

Rates of radiologically confirmed pneumonia as defined by the World Health Organization in Northern Territory Indigenous children

Kerry-Ann F O'Grady, Debbie M Taylor-Thomson, Anne B Chang, Paul J Torzillo, Peter S Morris, Grant A Mackenzie, Gavin R Wheaton, Paul A Bauert, Margaret P De Campo, John F De Campo and Alan R Ruben

Acute lower respiratory infections and pneumonia are major causes of morbidity in Indigenous children,^{1,2} but systematically evaluated data on the burden of these diseases are lacking. Most studies of disease resulting in hospitalisation have relied on hospital discharge diagnosis codes, which may be influenced by changes in clinician practices and coding procedures over time.

In 2001, the World Health Organization published guidelines for the standardised measurement in research of radiologically apparent pneumonia in children.³ These guidelines are now the benchmark on which burden of disease and intervention studies are based.

According to the WHO protocol, radiologically confirmed pneumonia — endpoint consolidation — is defined as “dense opacity ... fluffy consolidation of a portion or whole of a lobe or of the entire lung, often containing air bronchograms and sometimes associated with pleural effusion”.³ We studied the incidence of hospitalised, radiologically confirmed pneumonia in Northern Territory Indigenous children admitted to hospital over an 8-year period.

METHODS

Design

We conducted a historical observational study between 1 April 1997 and 31 March 2005 of all NT hospital admissions, irrespective of diagnosis, of Indigenous children aged ≥ 29 days and < 5 years at the time of admission. Admissions were excluded if the child did not reside in the NT, or the location of residence was unknown or not specified. All chest x-rays taken during all admissions were reviewed, but those taken more than 3 days from the date of admission were excluded as being more likely to represent nosocomial infections. The primary outcome was endpoint consolidation seen on a chest x-ray taken ≤ 3 days after admission.

Setting

In 2001, the NT had an estimated resident population of about 197 800 people⁴ dispersed across 1 346 200 km²; 29% of the

ABSTRACT

Objective: To determine the burden of hospitalised, radiologically confirmed pneumonia (World Health Organization protocol) in Northern Territory Indigenous children.

Design, setting and participants: Historical, observational study of all hospital admissions for any diagnosis of NT resident Indigenous children, aged between ≥ 29 days and < 5 years, 1 April 1997 to 31 March 2005.

Intervention: All chest radiographs taken during these admissions, regardless of diagnosis, were assessed for pneumonia in accordance with the WHO protocol.

Main outcome measure: The primary outcome was endpoint consolidation (dense fluffy consolidation [alveolar infiltrate] of a portion of a lobe or the entire lung) present on a chest radiograph within 3 days of hospitalisation.

Results: We analysed data on 24 115 hospitalised episodes of care for 9492 children and 13 683 chest radiographs. The average annual cumulative incidence of endpoint consolidation was 26.6 per 1000 population per year (95% CI, 25.3–27.9); 57.5 per 1000 per year in infants aged 1–11 months, 38.3 per 1000 per year in those aged 12–23 months, and 13.3 per 1000 per year in those aged 24–59 months. In all age groups, rates of endpoint consolidation in children in the arid southern region of NT were about twice that of children in the tropical northern region.

Conclusion: The rates of severe pneumonia in hospitalised NT Indigenous children are among the highest reported in the world. Reducing this unacceptable burden of disease should be a national health priority.

MJA 2010; 192: 592–595

See also page 586

population identify as Aboriginals or Torres Strait Islanders. Two climate zones exist in the NT: tropical in the north (the “Top End”) and arid in the south (the “Centre”). The average annual population of NT resident Indigenous children aged between ≥ 29 days and < 5 years over the study period was 7214 (range, 7047–7382).

All Indigenous children requiring hospitalisation are admitted to one of the five public hospitals in the NT, including those who need subsequent transfer to larger institutions in other states. The nearest public hospitals in other states are hundreds of kilometres from the NT borders. While not formally documented, expert opinion indicates that out-of-hospital deaths in the NT are rare.

X-ray facilities are not available in remote communities. However, given the high incidence of multiple morbidities in Indigenous children, clinical algorithms specify that all Indigenous children admitted to hospital with respiratory illnesses, gastroenteritis, malnutrition, failure to thrive and/or anaemia have a chest x-ray on admission.

