Lower Respiratory Tract Infections

Lower respiratory tract infections (LRTIs) including pneumonia, bronchiolitis, bronchitis (viral and bacterial) and pertussis (whooping cough) are among the most common paediatric diseases encountered in primary care, and are responsible for a large burden of avoidable morbidity and mortality in childhood.1 Individuals experiencing LRTIs may present with shortness of breath, high fever, coughing and fatigue, but the symptoms of LRTIs can be non-specific in very young children. While mild cases can be self-limiting, more serious infections may be life threatening and/or cause ongoing respiratory morbidity with irreversible lung changes.2

According to the World Health Organisation’s (WHO) estimates for 2002, LRTIs were the leading cause of death among all infectious diseases worldwide, accounting for 3.9 million deaths and 6.8% of all reported deaths that year.3 Since 1990, when the WHO began compiling and presenting statistics on the burden of lung infections, LRTIs have been found to consistently cause more burden (measured using the metric of disability-adjusted life years lost) than diseases such as HIV/AIDS, neoplasms, diarrhoeal disease, ischaemic heart disease, cerebrovascular disease, malaria, tuberculosis, chronic obstructive pulmonary disease (COPD), diabetes mellitus and asthma.4 Further concern is raised when recurrent, persistent or a severe LRTI develops into irreversible lung disease with chronic infection as seen with chronic suppurrative lung diseases including bronchiectasis.5

Surprisingly, LRTIs receive disproportionately little attention from the biomedical and public health communities.6 The disease does lack a single clear aetiological cause, but overall this important cause of human suffering does not receive due attention. Delivering preventative interventions for LRTIs has the potential for tremendous short- and long-term public health impact.

The aetiology of LRTIs

While acute bronchiolitis and bronchitis are mostly caused by viruses, bacterial pathogens are more predominant in community-acquired pneumonia (CAP) (although there is significant overlap).7 Most common are Streptococcus pneumoniae, Mycoplasma pneumoniae, Chlamydia pneumoniae, Moraxella catarrhalis, Influenza virus A and B, Haemophilus influenzae, respiratory syncytial virus (RSV), parainfluenza virus, adenovirus and Bordetella pertussis.8 These pathogens are usually spread by small droplets in the air. S. pneumoniae is estimated to be present in 25-30% of cases of paediatric CAP in the developed world. Viruses (predominantly RSV) are present in approximately 20% of cases of pneumonia.4 M. pneumoniae and C. pneumoniae tend to be found in older children (Table 1).

Table 1. Aetiology of pneumonia by age group in developed countries. (Adapted from Grant and Ingram 2000)9

<table>
<thead>
<tr>
<th>Age group</th>
<th>Predominant organisms (least frequent to most frequent in each group)</th>
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<tbody>
<tr>
<td>0 to 1 month</td>
<td>Group B streptococcus; Gram negative organisms</td>
</tr>
<tr>
<td>1 to 3 months</td>
<td>Chlamydia trachomatis; Respiratory syncytial virus (RSV); Bordetella pertussis</td>
</tr>
<tr>
<td>1 to 24 months</td>
<td>RSV, other respiratory viruses; Mixed viral or viral/bacterial infections; Bacterial infections (mostly Streptococcus pneumoniae and less frequently Haemophilus species, both typeable and nontypeable) and Mycoplasma pneumoniae</td>
</tr>
<tr>
<td>2 to 5 years</td>
<td>Respiratory viruses; Streptococcus pneumoniae; Haemophilus species; Mycoplasma pneumoniae; Chlamydia pneumoniae</td>
</tr>
<tr>
<td>6 to 18 years</td>
<td>Mycoplasma pneumoniae and Streptococcus pneumoniae are the predominant pathogens. Respiratory viruses account for &lt;15% of episodes of pneumonia in children &gt;5 years of age.</td>
</tr>
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</table>

*Other respiratory viruses = parainfluenza, influenza and adenoviruses.
In developed countries, CAP is a significant cause of hospitalisation and morbidity in children, and is the leading cause of death in less developed countries. In ‘Monitoring the Health of New Zealand Children and Young People’ over a 16 year period (1990-2006), both admissions and mortality for pneumonia have remained static – but hospitalisations for NZ children aged <5 years are 2-4 fold higher than other developed countries. In 2002-2006, the admission rates were highest among those aged 0-2 years, Pacific and Māori children, males and those living in the most deprived areas. Mortality was highest for those <1 year of age. A recent case control study looking at risk factors associated with pneumonia describes increased risk with lower weight for height, spending less time outside, previous chest infections, and the presence of mould in the child’s bedroom. For pneumonia resulting in hospitalisation, increased risks were seen with a maternal history of pneumonia, living in a more crowded household, with cigarette smokers and again mould in the child's bedroom.

