Acute respiratory tract infections in childhood

Most acute respiratory tract infections in developed countries are viral in aetiology and self-limiting. The use of antibiotics should only be considered if bacterial infection is suspected.

MERCI M.H. KUSEL
MB BS, PhD, Grad Cert Environ & Nutrit Med

PETER D. SLY
MB BS, FRACP, MD, DSc

Dr Kusel is Senior Research Officer, and Professor Sly is Head, Division of Clinical Sciences, Telethon Institute for Child Health Research, Perth, WA. Dr Kusel is also Adjunct Lecturer, School of Paediatrics and Child Health, University of WA and School of Public Health, Curtin University of Technology; and a family physician in Cottesloe. Professor Sly is also Professor, School of Paediatrics and Child Health, University of WA; Adjunct Professor, School of Public Health, Curtin University of Technology; Senior Principal Research Fellow, NHMRC; and Respiratory Paediatrician, Princess Margaret Hospital for Children, Perth, WA.

Acute respiratory infections (ARIs) are common causes of childhood morbidity. They are responsible for substantial numbers of doctor visits and school and parental workdays lost, and for general disruption of family function. Just under one-quarter (22.2%) of the Australian population reported a respiratory infection in the two weeks prior to the 1995 National Health Survey, and ARIs are responsible for nearly one-half of GP consultations with preschool-aged children.[1,2] Large amounts of money are expended by healthcare services and families in the management of these illnesses, and the world market for cough and cold remedies has been estimated to be about A$7 billion per year.[3]

Epidemiology

Patients with ARIs may present with a variety of symptoms, including sore throat, nasal congestion, cough, wheeze and fever.

Aetiological agents

Although all classes of micro-organisms are capable of causing ARIs, viruses are the most common aetiological agent in developed countries. Associations have been found between specific respiratory pathogens and clinical syndromes such as upper respiratory tract infection (URTI), croup, bronchiolitis, bronchitis and pneumonia, although there is considerable overlap (Table 1).[4-6]

Human metapneumovirus, a virus first described in 2001, has been found to be a leading cause of ARI in early childhood.[5,6] It has a disease spectrum similar to that of respiratory syncytial virus (RSV), including bronchiolitis and pneumonia. Peak incidence of infection occurs in late winter to early spring, with more boys affected than girls (in a ratio of 1.8 to 1). A recent study detected human metapneumovirus in an estimated 12% of infants and children hospitalised with respiratory tract infection.[5]

IN SUMMARY

- **Most acute respiratory infections (ARIs) in developed countries are viral in aetiology, uncomplicated and self-limiting.**
- **Human metapneumovirus is a leading cause of ARIs in early childhood.**
- **Respiratory viral infections are associated with most asthma exacerbations, particularly in children; rhinoviruses are the most commonly implicated virus.**
- **The use of antibiotics in treating ARIs should only be considered in the presence of bacterial sequelae.**
- **Although most children with ARIs can be managed in the community setting, some may be better referred to hospital.**
- **Prevention strategies for ARIs include avoidance of environmental tobacco smoke exposure and immunisation against pneumococcal disease, invasive *Haemophilus influenzae* type b infection and, in some children, influenza.**

Respiratory viral infections have also been found to be associated with 80 to 85% of asthma exacerbations, particularly in children; rhinoviruses were the most commonly isolated virus, accounting for two-thirds of positive viral specimens.[7]

Risk factors for ARIs

Various host and environmental factors increase the chance of an individual developing an ARI.

Host factors

Host factors associated with ARIs include age, gender, month of birth, birthweight, atopic status and the socioeconomic status of the family.

The incidence of ARIs in the first six months of life is generally low as children are protected by transplacentally acquired IgG antibody. The peak incidence is between the ages of 6 months and 5 years, with exposure through older siblings or day care attendance being the most critical determinant. Studies have found illness rates for both otitis media and lower respiratory infections (LRIs) to be substantially higher in boys than girls under the age of 6 years.[8,9] Children born in the winter months, when the prevalence of respiratory infections is high, are at higher risk of contracting an ARI, particularly if they are not breastfed. Children of low birthweight, from indigenous communities such as Aboriginal and Torres Strait Islanders, Maoris and Pacific Islanders, or from poor socioeconomic backgrounds are also at higher risk of ARIs, particularly pneumonia.[10]

Atopic children have not been found to be more prone to ARIs but, as mentioned above, respiratory infections have been shown to precipitate most asthma exacerbations in children.