Hospitalisation data

Up to 30 June 1998, the International classification of diseases, 9th revision, clinical modification (ICD-9-CM), was used for morbidity coding of records; for the remaining years, the 10th revision, Australian modification (ICD-10-AM) was used. Box 1 shows the hierarchy of diagnosis codes selected. Unique health record numbers permit linking of data and tracking of individuals in the NT public hospital system.

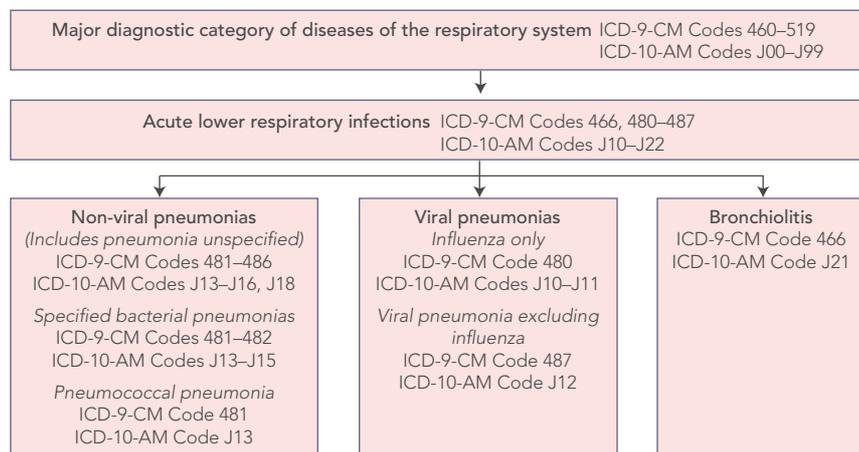
Radiological data

All chest x-rays corresponding to inpatient episodes of care were obtained, de-identified, and a randomly generated, unique study number was assigned to each film. Inpatient episodes of care for which no x-ray was taken, or the x-ray taken could not be found, were recorded as “not done”, or “missing”, respectively.

A panel of seven paediatric and respiratory physicians assigned the presence of endpoint consolidation (yes or no) for each



1 Hierarchical selection of ICD-9-CM and ICD-10-AM codes for analysis



ICD-9-CM = International classification of diseases, 9th revision, clinical modification.
ICD-10-AM = International classification of diseases, 10th revision, Australian modification.

2 Demographic characteristics of children hospitalised and the episodes of care

Characteristic	No. (%) children	No. (%) episodes
Sex		
Male	5 115 (53.9%)	13 281 (55.1%)
Female	4 376 (46.1%)	10 828 (44.9%)
Not specified	1 (0.0)	6 (0.02%)
Total	9 492 (100%)	24 115 (100%)
Age group (months) at the time of admission*		
1–11	5 426 (57.2%)	9 997 (41.5%)
12–23	4 432 (46.7%)	7 225 (30.0%)
24–59	4 291 (45.2%)	6 893 (28.6%)
Northern Territory region		
Top End	5 887 (62.0%)	13 402 (55.6%)
Centre	3 543 (37.3%)	10 612 (44.0%)
Key comorbidities diagnosed at least once†		
Gastrointestinal disorders	4 891 (51.5%)	8 439 (34.9%)
Metabolic disturbance‡	1 468 (15.5%)	2 319 (9.6%)
Anaemia	3 288 (34.6%)	4 977 (20.6%)

* Individual children may be represented more than once (eg, admitted when aged 1–11 months and readmitted when aged 12–23 months). † Number of episodes of care in which a comorbidity was diagnosed. ‡ Includes malnutrition, failure to thrive.

x-ray film, and each film was read independently by two readers. An expert panel consisting of two paediatric radiologists reviewed films in which there was disagreement about the presence of endpoint consolidation or the film's quality for determining this, reading them together for adjudication. All readers were trained and their skills calibrated against the set of training films provided by the WHO; a threshold of at least 80% agreement with the WHO diagnosis had to be met by each reader

before commencing study readings. Inter-observer agreement on the presence of endpoint consolidation was at least 90%.

Readers were blinded to all information about the episode, discharge diagnosis and vaccination status. The panel reviewing x-ray films for which agreement had not been reached was not aware of the reasons for disagreement, nor of the identity of the original readers. An unreadable film was considered negative for endpoint consolidation.

Statistical analyses

The primary analysis was the cumulative incidence of endpoint consolidation, stratified by age group of the child and NT health region, with calculation of incidence rate ratios. All instances of endpoint consolidation, irrespective of the discharge diagnosis, were included in the analysis to maximise the capture of cases and to ensure that the case definition for the primary analysis was systematically applied over time. Incidence rate ratios were computed to compare rates by NT region and sex. Denominators — the estimated resident population for each year of the study — were obtained from the Australian Bureau of Statistics and the NT Department of Health and Families. Data were analysed using Stata SE, version 9.1 (StataCorp, College Station, Tex, USA).