In the recent data looking at presence of virus in children admitted with LRTIs in South Auckland in the period 2009-2011 (post PCV7), there were 1885 children admitted and 1558 (83%) tested using PCR on a nasopharangeal aspirate. 1465 (94%) of those tested were positive for one or more respiratory viruses (unpublished data).

**Co-infection in CAP**

Co-infection with ≥2 pathogens is commonly present in CAP and viral-bacterial infections have been identified in a number of studies at rates ranging between 18-33%. Furthermore, it is not uncommon to find a history of influenza infection in the weeks preceding a diagnosis of CAP, with secondary infection caused by *S. pneumoniae, M. pneumoniae* or other pathogens. Increases in CAP admissions with these organisms mirror influenza epidemics. A positive correlation has also been shown between the presence of co-infections and disease severity in children with LRTIs.

**Pneumococcal disease and pneumonia**

Recent estimates of child death caused by *S. pneumoniae* range from 700,000 to 1 million every year worldwide, 11% of all deaths in HIV-negative children <5 years of age. In 2000, by using the proportion of pneumococcal pneumonia cases derived from four large vaccine efficacy trials and applying this to the WHO country-specific incidences of all-cause pneumonia cases and deaths, there were an estimated 14.5 million episodes of serious pneumococcal disease; 95.6% pneumonia, 3.7% invasive pneumococcal syndromes and 0.7% meningitis. Rates varied greatly by country from 188 to 6387 per 100,000 children. Even with these astonishing numbers, the authors commented that despite this being a rigorous calculation, pneumococcal disease is still likely underestimated. High incidence rates (up to 441/100,000 children. Even with these astonishing numbers, the authors commented that despite this being a rigorous calculation, pneumococcal disease is still likely underestimated. High incidence rates (up to 441/100,000 per year) have also been described in indigenous populations, including NZ Māori. *S. pneumoniae* remains the most common bacterial cause of CAP worldwide. Over 90 presently recognised serotypes are frequent colonisers of upper airways in human hosts existing mainly as a commensal bacterium. A new strain will often eliminate other competing pneumococcal serotypes and persist in adults (for weeks) and children (for months) with colonisation detectable in about 10% of healthy adults, 20-40% of healthy children and up to 60% of infants and children in day care settings. Specific clones appear to more often cause invasive pneumococcal disease (IPD) and/or pneumonia usually with rapid disease induction after recent acquisition. Virulence varies with tissue site and population density; pneumococci residing in biofilms are more likely to induce meningitis and pneumonia, but have less capacity for blood dissemination, which occurs with unattached, planktonic bacteria.

Risk factors associated with development of IPD and pneumococcal pneumonia are listed in Table 2. Pneumococcal pneumonia presents as a typically community-acquired pneumonia often with a predating upper airway infection. Diagnosis is often presumptive, with the limiting factor, especially in children, being the ability to get appropriate tissue for culture. Pneumococci grow readily on blood agar plates and can be detected by measuring the C polysaccharide (from the pneumococcal cell wall) in urine, which remains positive for weeks, or by streptococcal specific DNA sequences. For the latter, distinguishing pneumococcal colonisation from infection remains a challenge. Global estimates of disease do not include otitis media and sinusitis also commonly caused by *S. pneumoniae*. Table 2: Risk factors for pneumococcal pneumonia and invasive pneumococcal disease (Adapted from Van der Pol 2009).

