period (two in November and five in December), affecting at least 59 people. All outbreaks were thought to be caused by contaminated restaurant food. Of the seven outbreaks, three were reported directly to Public Health Units by the treating doctors or affected individuals, three were reported to the NSW Food Authority and one was identified from an investigation of *Salmonella* Singapore notifications clustered in time and location.

S. Singapore, *S.* Typhimurium and *Clostridium perfringens* caused illness in one outbreak each. However, despite thorough case interviews, the food vehicles could not be identified in these outbreaks as cases consumed multiple foods in each instance and no leftover foods were available for testing. In the remaining four outbreaks, the causative organism could not be identified due to either lack of stool collection from ill people and/or lack of sampling of suspected food vehicles.

Viral gastrointestinal disease

There were 115 outbreaks of gastroenteritis in institutions reported in NSW in the period (72 in November and 43 in December), affecting at least 1735 people. The previous 5-year average for this period was 51 outbreaks.

Of the 115 outbreaks:

- 52 outbreaks (45%) occurred in aged-care facilities; 41 (79%) of these had one or more stool samples collected – norovirus was confirmed in 17 (41%) outbreaks and rotavirus was confirmed in one (2%) outbreak.
- 46 outbreaks (40%) occurred in child-care centres; 7 (15%) of these had one or more stool samples collected – rotavirus was confirmed in one (14%) outbreak.
- 15 outbreaks (13%) occurred in hospitals; of these, one or more stool samples were collected in 14 (93%) outbreaks – norovirus was confirmed in 11 (79%) outbreaks and rotavirus was confirmed in one (7%) outbreak.
- Two outbreaks (2%) occurred in other health facilities and no stool samples were collected.

A stool specimen was collected in 62 outbreaks (54%); of these, no agent was identified in 32 outbreaks (52%).

Respiratory infections

Influenza

Influenza, as measured by the number of people who presented with influenza-like illness to 59 of the state's largest emergency departments, continued to circulate at low levels in NSW during November and December 2012. In addition, the number of people who tested positive for influenza A by diagnostic laboratories decreased to pre-seasonal levels throughout November and December after a peak in late June.

In November, there were:

- 68 presentations to emergency departments (rate 0.4 per 1000 presentations)
- 70 cases of laboratory-confirmed influenza including:
  - 14 (20%) influenza A
  - 56 (80%) influenza B.

In December, there were:

- 67 presentations to emergency departments (rate 0.4 per 1000 presentations)
- 45 cases of laboratory-confirmed influenza including:
  - 25 (56%) influenza A
  - 20 (44%) influenza B.

For a more detailed report on respiratory activity in NSW see: http://www.health.nsw.gov.au/PublicHealth/Infectious/influenza_reports.asp.

10.1071/NB13006

Vaccine-preventable diseases

Meningococcal disease

Five cases of meningococcal disease were notified in NSW in the period (three in November and two in December), a decrease from nine notified for the same period in 2011. The age of the cases ranged from 2 to 86 years; only one case was aged less than 5 years. An elderly woman from Hunter New England Local Health District died due to meningococcal B infection during this period.

Of the five cases, three (60%) were due to serogroup B (for which there is no vaccine), one (20%) was due to serogroup C, and one (20%) was due to serogroup Y. The notification of invasive meningococcal disease caused by serogroup C was in a 26-year old male traveller who had recently arrived from Europe.

Immunisation against meningococcal C disease is recommended for all children at the age of 12 months, as well as people at high risk of disease.[1]

Measles

Two cases of measles were notified in NSW in November and none in December. This was a decrease compared to the 77 notifications in September and October 2012. These two cases were the last associated with the measles virus genotype D8 outbreak that began in April. The outbreak was linked to a young traveller who was infected in Thailand.

The first case was a 13-year-old male from metropolitan Sydney with an unknown vaccination history. He was epidemiologically linked to his sister, who had previously been notified with laboratory-confirmed measles (measles virus genotype D8). The second case, the last of the outbreak, was a 14-year-old unvaccinated male from Sydney. The source of infection for this serologically-confirmed measles infection remains unknown.

Two doses of measles-mumps-rubella vaccine are recommended for all children (at 12 months and at 4 years of age),[1] as well as all young adults planning international travel.

Pertussis

There were 741 pertussis notifications in NSW during the reporting period (430 in November and 311 in December). This is approximately one-third of the 2120 cases notified for the same period in 2011, and represents the lowest number of notifications for this 2-month period since polymerase chain reaction diagnostic testing became widely adopted in 2008. Most cases were in the 5–9-year age group ($n = 212$), followed by the 10–14 ($n = 153$) and 0–4-year age groups ($n = 117$).