Ethics approval

The study was approved by the joint institutional Human Research Ethics Committee of the NT Department of Health and Community Services and the Menzies School of Health Research (HREC ID: 02/63), and by the Human Research Ethics Committee of Central Australia. Both committees have Indigenous Health Research Ethics Subcommittees.

RESULTS

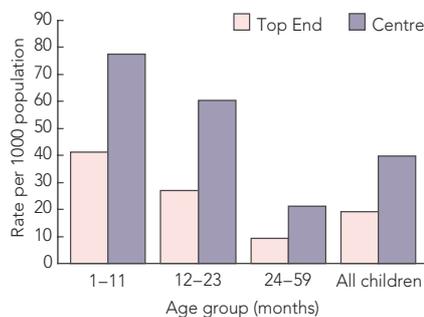
Final dataset

Between 1 April 1997 and 31 March 2005, there were 24 820 admitted episodes of care for 9787 Indigenous children (regardless of NT residence) aged between ≥ 29 days and < 5 years (median age, 2; range, 1–39 episodes per child). In 10 911 episodes (43.9%) no chest x-ray was taken, and in 64 episodes (0.3%) the film was missing; 18 224 x-rays were located and assessed for endpoint consolidation (median, 1; range, 0–142 per episode). The proportion of admissions in which x-rays were taken remained stable over the study period (an average of 56% of all hospitalisations).

Of the 24 820 admitted episodes of care, 705 episodes for 295 children and 4541 chest x-rays were excluded from the analysis as they did not meet eligibility criteria (child not an NT resident, x-ray taken ≥ 3 days after admission). The final dataset comprised 24 115 admitted episodes of care for 9492 children and 13 683 x-rays. Box 2 gives the demographic characteristics of the children and the episodes of care.



3 Average annual incidence of endpoint consolidation per 1000 population: by Northern Territory region and child's age group



Radiologically confirmed pneumonia

Overall, in 13 205 episodes of care (54.7%), irrespective of diagnosis, chest x-rays were taken within 3 days; endpoint consolidation was found in 11.6% (1535) of these; film quality was inadequate in 14.0% (1854).

The 1535 episodes of endpoint consolidation occurred in 1211 children with a range of 1–16 episodes per child (one episode, 937 children; two or more episodes, 274 children). Median age at the time of admission was 15 months (range, 1–59 months); 40.8% of episodes were for children aged <12 months and 23% were for children aged <6 months. Rates were 1.22 times higher for boys (95% CI, 1.19–1.26; $P < 0.001$), and 2.1 times higher in children in the southern region of NT (Centre) (95% CI, 1.6–2.8) compared with the Top End (Box 3). The average annual cumulative incidence of endpoint consolidation was 26.6 per 1000 population per year (95% CI, 25.3–27.9); 57.5 per 1000 per year in

infants aged 1–11 months, 38.3 per 1000 per year in those aged 12–23 months, and 13.3 per 1000 per year in those aged 24–59 months. Annual rates for each year of the study by age group are shown in Box 4.

Chest x-rays were taken within 3 days of admission in 6852 of the 8518 episodes (80.4%) with any diagnosis in the category, acute lower respiratory infection (ALRI). Film quality was inadequate for determining endpoint consolidation in 1305 (19.0%) episodes with ALRI. Endpoint consolidation was diagnosed in 20.4% of episodes with ICD-defined ALRI (1401/6852); 33.2% with non-viral pneumonia (1178/3551); 40.4% with pneumococcal pneumonia (21/52); 13.8% with influenza (32/232) (of which 3% had a concomitant diagnosis of non-viral pneumonia); and 9.2% with bronchiolitis (226/2455) (of which 43% had a concomitant diagnosis of non-viral pneumonia).

Sixty-four episodes with endpoint consolidation had no respiratory diagnosis recorded (4.2% of endpoint consolidation episodes). There were 258 diagnoses attached to these episodes; 59 (22.9%) were conditions listed under the major diagnostic category of infectious and parasitic diseases (predominantly gastrointestinal infections); 55 (21.3%) were haematological and metabolic disorders; 36 (14.0%) were related to external causes and injury (eg, trauma or near drowning) and 10 (3.9%) were ear diseases. The remainder were scattered across other diagnostic categories. As coding errors cannot be excluded, these episodes were included in the analysis.