Environmental factors

Environmental factors shown to be associated with ARIs include air pollution, environmental tobacco smoke exposure, poverty, lack of breastfeeding, day care attendance and overcrowding.[9,11-15] Children in day care have been shown to have not only more infections but also infections of longer duration.[12]

Classification of ARIs

ARIs can be classified several ways but the most commonly used method, and the one preferred by most clinicians, is by site of primary pathology, with separation of upper from lower respiratory tracts at the level of the larynx.

URTIs

Little is known about the frequency of URTIs as generally they are common, have few complications and resolve spontaneously without medical attention. URTI symptoms are not clear cut, and there is strong overlap with hay fever symptoms.

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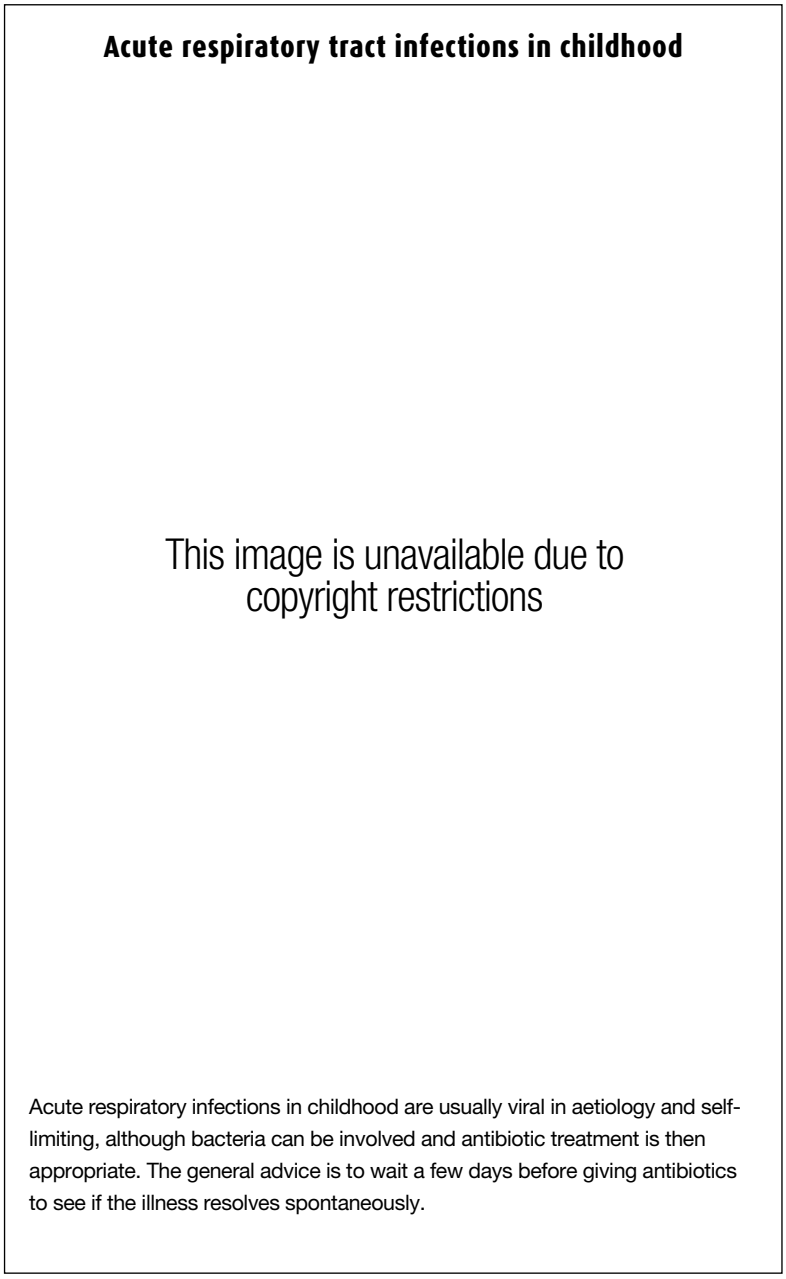

Acute respiratory infections in childhood are usually viral in aetiology and self-limiting, although bacteria can be involved and antibiotic treatment is then appropriate. The general advice is to wait a few days before giving antibiotics to see if the illness resolves spontaneously.

