

## Drug treatments of childhood coughs

## SUMMARY

Appropriate management of cough in children depends upon accurate assessment. The diagnosis is often unclear at the initial presentation.

Acute cough is frequently caused by a viral infection, and often no specific therapy is indicated. Urgent treatment may be needed if history suggests a more serious disorder such as a foreign body or pneumonia.

When treating children with chronic cough, paediatric-specific algorithms should be used. Empirical use of medicines without looking for a specific cause should be avoided.

In the absence of an alternative specific cause of cough, chronic wet cough (lasting at least four weeks) is most frequently due to protracted bacterial bronchitis. Antibiotics are indicated.

### Introduction

Cough is the most common symptom presented to GPs and pharmacists in Australia. An Australian study found that 'one in three (28.7%) respiratory episodes were associated with a doctor's visit, and one in four (23%) necessitated time off school or work'.<sup>1</sup> When a child first presents with cough, determining the precise diagnosis is not always possible.

#### Acute cough

Acute cough in a child may represent a variety of pathologies, from self-resolving viral-induced acute respiratory infection to acute severe respiratory disease or an acute presentation of an underlying chronic disorder. Appropriate management depends on accurate assessment. Patient history should include:<sup>2</sup>

- cough duration (acute <2 weeks, sub-acute 2-4 weeks, chronic >4 weeks)
- characteristics of cough (whooping cough, wet vs dry cough)
- questions about choking episodes and previous respiratory illness
- associated wheeze
- other symptoms such as weight loss, appetite or rash
- immunisation history.

In the differential diagnosis, it is important to consider inhaled foreign body, pneumonia and other treatable infections like pertussis and underlying lung disease such as bronchiectasis.

## Uncomplicated acute upper respiratory infections

It is commonly said that young children have up to 6–12 acute respiratory infections per year. However,

a Melbourne-based community study involving 600 families showed fewer episodes and an age-dependent trend (see Table).<sup>1</sup> The mean duration of episodes was 6.3 days (range 1–70 days) and younger children were more likely to have a longer duration of cough (6.8 days in youngest age group and 5.5 days in oldest group).

#### Management

Supportive therapy is the mainstay of treatment for viral acute respiratory infections. Paracetamol and ibuprofen are useful for related symptoms. Over-the-counter cough and cold medicines are not recommended due to a lack of proven efficacy and the possibility that they may present a safety risk.<sup>3</sup> The Therapeutic Goods Administration now recommends that they should not be used in children under 6 years and only in children aged 6–11 years on advice from a doctor.<sup>4</sup>

Honey,<sup>5,6</sup> and menthol-based rubs<sup>7</sup> may reduce the impact of nocturnal cough. It is reasonable to recommend one teaspoon of honey before bedtime for children aged over one year. Honey should be avoided in children under one year due to the risk of botulism.

TableAustralian rates of uncomplicated<br/>acute upper respiratory infections<br/>in children and young adults 1

Age (years)	Mean number of episodes a year
0-1	3.8
2-3	3.3
4-5	2.8
6–10	2.2
11-20	2

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#### Key words

asthma, bronchiectasis, bronchiolitis, bronchitis, croup, pertussis, pneumonia

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#### **Childhood coughs**

Antibiotics should be avoided for the treatment of acute cough associated with mild upper respiratory tract infection, as the cough is most likely viral in origin. A recent Cochrane review reported that in cases of confirmed or suspected exposure to influenza in healthy children, oseltamivir shortens the time to first alleviation of symptoms by 29 hours (95% confidence interval 12–47 hours, p=0.001).<sup>8</sup> No effect however was seen in children with asthma. Oseltamivir may reduce the risk of otitis media in children aged 1–5 years, especially if commenced within the first 12 hours, but is associated with a significantly increased risk of vomiting.<sup>9</sup> Laboratory-based polymerase chain reaction (PCR) techniques enable rapid influenza diagnosis.<sup>10</sup>

Management of acute cough should include counselling and advice on:

- the expected duration of cough (typically 5–7 days, but up to 3 weeks)
- when to come back and see the GP and when to seek urgent medical review (for example suspected foreign body, tachypnoea, dyspnoea, vomiting, inability to feed, persistent fever, lethargy)
- avoidance of passive smoke exposure.

#### Specific causes of acute cough

A number of specific diseases need to be considered in a child presenting with acute cough. Many of these have specific symptoms and signs.