**Definite risk factors** (high risk)
- <2 years of age; >65 years of age
- Asplenia or hyposplenia
- Alcoholism
- Diabetes mellitus
- Antecedent influenza
- Defects in humoral immunity (complement or immunoglobulin)
- HIV infection
- Recent acquisition of a new virulent strain

**Probable risk factors** (moderate risk)
- Genetic polymorphisms (eg, complement, MBL, IRAK-4, Mal, MyD88)
- Isolated populations
- Poverty, crowding, low pneumococcal vaccine use
- Cigarette smoking
- Chronic lung disease
- Severe liver disease
- Other antecedent viral infections
- Poor mucociliary function

**Possible risk factors** (low risk)
- Recent exposure to antibiotics
- Defects in cellular immunity and neutrophil defects
- Diminished cough reflex, aspiration pneumonitis
- Proton-pump inhibitors and other gastric-acid inhibitors
- Large organism burden in upper airways
- Childhood day care

*Many clinical studies. Some clinical and laboratory studies. Few clinical studies BMB = mannose-binding lectin; IRAK = interleukin-1 receptor-associated kinase; Mal, MyD88 = Myeloid differentiation primary response factor 88 adaptor-like

**Complications of CAP**

Empyema occurs in 1 in 150 children hospitalised with pneumonia or 0.6%, with a recent increase documented in the 0-4 year age group. Chronic suppurative lung disease is an entity that encompasses protracted bacterial bronchitis, chronic lower respiratory tract infection and bronchiectasis, and is thought to be a continuum of disease. A cohort study of Alaskan children <3 years of age admitted to hospital with LRTI demonstrated moist cough (46%), chronic bronchitis (22%) and bronchiectasis (10%) by age 5 to 8 years. A case control study of Australian Aboriginal children demonstrated that a history of hospitalised pneumonia gave an odds ratio (OR) of 15.2 for developing bronchiectasis.

**Protracted bacterial bronchitis to bronchiectasis**

Chronic wet cough (lasting >4 weeks) is a common paediatric complaint. While there is a wide differential diagnosis (asthma, cystic fibrosis, immunodeficiency, foreign body aspiration, anatomical airway abnormality), it is often associated with persisting bacterial infections of the lower airways. Studies have identified *H. influenzae, S. pneumoniae, M. catarrhalis, S. aureus* and *Klebsiella pneumoniae* as responsible pathogens and it would appear that children with airway malacia might be more susceptible. Investigations of children with chronic cough and/or recurrent LRTIs have diagnosed high rates of bronchiectasis, with the limiting factor being access to CT scan, which currently remains the diagnostic gold standard. We have determined both higher rates and more widespread disease in NZ children than reported elsewhere. While the diagnosis of bronchiectasis increases with age, it is thought that 50% develop the disease in childhood. In the US, reported prevalence in adults ranges from the pneumococcal cell wall) in urine, which remains positive for weeks, or by
The burden of LRTIs in New Zealand children

A 2006 review undertaken by The Asthma and Respiratory Foundation of New Zealand emphasised the disturbing fact that NZ rates for respiratory conditions are higher than in comparable countries.1 In fact, the majority of the top 10 causes of potentially avoidable NZ hospital admissions in 1999 for individuals aged 0-24 years were respiratory conditions.2

During the period 2002 to 2006, bronchiolitis, asthma and pneumonia were the main causes of hospital admissions due to LRTIs in children aged 0-14 years, with rates of 5.4 per 1000, 5.3 per 1000 and 3.9 per 1000, respectively.2 Pneumonia was estimated to account for 63.6% of all deaths attributed to LRTI in NZ children. Based on admissions data from 2000-2007, episode rates for pneumonia were highest in the second 6 months of life and declined over the first 5 years, with mean rates of 464 per 100 000 for children aged <2 years and 295 per 100 000 for children aged <5 years.3

Of ongoing concern, the burden of paediatric respiratory disease falls heavily on Māori and Pacific Island children, who exhibit higher rates of CAP, empyema and bronchiectasis, and have a tendency to be hospitalised with more severe pneumonia than European children in NZ.1,13-16 In fact, Pacific children in this country have hospitalisation rates for LRTIs almost three times that of other NZ children.17 This may partly be attributable to lower quality living environments (poorer nutritional status, cigarette smoke exposure and lower housing quality), which increase both the risk of, and hospitalisation with, pneumonia.18 Analysis of WHO data suggests that poverty is associated with a more than 20-fold increase in the relative burden of lung infections.19