Table 1. Associations of viruses and clinical respiratory syndromes[4-6]

Virus	Clinical syndrome
Rhinoviruses and coronaviruses	Upper respiratory tract infection
Respiratory syncytial virus, human metapneumovirus	Upper respiratory tract infection, bronchiolitis, pneumonia
Parainfluenza viruses 1 to 3, human metapneumovirus	Croup
Influenza viruses	Bronchitis
Influenza viruses A and B, parainfluenza viruses 2 and 3	Pneumonia

Children have been reported to have, on average, 6.2 URTI episodes in the first year of life, and 6.5 episodes in the second year.[8,9,16] The incidence of otitis media is greatest in young children between 6 and 18 months of age, and 90% of all children have at least one episode of acute otitis media by the age of 2 years.[17] Complications such as sinusitis, mastoiditis and peritonsillar abscesses are uncommon and dependent on several factors, including the child's age and offending organism.

Acute epiglottitis, a condition that presents with symptoms of fever, difficulty swallowing, drooling and inspiratory stridor, has previously been a cause of life threatening airway obstruction in children. However, with the introduction of the conjugate vaccine for *Haemophilus influenzae* type b for infants, the incidence of acute epiglottitis in the developed world has reduced, with most cases now occurring in unimmunised older children and adults.[18]

LRIs

LRIs are classified by the primary anatomical site affected and include laryngotracheobronchitis (croup), bronchiolitis, bronchitis and pneumonia. Although more than one site can be affected, most patients have a predominant site of involvement. Close associations have been shown between sites of involvement and causative agents (see Table 1).

Croup

Croup is an extremely common illness, usually occurring in young children aged between 6 and 36 months. Clinical diagnosis is based on the symptom complex of coryza, fever, hoarseness, harsh barking cough, stridor and respiratory distress, usually worse at night. It affects more boys than girls, and although usually mild and self-limiting, it can occasionally cause severe obstruction requiring hospitalisation. It is important to exclude other conditions, such as foreign body inhalation.

Early intervention reduces symptom severity, rates of return to GPs, emergency department visits and hospital admissions.

Bronchiolitis

Acute bronchiolitis is the best known LRI of young children and RSV is the agent most often detected in children under the age of 2 years.[1,2] Passively acquired maternal RSV antibodies offer poor protection against with this virus, making infants prone to this infection. In temperate climates, RSV infection peaks in winter and early spring; although these infections occur every year, the severities of the annual epidemics vary. More than 85% of children will have been exposed to RSV by their second winter, and about 40% will have lower respiratory tract involvement with associated wheezing, thus causing confusion with a diagnosis of asthma.

The characteristic presentation of bronchiolitis is that of a young infant with symptoms of a cold, with rhinitis or nasal congestion followed within a couple of days by a fever, intermittent spluttering cough and sometimes wheeze. Only about 1% of patients with bronchiolitis require hospitalisation, but reinfections are common as RSV IgG antibodies offer poor protection.

Bronchitis

Although almost all children suffer from at least one bout of bronchitis each year, especially during infancy, it is difficult to quantify 'normal' frequencies.[19] Population studies in Australia have shown that 15 to 25% of secondary schoolchildren suffer at least one episode of bronchitis each year.[20]

Acute bronchitis is generally seen in association with an URTI. The hallmark of the condition is the presence of cough that is initially dry and irritating but, with the natural progression of illness, becomes moist and productive over a seven to 10-day period.[21] Bronchitis has been found to be the most common cause of chronic cough in children.[21] Although cough is a common symptom in children presenting to GPs, persistent cough can be a source of great parental anxiety, often requiring referral to paediatricians or respiratory physicians. Guidelines on the management of cough in children are clearly set out in the position statement of the Thoracic Society of Australia and New Zealand on the definitions and clinical evaluation of cough in children.[22]