Direct protection for young infants remains available through free vaccination for pertussis that is administered at 2, 4 and 6 months of age. The first dose can be provided as early as 6 weeks of age. There is also a booster dose at 3½ to 4 years. New parents and grandparents should also discuss the benefits of pertussis vaccination for themselves with their general practitioner.

Sexually transmissible infections and bloodborne viruses

Chlamydia

After reaching a peak of 2047 notifications in February 2012, the number of monthly chlamydia notifications has decreased. There were 3291 notifications in NSW in November and December 2012, identical to the same period in 2011. A spike in chlamydia notifications is often seen at the beginning of the year, though it was particularly high in 2012.

Gonorrhoea

There were 635 confirmed cases of gonorrhoea notified in NSW in November and December, an increase of 5.8% compared to the same period in 2011 ($n = 600$). The majority of notifications were in males ($n = 508$), and the most commonly notified age group was 20–24 years ($n = 134$).

Syphilis

There were 58 syphilis notifications in NSW in November and 30 in December, a decrease since the monthly peak of 78 notifications in July. Delayed reporting may account for some of this decrease.

Lymphogranuloma venereum

There was an increase in the number of notifications of lymphogranuloma venereum in the second half of 2012. There were 11 notifications in NSW in November and December, which is higher than the same period in 2011 ($n = 4$). Of the 11 notifications, all were male, ranging in age from 18 to 75 years.

Reference

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Figure 1. Reports of selected communicable diseases, NSW, Jan 2004 to Dec 2012, by month of onset.
Preliminary data: case counts in recent months may increase because of reporting delays.
Laboratory-confirmed cases only, except for measles, meningococcal disease and pertussis.
BFV = Barmah Forest virus infections, RRV = Ross River virus infections, lab conf = laboratory confirmed, Men Gp C and Gp B = meningococcal disease due to serogroup C and serogroup B infection, other/unk = other or unknown serogroups.
NB: Multiple series in graphs are stacked, except gastroenteritis outbreaks.
NB: Outbreaks are more likely to be reported by nursing homes and hospitals than by other institutions.