The overall incidence of bronchiectasis in NZ children aged 0-14 years was 3.7 per 100 000 per year during 2001 and 2002, an incidence seven times that seen in Finland.20 This analysis also showed that the incidence of bronchiectasis varied greatly with ethnicity (1.5-17.8 per 100,000 per year) and was highest in Pacific children. The median age at diagnosis was 5.2 years and the majority of children had experienced symptoms for more than 2 years. In most developed countries the incidence of bronchiectasis is falling, but this does not appear to be the case in NZ.21,22

The incidence of pertussis in NZ is lower than the other types of LRTIs, however, the incidence is still unacceptable high, with 1272 confirmed cases reported to the Ministry of Health (MOH) from Jan–Aug this year.23 For the burden of pertussis to decrease further, immunisation coverage and on-time immunisation need to increase significantly to the MOH target of 95% of infants fully vaccinated at ages 6 and 16 months.24

The economic burden of LRTIs

By far the biggest economic cost of LRTIs is associated with pneumonia. In 2000, it was estimated that NZ spent at least $7 million per year on direct medical costs associated with pneumonia in children.19 This is believed to be an underestimate, because the calculations only took into account direct medical costs. A 2010 evaluation estimated the total NZ cost associated with pneumococcal disease and otitis media to be $10 million, with 48% of this cost estimated to result from pneumococcal pneumonia.25 In addition, children who suffer from pneumonia may have poorer lung function in adulthood, and a higher risk of developing bronchiectasis, therefore engendering further associated healthcare costs.

While lung infections threaten all economic groups improving immunisation rates, fighting poverty, improving the home environment, and better access to health care for lower socioeconomic groups will significantly decrease the burden of LRTIs.26

Bronchoscopy revealed purulent bronchitis in 152 adult patients over a single year at Middlemore Hospital, with an incidence of 50 per 100,000, again likely underreported. In reviewing 307 exacerbations of bronchiectasis in 152 adult patients over a single year at Middlemore Hospital, 46% had at last one readmission and 21% died within 12 months.27

Protracted bacterial bronchitis in young children: association with airway malacia28

Authors: Kompare M and Weinberger M

Summary: This retrospective study reviewed clinical data on 70 children <60 months of age with a ≥1 month (median 5 months) history of cough, wheeze and/or noisy breathing who were seen between 1999 and 2009 at the Pediatric Pulmonary Clinic at Maimonides Infants and Children’s Hospital in New York from 2004 to 2008. Laryngomalacia and/or tracheomalacia were present in 33 (50.3%) children. Bronchoscopy revealed purulent bronchitis in 110 (56%) children. BAL bacterial cultures were positive in 91 (46%) children and revealed nontypeable H. influenzae (49%), S. pneumoniae (20%), M. catarrhalis (17%), S. aureus (12%), and K. pneumoniae (1 patient). Children with nonpurulent bronchitis (n = 87) had a significantly lower rate of positive bacterial cultures than those with purulent bronchitis (19.8 vs 69.8%; p < 0.001).

Comment: see right

Specialist Commentary on Current Studies

SPECIALIST COMMENTARY ON CURRENT STUDIES

Bronchoscopic findings in children with chronic wet cough26

Authors: Zgherea D et al

Summary: The frequency of bacterial bronchitis in children with chronic wet cough and the type of pathogen present in bronchoalveolar lavage (BAL) was investigated in this retrospective review of data from 197 children aged 0 to 3 years who were referred to the Pediatric Pulmonary Clinic at Maimonides Infants and Children’s Hospital in New York from 2004 to 2008. Laryngomalacia and/or tracheomalacia were present in 33 (50.3%) children. Bronchoscopy revealed purulent bronchitis in 110 (56%) children. BAL bacterial cultures were positive in 91 (46%) children and revealed nontypeable H. influenzae (49%), S. pneumoniae (20%), M. catarrhalis (17%), S. aureus (12%), and K. pneumoniae (1 patient). Children with nonpurulent bronchitis (n = 87) had a significantly lower rate of positive bacterial cultures than those with purulent bronchitis (19.8 vs 69.8%; p < 0.001).