Pneumonia

Pneumonia is most common in children under the age of 2 years, with incidence rates of 40 per 1000 in preschool-aged children and 9 per 1000 in children aged 9 to 15 years.[23] Poor socioeconomic background, crowded living conditions, large families, environmental tobacco smoke exposure, prematurity, and medical conditions that reduce local defences (such as

decreased cough reflex and impaired mucociliary clearing) or immunological responses (such as cystic fibrosis) confer increased susceptibility.

Although the majority of cases of pneumonia have a viral aetiology, bacteria (most commonly *Streptococcus pneumonia*e and *H. influenzae*) cause about 30 to 40% of cases. The bacteria often responsible for pneumonia are oropharyngeal commensals, and a preceding viral infection facilitates their passage into the lower respiratory tract. The signs and symptoms of bacterial and viral pneumonias overlap, often making specific diagnosis difficult. Diagnosis is further complicated by more than half of children with bacterial pneumonia having concurrent viral infections. Nasopharyngeal aspirates, blood cultures and chest x-ray may help to identify the aetiological agent for choice of antibiotic treatment. However, treatment is often instigated in the general practice setting before specific identification of the pathogen, using information gathered from the child's age, symptoms and signs, and chest x-ray appearances to formulate a treatment regimen.

Management

The vast majority of ARIs are self-limiting and uncomplicated, and the use of antibiotics, antihistamines or decongestants do not reduce symptoms, alter the course or prevent complications.[24] The clinical approach to treatment regimens for ARIs in childhood is summarised in Tables 2 and 3. The treatment of croup and bronchiolitis and the use of antibiotics in ARIs are discussed in more detail below.

Croup

Most children with croup respond to a single, oral dose of corticosteroids.[25] For those who do not tolerate the oral preparation, nebulised budesonide (Pulmicort Respules) or intramuscular dexamethasone (Dexamethasone Sodium Phosphate Injection) are reasonable alternatives. In severe croup, nebulised adrenaline (1:1000) has been shown to result in rapid clinical improvement, but because the effect is short lasting (usually only two to three hours), admission of the child to hospital for observation is recommended.[26,27]

Bronchiolitis

Bronchodilators, adrenaline and corticosteroids have all been used in the treatment of bronchiolitis, both in the outpatient setting as well as in hospitalised infants. Clinical randomised trials have failed to

Table 2. Summary of treatment regimens for ARIs*

Condition	Treatment options
Common cold	Symptomatic treatment
Acute bronchitis	Symptomatic treatment
Bronchiolitis	Symptomatic treatment
Croup	Corticosteroids – single oral dose or nebulised budesonide† or intramuscular dexamethasone.‡ Nebulised adrenaline if severe.
Pharyngitis/tonsillitis	85% of cases resolve in 1 week with symptomatic treatment. Consider antibiotics if: – severe tonsillitis suggestive of group B *Streptococcus* infection – communities at risk of rheumatic fever, e.g. Aboriginal and Torres Strait Islanders – existing rheumatic heart disease – scarlet fever/quinsy
Acute otitis media	66% of patients will be pain-free after 24 hours with symptomatic treatment. Children without fever and vomiting: – if 6 to 24 months of age, delay antibiotics for 24 hours and review by telephone and/or visit – if more than 24 months of age, delay antibiotics for 48 hours and reassess Children with fever and vomiting: antibiotic therapy may be indicated
Otitis media with effusion	Consider antibiotics in those with chronic course or no preceding history of acute otitis media
Acute sinusitis	70% of patients spontaneously recover with symptomatic treatment. Consider antibiotics if the patient has more than three of the following: – mucopurulent discharge for more than 7 to 10 days – facial pain/tenderness over sinuses – poor response to decongestants – prolonged fever – headache
Pneumonia	If thought to be viral, symptomatic treatment; if thought to have a bacterial component, antibiotic treatment

* See Table 3 for antibiotics of choice if the decision is made to treat with antibiotics; † Nebulised budesonide: Pulmicort Respules; ‡ Dexamethasone: Dexamethasone Sodium Phosphate Injection.