NSW Population	
Male	50%
<5 y	7%
5–24 y	27%
25–64 y	53%
65+ y	13%
Rural	46%

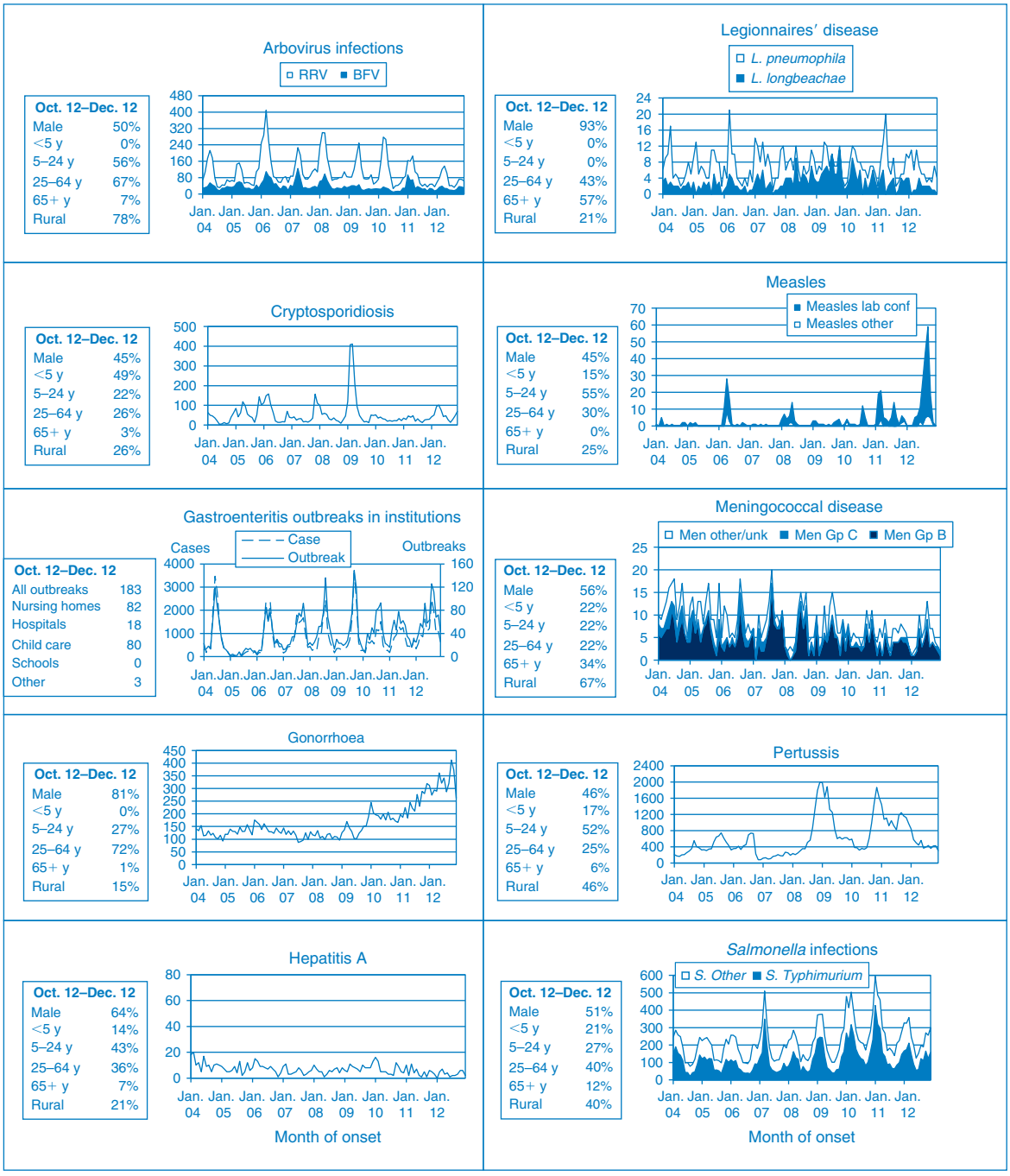

Table 1. Notifications of scheduled medical conditions with an onset date in November 2012 by Local Health District, NSW

Condition	Local Health District																Total	
	Murrumbidgee (including Albury)	Southern NSW	Western NSW	Far West	Hunter New England	Northern NSW	Mid North Coast	Central Coast	Northern Sydney	South Eastern Sydney	Illawarra Shoalhaven	Sydney	South Western Sydney	Western Sydney	Nepean Blue Mountains	Justice Health	For Nov[b]	Year to date[b]
Bloodborne and sexually transmissible																		
Chancroid[a]	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Chlamydia (genital)[a]	55	46	69	8	272	82	21	85	159	353	85	182	166	174	80	11	1851	19 801
Gonorrhoea[a]	–	5	2	2	26	5	2	10	29	129	9	75	26	44	6	3	373	3826
Hepatitis B – acute viral[a]	–	–	–	–	2	–	–	–	–	–	–	–	–	–	–	–	2	22
Hepatitis B – other[a]	2	–	3	–	6	–	–	1	25	21	3	35	37	32	6	1	172	2133
Hepatitis C – acute viral[a]	–	–	1	–	–	–	–	–	–	–	–	–	–	–	1	–	2	47
Hepatitis C – other[a]	11	4	14	2	32	17	8	22	11	14	15	24	44	28	12	25	283	3009
Hepatitis D – unspecified[a]	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	5
Lymphogranuloma venereum	–	–	–	–	–	–	–	–	–	3	–	–	1	–	–	–	4	28
Syphilis	–	–	–	–	7	–	–	1	4	17	4	12	5	7	1	–	58	739
Vectorborne																		
Barmah Forest virus[a]	2	–	1	–	12	16	4	–	–	–	–	–	–	–	–	–	35	313
Ross River virus[a]	9	1	6	–	5	8	4	2	–	–	–	–	–	–	2	–	37	563
Arboviral infection (other)[a]	–	–	–	–	1	3	–	–	4	4	–	–	–	2	1	–	15	265
Malaria[a]	–	1	–	–	1	–	1	–	–	–	–	–	–	3	–	–	6	67
Zoonoses																		
Anthrax[a]	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Brucellosis[a]	–	–	–	–	1	–	–	–	–	–	–	–	–	–	–	–	1	4
Leptospirosis[a]	–	–	1	–	–	–	–	–	–	–	–	–	–	–	–	–	1	18
Lyssavirus[a]	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Psittacosis[a]	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	13
Q fever[a]	–	3	2	–	1	1	1	–	–	–	1	–	–	–	–	–	9	98
Respiratory and other																		
Blood lead level[a]	6	1	6	6	3	1	–	1	1	3	1	3	1	–	1	–	34	532