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Combined commentary: These two studies describe bronchoscopy and lavage findings in very young age groups (<3 years and <5 years) referred for chronic cough and other symptoms. Significant findings were single positive organisms in 46% in one study and two or more organisms found in almost 50% in the second study, with a strong association with the presence of tracheo-bronchomalacia in both at 30% and 74%. Both studies were retrospective, have small numbers (but this procedure is a significant undertaking in young children) and have no control group. Tracheomalacia is said to occur in 1 in 2100 newborns,44 thus it was very prevalent in these studies, although the accuracy of normative data could be questioned as we rarely bronchoscope normal healthy children.

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Respiratory bacterial pathogens in the nasopharynx and lower airways of Australian indigenous children with bronchiectasis

Authors: Hare KM et al

Summary: This Australian study involving 45 indigenous children with bronchiectasis and 30 non-indigenous children with non-bronchiectatic respiratory conditions was undertaken in order to test the hypothesis that bacterial density, strain diversity and concordance of pathogens between upper and lower airways are higher in paediatric patients with bronchiectasis than in those with non-bronchiectatic conditions. Nasopharyngeal swab and bronchoalveolar lavage fluid culture was undertaken for all subjects and revealed that nasopharyngeal carriage of nontypeable H. influenzae, S. pneumoniae and M. catarrhalis, and lower respiratory tract infection with nontypeable H. influenzae were significantly more frequent in children with bronchiectasis than those without the condition (47% vs 3%). While strain concordance between the upper and lower airways was high in both infected subgroups, bronchoalveolar lavage specimens from infected indigenous children revealed greater strain diversity (71% vs 0%). These findings suggest a possible pathogenic role of recurrent aspiration of nasopharyngeal secretions in Australian indigenous children with bronchiectasis.

In all three studies, nontypeable H. influenzae and S. pneumoniae are common infecting agents.

Microbiology of bronchoalveolar lavage fluid in children with acute nonresponding or recurrent community-acquired pneumonia: Identification of nontypeable Haemophilus influenzae as a major pathogen

Authors: De Schutter I et al

Summary: Researchers from Belgium conducted a retrospective study of CAP aetiology in two groups of children, those with acute nonresponsive CAP (NR-CAP; n = 127) and those with recurrent CAP (Rec-CAP; n = 123). Both groups underwent flexible bronchoscopy with bronchoalveolar lavage and, where available, serological test results, blood and pleural fluid culture results and nasopharyngeal secretion findings were assessed. In 76% of cases an infectious agent was identified, and in 51.2% of those cases, aerobic bacteria were isolated (H. influenzae 75%; M. catarrhalis 28.9%; S. pneumoniae 13.3%). H. influenzae was detected in 51.2% of Rec-CAP cases and in 26.0% of NR-CAP cases. M. pneumoniae was the most common pathogen identified in the NR-CAP group (34.9%) and occurred in 19.3% of the Rec-CAP group. Of the H. influenzae strains, 97.9% were nontypeable. In 30.4% of cases a virus was identified (parainfluenza viruses, influenza viruses and RSV were the most frequently detected viruses), and 18.9% of NR-CAP and 30.1% of Rec-CAP cases exhibited mixed infections.

Comment: Another, but this time prospective, bronchoscopy and lavage study in a young group of 75 children determined high upper and lower airway bacterial concordance. The findings support, but do not definitively prove, a possible pathogenic role of recurrent aspiration of nasopharyngeal secretions in Australian indigenous children who have developed bronchiectasis or protracted bacterial bronchitis. This is likely to be relevant to all children who develop bronchiectasis.

Reduction in hospitalizations for pneumonia associated with the introduction of a pneumococcal conjugate vaccination schedule without a booster dose in Australia

Authors: Jardine A et al

Summary: Nearer to home, the pneumococcal vaccine programme in Australia (which includes a 3-dose PCV7 primary schedule, but no booster) showed significant reductions in adjusted all-cause pneumonia in children aged <2 years (38% reduction; 95% CI 36-40%) and 2-4 years (29% reduction; 95% CI 26-31%), with reductions also in older age groups, with those aged 5-17 years, 18-39 years, 40-64 years and ≥65 years showing between 3% and 11% reductions. There was almost a 70% reduction in rates of presumptive pneumococcal pneumonia, a 40% reduction for pneumonia of unspecified cause and no reduction in pneumonia coded as due to other organisms. This study also shows why all-cause pneumonia is an important marker of success, as of the over half a million recorded hospitalisations for pneumonia across the study period, 85% of coding did not specify a causative organism, pneumococcal pneumonia was coded in 5% and other pathogens were coded in 9.9%.