Table 3. Antibiotics of choice for treatment of ARIs

Condition	No penicillin hypersensitivity	Penicillin hypersensitivity	Duration of treatment
Pharyngitis/tonsillitis	Phenoxymethylpenicillin (penicillin V) 10 mg/kg (up to 500 mg) orally, 12 hourly	Roxithromycin* 4 mg/kg (up to 150 mg) orally, 12 hourly	10 days
Acute otitis media	Amoxycillin 15 mg/kg (up to 500 mg) orally, 8 hourly, or amoxycillin 30 mg/kg (up to 1000 mg) orally, 12 hourly If poor response to above, amoxycillin + potassium clavulanate 22.5 + 3.2 mg/kg (up to 875 + 125 mg) orally, 8 hourly	Cefuroxime† 10 mg/kg (up to 500 mg) orally, 12 hourly Cefaclor 10 mg/kg (up to 250 mg) orally, 8 hourly	5 to 7 days
Otitis media with effusion	As for acute otitis media but longer duration	As for acute otitis media but longer duration	10 to 30 days
Acute sinusitis	Amoxycillin 15 mg/kg (up to 500 mg) orally, 8 hourly If poor response to above, amoxycillin + potassium clavulanate 22.5 + 32 mg/kg (up to 875 + 125 mg) orally, 8 hourly	Cefuroxime† 10 mg/kg (up to 500 mg) orally, 12 hourly Cefaclor 10 mg/kg (up to 250 mg) orally, 8 hourly Doxycycline (children over 8 yrs) 4 mg/kg (up to 200 mg) orally initially then 2 mg/kg daily	5 to 7 days
Pneumonia	Amoxycillin 15 mg/kg (up to 500 mg) orally, 8 hourly followed by Roxithromycin 4 mg/kg (up to 150 mg) orally, 12 hourly	Cefuroxime 10 mg/kg (up to 500 mg) orally, 12 hourly followed by Roxithromycin 4 mg/kg (up to 150 mg) orally, 12 hourly	7 days 7 days

* Roxithromycin: Biaxsig, Roxar, Roximycin, Rulide; † Cefuroxime: Zinnat.

demonstrate clinical benefit.[28-30] Current evidence thus does not support the use of bronchodilators, antibiotics or corticosteroids in managing this condition and the efficacious management of fever, hydration and hypoxia remain the key components of care. The search for effective therapy for bronchiolitis continues as newer strategies like the antiviral agent ribavirin, the immunomodifier palivizumab and the leukotriene receptor antagonist montelukast have been demonstrated to have limited or no role.[30]

Antibiotics and ARIs

Inappropriate antibiotic prescription for ARIs, most of which are viral in aetiology, has led to an alarming increase in antibiotic resistance among respiratory bacteria. Although consumers are becoming more aware of the risks and benefits of antibiotics, there is still an expectation for GPs to prescribe antibiotics when children present with acute otitis media, bronchitis or pneumonia, as these conditions are often considered by parents and other carers as being more severe and thus warranting antibiotics. Studies have shown that asking patients to wait three or more days and only have antibiotics dispensed if the condition has not improved spontaneously has been shown to be effective in reducing use of antibiotics for ARIs.[31]

Antibiotics have been reported as being prescribed for ARIs in the primary care setting at markedly differing rates in different countries, varying from 60 to 70% in the UK, the USA, Canada, Mexico and Italy to 26% in Malaysia and 8.5% in India.[32-39] Some of these studies also showed higher rates of antibiotic prescription for LRIs compared with URTIs.[34,37]

In Australia, although the prescription of antibiotics has decreased from 24 million prescriptions dispensed in 1990-91 to 20 million in 2002-03, 35% of GP visits for URTIs in 2002-03 resulted in antibiotic prescription.[40]

Referral to hospital

Although most children with ARIs can be managed in the community setting, some may be better referred to hospital. General indicators for hospital referral include:

- age less than 3 months
- fever above 38°C, refusal to feed, vomiting, toxic looking child
- rapid breathing, moderate to severe chest retraction with or without cyanosis
- failure of previous antibiotic therapy
- severe underlying disorders, such as heart disease or cystic fibrosis
- recurrent episodes of pneumonia.