There were differing seasonal patterns of endpoint consolidation and other respiratory diagnoses between the NT regions. Episodes of endpoint consolidation were

more frequent in the winter and spring months in the Central Australian region of NT; in the Top End region, episodes were more evenly distributed across the year.

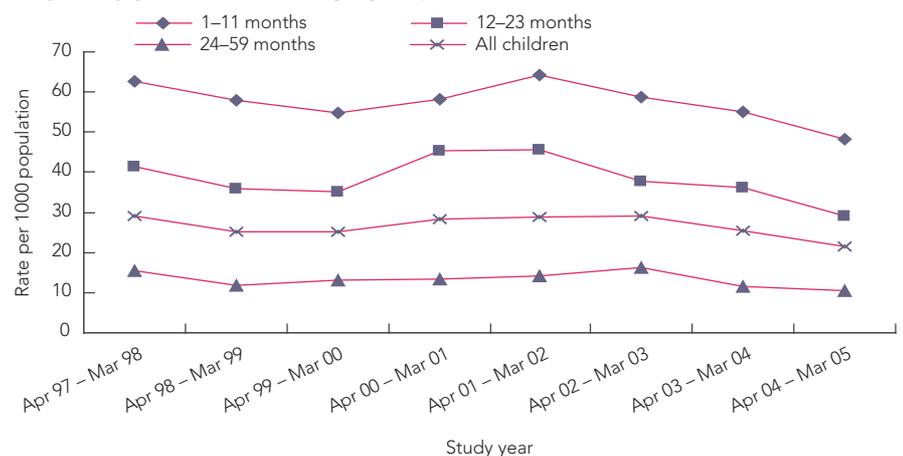
DISCUSSION

We found that the annual incidence of endpoint consolidation in NT children under 5 years of age approximates 3%, and in infants aged under 12 months it is as high as 7%. Differences in study design, case ascertainment, and populations complicate direct comparisons; however, rates of WHO-defined endpoint consolidation in NT children are between three and 25 times higher than found elsewhere. The rates in children aged less than 12 months in the Central Australian region of the NT are the highest reported in the world.

Case ascertainment differences may partially explain the high rates of endpoint consolidation we found. First, the entire NT hospitalised population was included, and hospital access has been improving over the past two decades; and, second, we included remote-living children. Comparable data on children in other disadvantaged populations are from studies in predominantly urban or peri-urban populations; children from rural and remote areas, with substantially less access to health services and with differing risk-factor profiles, would have been missed. These studies are from The Gambia (53.0/1000; aged 1–11 months),⁵ Philippines (13.5/1000; aged 6 weeks to 23 months),⁶ Indonesia (8.9/1000; aged 1.5–23 months),⁷ Chile (5.0/1000; aged 4–23 months),⁸ Fiji (4.3/1000; aged 1–59 months),⁹ Uruguay (up to 16.9/1000; aged 0–59 months)¹⁰ and South Africa (4.9/1000; aged 1.5–30 months).¹¹ Furthermore, we included all chest x-rays taken within the first 3 days of admission. Studies including only x-rays taken on the day of admission may miss some cases, as clinical pneumonia may precede radiologically confirmed endpoint consolidation.

Indigenous children in the NT may have a different risk factor and health care access profile, predisposing them to infection and hospitalisation. Underlying medical conditions or comorbidities (eg, malnutrition, anaemia and gastrointestinal infections) are common,^{12,13} and the high prevalence of low-birthweight infants is well documented.^{14–16} Overcrowding, excessive pneumococci and non-typeable *Haemophilus influenzae* carriage rates in early infancy,^{17,18} and repeated infections leading to bron-

4 Cumulative incidence of endpoint consolidation per 1000 population per year, by study year and child's age group



chiectasis and chronic lung disease^{19,20} may play an important role in disease burden.

The major limitations of our study were its retrospective nature, the inclusion of hospitalised children only, and the use of a specific case definition as the primary outcome. The results should be viewed as an underestimate of the true incidence of disease. Most children with ALRI are treated in the community without a chest x-ray and antibiotic use is high.