Influenza[a]	3	2	4	3	30	8	2	1	6	32	1	10	12	13	6	–	133	7896
Invasive pneumococcal infection[a]	2	1	3	1	4	–	1	2	3	4	3	4	6	6	5	–	45	531
Legionella longbeachae infection[a]	–	–	–	–	–	–	–	–	–	–	–	–	–	1	–	–	1	24
Legionella pneumophila infection[a]	–	–	–	–	–	–	–	–	3	1	–	–	–	2	–	–	6	57
Legionnaires' disease (other)[a]	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	8
Leprosy	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Meningococcal infection (invasive)[a]	1	–	–	–	1	–	–	–	–	1	–	–	–	–	–	–	3	63
Tuberculosis	1	–	–	–	1	–	–	–	1	4	1	4	7	7	–	–	26	357
Vaccine-preventable																		
Adverse event after immunisation	–	–	–	–	2	–	–	1	4	–	–	–	2	2	–	–	11	181
H. influenzae b infection (invasive)[a]	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	2
Measles	–	–	–	–	–	–	–	–	–	–	–	–	1	1	–	–	2	173
Mumps[a]	–	–	–	–	–	–	–	–	–	–	1	–	–	–	1	–	2	99
Pertussis	35	18	23	–	58	13	5	21	55	84	29	9	17	44	19	–	430	5498
Rubella[a]	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	10
Tetanus	–	–	–	1	–	–	–	–	–	–	–	–	–	–	–	–	1	1
Enteric																		
Botulism	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Cholera[a]	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	2
Cryptosporidiosis[a]	1	–	3	–	4	2	–	1	3	18	1	7	3	2	2	–	47	611
Giardiasis[a]	3	3	7	–	16	–	–	5	23	35	9	21	6	17	10	–	155	1879
Haemolytic uraemic syndrome	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	9
Hepatitis A[a]	–	–	1	–	–	–	–	–	–	–	–	2	3	–	–	–	6	40
Hepatitis E[a]	–	–	–	–	–	–	–	–	–	–	–	1	–	1	–	–	2	10
Listeriosis[a]	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	31
Rotavirus[a]	17	4	5	–	32	6	–	1	13	12	–	9	12	11	5	–	127	1707
Salmonellosis[a]	11	7	12	–	37	15	6	10	34	25	17	16	25	24	17	–	256	2638
Shigellosis[a]	–	–	–	–	–	1	–	1	3	4	2	–	3	–	1	–	15	117
Typhoid[a]	–	–	–	–	–	–	–	–	–	–	–	–	–	1	–	–	1	36
Verotoxin-producing *E. coli*[a]	–	–	–	–	–	–	–	1	–	–	–	–	–	–	–	–	1	10
Miscellaneous																		
Creutzfeldt–Jakob disease	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	7
Meningococcal conjunctivitis	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–