High levels of parental anxiety, difficult social circumstances and the distance between home and primary health care facility are other considerations.

Prevention strategies

A systematic public health approach is necessary in the management of ARIs to maximise preventive measures and minimise transmission rates. This will reduce prevalence rates and economic impact, as well as inappropriate prescribing of antibiotics.

Reduce exposure to environmental tobacco smoke

Environmental tobacco smoke exposure has been found to be associated with increased risk to all types of ARI. Reducing children's exposure to environmental tobacco smoke should be a primary aim of all health care providers and politicians. This can be achieved by increased parental education about the detrimental effects of environmental tobacco smoke exposure on children's developing lungs. Governments should increase taxes on cigarettes and tobacco products and use the revenue obtained for further public education. Legislation should be put in place to ban smoking in public places as well as in private vehicles, and all tobacco advertising ceased.

Vaccine preventable ARIs

In Australia and the USA, pneumonia and influenza are the only infectious diseases in the top 10 causes of death.[1] *S. pneumoniae* is the leading cause of bacterial pneumonia, meningitis, sinusitis and acute otitis media in children and adults worldwide, with young children at special risk of pneumococcal disease with high rates of sequelae. Influenza, a highly contagious ARI caused by influenza viruses A and B, has been estimated to affect 10 to 20% of a community during a season, but rates of 40% to 50% within institutions have been reported.[41] Rates of infection tend to be highest in school-aged children. Although influenza is generally self-limiting, complications (such as pneumonia) tend to occur more often in the young and the elderly and it is associated with asthma exacerbations.[7,42]

Immunisation is effective in reducing the incidence and transmission of disease, as demonstrated by the reduction of invasive *H. influenzae* disease such as epiglottitis, meningitis and pneumonia with the introduction of vaccination against *H. influenzae* type b (Hib).[18,43] Thus immunisation should be the mainstay for prevention of LRIs. Hib vaccination is now included in the standard Australian infant vaccination schedule; available haemophilus b conjugate vaccines are Hiberix and Liquid PedvaxHIB.

Several vaccines are available in Australia to prevent pneumococcal disease and influenza, the most common causes of LRIs. However, they have been underutilised even though they have been shown to lower the incidence and transmission of pneumococcal disease and the mortality from influenza.[44-46]

The pneumococcal conjugate vaccine Prevenar has been included in the standard Australian infant vaccination schedule since 2005. Its use should result in a significant decrease in the incidence and transmission of invasive pneumococcal disease, as has been shown in other countries where pneumococcal conjugate vaccine has been introduced in infants.[44, 47]

Influenza vaccination is currently recommended only for the elderly, health care workers and those individuals, including children, who have chronic conditions such as heart disease and asthma. Vaccines suitable for children and infants are Fluarix, Fluvax, Vaxigrip and Vaxigrip Junior. It may be economically prudent to increase vaccine coverage by vaccinating all children over the age of 2 years to reduce the burden of this highly infectious disease.

Respiratory tract complications of measles include otitis media, bronchitis and pneumonia. Widespread measles vaccination in Australia has resulted in a low incidence of this childhood illness and its concomitant respiratory tract complications. Measles outbreaks do, however, still occur, particularly in unimmunised individuals.

Conclusion

Most ARIs in developed countries are viral in aetiology and self-limiting. Antibiotics have not been found to influence the course of most mild ARIs or prevent complications and should thus only be considered in the presence of bacterial sequelae. Public education to raise awareness of the detrimental effects of environmental tobacco smoke exposure, as well as increasing the uptake of immunisation against pneumococcal disease, influenza, *H. influenzae* type b infection and measles, are other measures that clinicians can use to reduce the burden of ARI. MT

A list of references is available on request to the editorial office.

DECLARATION OF INTEREST: None.

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MERCI M.H. KUSEL MB BS, PhD, Grad Cert Environ & Nutrit Med **PETER D. SLY** MB BS, FRACP, MD, DSc

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