Measurement error leading to an overestimation of disease incidence is unlikely. All readers were blinded to the clinical diagnosis associated with each chest x-ray film. While readers might have been influenced by knowing that they were examining x-rays from a high-risk population, the incidence of end-point consolidation found was lower than that anticipated from a priori estimates based on data from Central Australia.²¹ Furthermore, the proportion of admitted episodes of care deemed positive for endpoint consolidation (20% of all episodes of ALRI in which a chest x-ray was taken) was similar to that reported in other studies.^{5,11,22}

The rates of pneumonia in Indigenous children hospitalised in the NT are among the highest reported in the world. This is unacceptable in a wealthy country like Australia, and reducing this disease burden should be a national priority. Ongoing surveillance programs incorporating aetiological studies and innovative interventions are urgently required.

ACKNOWLEDGEMENTS

We thank Ross Andrews, Joan Cunningham (Menzies School of Health Research); Terry Nolan (University of Melbourne); John Carlin, Suzanna Vidmar (Murdoch Childrens Research Institute); Jane Benson (Johns Hopkins University Hospital); and Kim Mulholland, Tilman Ruff, and Thomas Cherian.

Kerry-Ann O’Grady was supported by a National Health and Medical Research Council (NHMRC) Postgraduate Training Scholarship in Indigenous Health, and by the Australian Academy of Science’s Douglas and Lola Douglas Scholarship in Medical Research.

COMPETING INTERESTS

Wyeth Vaccines provided funding for the study, but had no role in the design, data collection, analysis and interpretation, writing, or publication of the article. Kerry-Ann O’Grady has been a senior research officer on sponsored vaccine trials (Glaxo-SmithKline, Wyeth, Merck Sharp & Dohme, MedImmune, and CSL) and a recipient of funds for epidemiological research (GlaxoSmithKline).

AUTHOR DETAILS

Kerry-Ann F O’Grady, GDipPH, MAppEpid, PhD, NHMRC Post-Doctoral Training Fellow, Child Health Division^{1,2,3}

Debbie M Taylor-Thomson, BPharm, Senior Project Officer, Menzies School of Health Research¹

Anne B Chang, FRACP, MPHTM, PhD, Professor, and Head, Child Health Division¹

Paul J Torzillo, AM, MB BS, FRACP, FJFICM, Associate Professor, Department of Respiratory Medicine,⁴ and Director, Nganampa Health Service

Peter S Morris, MB BS, FRACP, PhD, Paediatrician and Deputy Leader, Child Health Division^{1,5}

Grant A Mackenzie, MB BS, PhD, Clinical Epidemiologist⁶

Gavin R Wheaton, MB BS, FRACP, FCSANZ, Cardiologist, Women’s and Children’s Hospital Adelaide⁷

Paul A Bauert, MB BS, FRACP, Head, Department of Paediatrics⁸

Margaret P De Campo, FRANZCR, MPH, GDipEpiBiostats, Associate Professor, Department of Medicine⁹

John F De Campo, FRANZCR, MHA, FRACMA, Professor, Department of Medicine⁹

Alan R Ruben, MB BS, MAppEpid, Paediatrician⁵

- 1 Menzies School of Health Research, Charles Darwin University, Darwin, NT.
- 2 School of Population Health and Department of Paediatrics, University of Melbourne, Melbourne, VIC.
- 3 Vaccine and Immunisation Research Group, Murdoch Childrens Research Institute, Melbourne, VIC.
- 4 Royal Prince Alfred Hospital, University of Sydney, Sydney, NSW.
- 5 Northern Territory Clinical School, Flinders University, Darwin, NT.
- 6 Bacterial Diseases Program, Medical Research Council (UK) Laboratories, Fajara, The Gambia.
- 7 Department of Clinical Effectiveness, School of Medicine, Faculty of Health Sciences, Flinders University, Adelaide, SA.
- 8 Royal Darwin Hospital, Darwin, NT.
- 9 Bond University, Gold Coast, QLD.

Correspondence: k.ogradey@uq.edu.au

REFERENCES

- 1 Carville KS, Lehmann D, Hall G, et al. Infection is the major component of the disease burden in Aboriginal and non-Aboriginal Australian children: a population-based study. *Pediatr Infect Dis J* 2007; 26: 210-216.
- 2 Burgner D, Richmond P. The burden of pneumonia in children: an Australian perspective. *Paediatr Respir Rev* 2005; 6: 94-100.
- 3 World Health Organization Pneumonia Vaccine Trial Investigators Group. Standardization of interpretation of chest radiographs for the diagnosis of pneumonia in children. Geneva: World Health Organization Department of Vaccines and Biologicals, 2001. <http://www.who.int/vaccines-documents/DocsPDF01/www616.pdf> (accessed Mar 2010).
- 4 Australian Bureau of Statistics. Census of population and housing: selected social and housing characteristics for Statistical Local Areas, Northern Territory, 2001. (ABS Cat. No. 2015.7.)
- 5 Cutts FT, Zaman SM, Enwere G, et al. Efficacy of nine-valent pneumococcal conjugate vaccine against pneumonia and invasive pneumococcal disease in The Gambia: randomised, double-blind,