[a]Laboratory-confirmed cases only. [b]Includes cases with unknown postcode.
NB: Data are current and accurate as at the preparation date. The number of cases reported is, however, subject to change, as cases may be entered at a later date or retracted upon further investigation.
Data are reported by Local Health District of residence (geocoded to 2011 boundaries).
Source: Notifiable Conditions Information Management System, NSW Ministry of Health.

Table 2. Notifications of scheduled medical conditions with an onset date in December 2012 by Local Health District, NSW

Condition	Local Health District																Total	
	Murrumbidgee (including Albury)	Southern NSW	Western NSW	Far West	Hunter New England	Northern NSW	Mid North Coast	Central Coast	Northern Sydney	South Eastern Sydney	Illawarra Shoalhaven	Sydney	South Western Sydney	Western Sydney	Nepean Blue Mountains	Justice Health	For Dec[b]	Year to date[b]
Bloodborne and sexually transmissible																		
Chancroid[a]	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Chlamydia (genital)[a]	60	24	57	6	223	50	30	75	123	220	81	141	126	142	70	11	1440	21 241
Gonorrhoea[a]	1	1	6	1	14	6	2	7	14	74	5	64	13	43	10	1	262	4088
Hepatitis B – acute viral[a]	–	–	–	–	2	1	–	–	–	2	–	–	1	–	1	–	7	29
Hepatitis B – other[a]	2	1	1	1	5	1	–	3	25	8	1	23	33	50	1	2	157	2290
Hepatitis C – acute viral[a]	–	–	3	–	–	–	–	–	–	–	–	–	–	–	–	1	4	51
Hepatitis C – other[a]	10	11	10	1	28	18	4	13	12	12	21	17	20	20	9	18	224	3233
Hepatitis D – unspecified[a]	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	5
Lymphogranuloma venereum	–	–	–	–	–	–	–	–	–	5	–	2	–	–	–	–	7	35
Syphilis	–	–	–	–	1	1	–	1	4	12	3	1	1	5	1	–	30	769
Vectorborne																		
Barmah Forest virus[a]	–	–	–	–	12	6	5	2	1	–	3	1	–	–	–	–	30	343
Ross River virus[a]	8	1	4	1	6	6	1	1	2	–	2	–	1	–	2	–	35	598
Arboviral infection (other)[a]	–	–	–	–	2	2	–	–	4	–	1	1	2	1	–	–	13	278
Malaria[a]	–	–	–	–	1	–	–	–	–	–	–	–	–	1	–	–	2	69
Zoonoses																		
Anthrax[a]	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Brucellosis[a]	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	4
Leptospirosis[a]	–	–	–	–	1	–	–	–	–	–	–	–	–	–	–	–	1	19
Lyssavirus[a]	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Psittacosis[a]	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	13
Q fever[a]	–	–	–	–	2	1	1	–	1	–	–	–	–	–	–	–	5	103
Respiratory and other																		
Blood lead level[a]	–	–	7	–	6	–	–	1	–	1	–	–	–	1	3	–	19	551
Influenza[a]	1	1	4	2	11	6	1	1	11	23	5	5	10	4	3	–	88	7984
Invasive pneumococcal infection[a]	1	1	–	–	5	1	1	1	2	6	5	–	2	4	3	–	32	563
Legionella longbeachae infection[a]	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	24
Legionella pneumophila infection[a]	–	–	–	–	–	–	–	–	2	–	1	–	–	1	–	–	4	61
Legionnaires' disease (other)[a]	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	8
Leprosy	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Meningococcal infection (invasive)[a]	–	1	–	–	–	–	–	–	–	–	–	1	–	–	–	–	2	65
Tuberculosis	1	–	–	–	1	–	–	–	–	3	–	5	7	1	–	–	18	375
Vaccine-preventable																		
Adverse event after immunisation	1	–	2	–	1	–	–	–	–	–	1	–	1	1	–	–	7	188
H. influenzae b infection (invasive)[a]	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	2
Measles	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	173
Mumps[a]	–	–	–	–	–	2	–	–	–	1	–	–	1	1	–	–	5	104
Pertussis	29	16	12	–	28	19	1	14	51	38	22	13	14	41	13	–	311	5809
Rubella[a]	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	10
Tetanus	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1
Enteric																		
Botulism	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Cholera[a]	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	2
Cryptosporidiosis[a]	1	1	6	–	6	4	–	1	6	18	3	10	5	7	1	–	69	680
Giardiasis[a]	5	3	9	–	20	1	1	3	21	29	2	13	11	5	4	–	127	2006
Haemolytic uraemic syndrome	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	9
Hepatitis A[a]	–	–	–	–	–	–	–	–	1	–	–	–	–	1	–	–	2	42
Hepatitis E[a]	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	10
Listeriosis[a]	–	–	–	–	–	–	–	–	1	3	3	1	1	–	–	–	9	40
Rotavirus[a]	4	3	3	–	15	5	–	–	–	6	–	2	2	4	1	–	45	1752
Salmonellosis[a]	20	3	9	1	31	19	14	10	37	40	15	22	26	38	15	–	300	2938
Shigellosis[a]	–	–	–	–	–	1	–	–	1	1	–	1	–	–	–	–	4	121
Typhoid[a]	–	–	–	–	–	–	–	–	1	2	–	–	2	1	–	–	6	42
Verotoxin-producing *E. coli*[a]	–	–	–	–	1	–	–	–	–	–	–	–	–	–	–	–	1	11
Miscellaneous																		
Creutzfeldt–Jakob disease	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	7
Meningococcal conjunctivitis	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–

[a]Laboratory-confirmed cases only. [b]Includes cases with unknown postcode.
NB: Data are current and accurate as at the preparation date. The number of cases reported is, however, subject to change, as cases may be entered at a later date or retracted upon further investigation.
Data are reported by Local Health District of residence (geocoded to 2011 boundaries).
Source: Notifiable Conditions Information Management System, NSW Ministry of Health.

Contents

NSW PUBLIC HEALTH BULLETIN

The *NSW Public Health Bulletin* is a peer-reviewed journal produced by the NSW Ministry of Health and indexed in Medline. It has a NSW focus, however, it aims to support the practice of public health more broadly.

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eISSN 1834-8610

The *Bulletin* uses digital publishing at all stages of production as a priority over print. The *Bulletin* is printed on archival quality, chlorine-free paper using low volatility vegetable-based inks and uses computer-to-plate technology. The acid-free paper meets the standards of the American National Standards Institute for Information Sciences–Permanence of Paper for Printed Library Materials, ANSI Z39.48-1992.

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