Summary/comment: A Research Review publication

National hospitalization trends for pediatric pneumonia and associated complications

Authors: Lee GE et al

Summary/comment: These researchers determined current rates and trends in hospitalisations for CAP in the US in their cross-sectional, retrospective, cohort study using data from 38 US states from the 1997, 2000, 2003 and 2006 Kids’ Inpatient Database, representing 88.8% of the population. They analysed data from two periods (1997 and 2006), corresponding to before and after the introduction of the seven-valent pneumococcal vaccine (PCV7), which was licenced for use in the US in 2000 and subsequently became part of the routine childhood immunisation schedule. During the entire time period investigated, there were 619,102 CAP discharges. While overall rates of CAP discharges did not change significantly between 1997 and 2006, a 22% decrease in children under 1 year of age was evident, with 90% of this decrease having been seen by 2003. However, minimal interval changes were seen for the next age group (1-5 years), and rates increased for the older age groups; 6-12 years (21.9% increase), 13-18 years (40.5% increase). The youngest age group also had the highest frequency of complications (local, systemic, metastatic), but these decreased by 25.5% with the vaccine programme. The reason for the increase in CAP discharges in the older age groups is unclear, but could possibly be due to pneumococcal serotype replacement or changes in the epidemiological features of other pathogens, such as methicillin-resistant S. aureus or atypical organisms.

Summary/comment: A Research Review publication

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Impact of pneumococcal conjugate vaccination of infants on pneumonia and influenza hospitalization and mortality in all age groups in the United States

Authors: Simonsen L et al

Summary: PCV7 was introduced in the US in 2000. This study incorporated data from Health Care Utilization Project State Inpatient Databases (SID) for 1996 to 2006 from 10 states, in order to assess the impact of infant immunisation on pneumococcal pneumonia hospitalisations and mortality across all age groups. Compared with 1996–1999 baseline data, 2005-2006 data revealed a significant reduction in both pneumococcal pneumonia and invasive pneumococcal pneumonia hospitalisations, and deaths across all age groups, with a 47% (95% CI 38–54%) reduction in non-bacteraemic pneumococcal pneumonia in infants aged <2 years and a 54% reduction (95% CI 53–56%) in adults aged >65 years. Modelling estimated 788,838 (95% CI 695,406–875,476) fewer pneumococcal pneumonia-related hospitalisations between 2000 and 2006, following the introduction of infant PCV7 immunisation and 90% of this reduction was attributed to herd immunity among adults ≥18 years. The study also revealed that US states with greater infant PCV7 immunisation coverage had significantly fewer paediatric influenza-associated pneumonia hospitalisations, indicating that PCV7 immunisation also reduces influenza-attributable pneumonia in children.

Comment: In addition to confirming that the pneumococcal vaccination programme reduces invasive pneumococcal disease, pneumococcal pneumonia hospitalisations and all pneumonia hospitalisations in the vaccine-targeted age group, this study shows positive effects for all ages, notably the most senior age group, through herd immunity. It also suggests that the pneumococcal vaccination programme is associated with reduced hospitalisation for influenza pneumonia in children. Other studies have shown a 31% reduction in admission for viral pneumonia following pneumococcal vaccination and correspondingly increased rates of pneumococcal pneumonia during times of influenza epidemics.