- placebo-controlled trial. *Lancet* 2005; 365: 1139-1146.
- 6 Lucero MG, Nohynek H, Williams G, et al. Efficacy of an 11-valent pneumococcal conjugate vaccine against radiologically confirmed pneumonia among children less than 2 years of age in the Philippines: a randomized, double-blind, placebo-controlled trial. *Pediatr Infect Dis J* 2009; 28: 455-462.
- 7 Gessner BD, Sutanto A, Linehan M, et al. Incidences of vaccine-preventable *Haemophilus influenzae* type b pneumonia and meningitis in Indonesian children: hamlet-randomised vaccine-probe trial. *Lancet* 2005; 365: 43-52.
- 8 Levine OS, Lagos R, Munoz A, et al. Defining the burden of pneumonia in children preventable by vaccination against *Haemophilus influenzae* type b. *Pediatr Infect Dis J* 1999; 18: 1060-1064.
- 9 Magree HC, Russell FM, Sa’aga R, et al. Chest x-ray confirmed pneumonia in children in Fiji. *Bull World Health Organ* 2005; 83: 427-434.
- 10 Hortal M, Estevan M, Iraola I, De Mucio B. A population-based assessment of the disease burden of consolidated pneumonia in hospitalized children under five years of age. *Int J Infect Dis* 2007; 11: 273-277.
- 11 Klugman KP, Madhi SA, Heubner R, et al. A trial of a 9-valent pneumococcal conjugate vaccine in children with and those without HIV infection. *N Engl J Med* 2003; 349: 1341-1348.
- 12 Paterson B, Ruben A, Nossar V. School screening in remote Aboriginal communities — results of an evaluation. *Aust N Z J Public Health* 1998; 22: 685-689.
- 13 Ruben AR, Walker AC. Malnutrition among rural Aboriginal children in the Top End of the Northern Territory. *Med J Aust* 1995; 162: 400-403.
- 14 Mackerras DE, Reid A, Sayers SM, et al. Growth and morbidity in children in the Aboriginal Birth Cohort Study: the urban-remote differential. *Med J Aust* 2003; 178: 56-60.
- 15 Gogna NK, Smiley M, Walker AC, Fullerton P. Low birthweight and mortality in Australian Aboriginal babies at the Royal Darwin Hospital: a 15-year study. *Aust Paediatr J* 1986; 22: 281-284.
- 16 Rousham EK, Gracey M. Factors affecting birth-weight of rural Australian Aborigines. *Ann Hum Biol* 2002; 29: 363-372.
- 17 Leach AJ, Boswell JB, Asche V, et al. Bacterial colonization of the nasopharynx predicts very early onset and persistence of otitis media in Australian Aboriginal infants. *Pediatr Infect Dis J* 1994; 13: 983-989.
- 18 Smith-Vaughan HC, Leach AJ, Shelby-James TM, et al. Carriage of multiple ribotypes of non-encapsulated *Haemophilus influenzae* in Aboriginal infants with otitis media. *Epidemiol Infect* 1996; 116: 177-183.
- 19 Valery PC, Torzillo PJ, Mulholland K, et al. Hospital-based case-control study of bronchiectasis in Indigenous children in Central Australia. *Pediatr Infect Dis J* 2004; 23: 902-908.
- 20 Chang AB, Masel JP, Boyce NC, Torzillo PJ. Respiratory morbidity in central Australian Aboriginal children with alveolar lobar abnormalities. *Med J Aust* 2003; 178: 490-494.
- 21 Torzillo P, Dixon J, Manning K, et al. Etiology of acute lower respiratory tract infection in Central Australian Aboriginal children. *Pediatr Infect Dis J* 1999; 18: 714-721.
- 22 Hansen J, Black S, Shinefield H, et al. Effectiveness of heptavalent pneumococcal conjugate vaccine in children younger than 5 years of age for prevention of pneumonia: updated analysis using World Health Organization standardized interpretation of chest radiographs. *Pediatr Infect Dis J* 2006; 25: 779-781.

(Received 20 Jul 2009, accepted 7 Oct 2009) □