Risk factors for community-acquired pneumonia in pre-school-aged children

Authors: Grant CC et al

Summary/comment: This study involving children <5 years of age living in the Auckland central region confirms some risk factors for the development of early childhood pneumonia and reveals others. During the period 2002 to 2004, children hospitalised with pneumonia (n= 289) plus children with pneumonia discharged from the Emergency Department (n= 139) were compared with a random community sample of children without pneumonia (n= 351). Multivariate analysis indicate that factors independently associated with pneumonia included being lower weight for height (OR 1.28; 95% CI 1.10–1.51), spending <30 minutes a day outside in the past 4 weeks (OR 1.96; 95% CI 1.11–3.47) and mould in the bedroom (OR 1.93; 95% CI 1.24–3.02). Not being breastfed (OR 0.46; 95% CI 0.27–0.80), which the authors suggested might be due to earlier recognition of clinical symptoms by parents with previous experience of the condition. Other factors that independently (multivariate analysis) increased the risk of hospitalisation included a maternal history of pneumonia (OR 4.03; 95% CI 1.25–16.18), an indoor environment of crowded households (OR 2.87; 95% CI 1.33–6.41), presence of cigarette smoke (OR 1.99; 95% CI 1.05–3.81), and a mouldy bedroom (OR 2.39; 95% CI 1.25–4.72). The observed influence of less time outdoors could be due to a lack of exposure to sun and potential vitamin D deficiency, or an increased exposure to the deleterious indoor environment. It does confirm that there are many environmental factors that could be addressed to reduce childhood pneumonia rates in NZ.

Expert’s concluding remarks

Pneumococcal vaccination programmes have proven efficacy elsewhere, and although only commenced in the last few years for NZ children, are likely to be hugely beneficial given our burden of disease. As well as reducing pneumococcal pneumonia in the young age groups, it could also affect the numbers of ‘all-cause’ pneumonia, and herd immunity for other age groups. It will be interesting to quantify the effects here in NZ and the effects on other highly morbid conditions such as otitis media and sinusitis research underway.

Complications of CAP and the presence of chronic wet cough should also be taken more seriously in our country. Given that 2-4 years of symptoms occur before a bronchiectasis diagnosis is made and appropriate treatment is instigated, it is likely that ongoing damage is occurring and contributing to the severity of the disease seen here in NZ. The association with tracheomalacia is noted and the possible upper and lower airway concordance suggests oral aspiration may be seeding the lower airway with bacteria. S. pneumoniae remains an issue here, although nontypeable H. influenzae is by far the most common organism in established disease. Prevention of LRTIs, including CAP, by immunisation (and immunisation on time) would be hugely beneficial. As with most health issues – attention to living conditions, smoking, nutrition and improved access to healthcare also needs to be addressed across our communities to improve outcomes.

Serotype-specific hyporesponsiveness to pneumococcal conjugate vaccine in infants carrying pneumococcus at the time of vaccination

Authors: Väkeväinen M et al

Summary: This study investigated 1111 Filipino infants who were recruited into an immunogenicity and carriage study of an 11-valent pneumococcal conjugate vaccine (PCV11) efficacy trial. Infants received either PCV11 or placebo at 6, 10 and 14 weeks of age. Analysis of sera revealed that antibody concentrations to 6B, 19F and 23F were significantly lower at 18 weeks and 9 months of age among children who were carriers of the specific serotype 6 weeks of age than among non-carriers of the serotype; this hyporesponsiveness was specific to the carried serotype. PCV11-induced specific antibody concentrations among carriers did not differ significantly from those in placebo recipients, whereas highly significant differences were seen among non-carriers.

Comment: Nasopharyngeal pneumococcal carriage occurs from early infancy with wide differences described in different populations. This study follows up previous concerns that, subsequent to invasive pneumococcal disease, affected children did not respond to their infecting serotype when immunised with the pneumococcal vaccine. Similarly in this study, of the 555 children in the vaccination arm, 96% had nasopharyngeal carriage of pneumococcus and in 28% this included one of the vaccine serotypes. These children had significantly lower pneumococcal antibodies at both 18 weeks of age and 9 months of age (1 month and 4½ months after the scheduled third dose) than those with non-vaccine serotype nasal carriage. This hyporesponsiveness requires further research – as this may be a barrier to overall success of vaccination programmes, especially in developing countries with known high prevalence of pneumococcal carriage.
A Research Review publication

This publication is an independent review of significant research in the area of paediatric lower respiratory tract infections. It provides summaries and opinions of published data that are the opinion of the writer rather than that of the scientific journal or research group. It is suggested the reader reviews the full trial data before forming a final conclusion on any recommendations.

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