#### Croup

The acute or sub-acute onset of a barking 'brassy' cough, hoarse voice, stridor with or without evidence of upper airway obstruction, is characteristic of croup. It often begins with a viral upper respiratory tract infection (for example rhinorrhoea, sore throat with or without fever) and typically affects children aged 1–6 years. Children outside this age range or with severe or recurrent stridor or other symptoms require careful evaluation for an underlying airway lesion. Children with bacterial causes of stridor such as tracheitis or epiglottitis usually appear more toxic.

Prednisolone 1–2 mg/kg orally for two consecutive days is effective for croup. Dexamethasone 0.15 mg/kg orally is an appropriate alternative therapy. In severe croup, when a child has ongoing stridor at rest, increasing fatigue and marked tachycardia with or without signs of impending hypoxaemia (for example, lethargy and increased irritability), urgent transfer to an emergency facility is recommended. Potentially distressing interventions, such as throat examination, should be avoided, as these may worsen respiratory obstruction.

#### Pneumonia

Children with pneumonia often have cough, fever and tachypnoea, but occasionally present with fever and

upper abdominal pain. Signs of severity include grunt and intercostal recession. Wheeze is usually absent in bacterial pneumonia.

A chest X-ray does not need to be performed routinely in all children with suspected pneumonia. However, it should be considered in any child with an atypical presentation (recurrent pneumonia, prolonged fever, signs of pleural effusion) or severe pneumonia requiring hospital admission.<sup>11</sup>

Recommendations for antimicrobial therapy vary according to the age of the child, context, presence of underlying disease (risk factors), presence of hypoxaemia, non-respiratory symptoms (such as vomiting), length and severity of symptoms and the presence of complications. Guidelines for antimicrobial therapy should be consulted.<sup>11-13</sup> For a child with subacute onset and prominent cough (with or without headache or sore throat), or who is not improving, mycoplasma pneumonia should be suspected.<sup>13</sup>

Indications for hospitalisation for community-acquired pneumonia include:

- very young children (less than 6 months) with suspected bacterial pneumonia<sup>12</sup>
- clinical evidence of moderate to severe pneumonia, including hypoxaemia and signs of respiratory distress<sup>12</sup>
- significant comorbidities or factors which predispose to more severe disease e.g. immunodeficiency, congenital heart disease, bronchiectasis<sup>11</sup>
- pneumonia suspected or confirmed to be secondary to a pathogen with increased virulence e.g. community-acquired methicillin-resistant *Staphylococcus aureus* (MRSA)<sup>12</sup>
- dehydration or inability to tolerate oral therapies<sup>11</sup>
- significant parental concern or anxiety<sup>11</sup>
- family unable to provide appropriate care or adhere to management plan<sup>12</sup>
- toxic-looking child e.g. pale or cyanotic, lethargic or inconsolably irritable
- complicated pneumonia e.g. empyema
- poor response after 48 hours of oral antibiotics.

All children with suspected pneumonia should be followed up regularly to ensure complete resolution of their symptoms. A repeat chest X-ray is not routinely performed following simple pneumonia unless there are persisting symptoms.<sup>11</sup>

#### Bronchiolitis

Children under two years presenting acutely with cough, tachypnoea (with or without poor feeding) and often with a history of a viral prodrome may have viral bronchiolitis. Clinical examination reveals hyperinflation with widespread wheeze and crackles on chest auscultation. Respiratory syncytial virus is the most common infection associated with bronchiolitis.

Any infant with apnoeas, hypoxia (oxygen saturations ≤92%), dehydration or poor feeding requires hospital admission for supplemental oxygen with or without hydration therapy. Children frequently worsen in the first 72 hours before showing improvement. The cough can persist for 2–3 weeks after other symptoms resolve. There is no evidence for the routine use of antibiotics, steroids or asthma drugs in viral bronchiolitis.

#### Pertussis

Pertussis (whooping cough) typically presents with cough lasting two or more weeks with cough paroxysms, inspiratory whoop or post-tussive vomiting. Confirmation with a PCR-positive nasopharyngeal aspirate or swab is recommended. If there is a high clinical suspicion, start antibiotics before receiving the test results. Clarithromycin (7.5 mg/kg up to 500 mg orally, 12-hourly for 7 days) or erythromycin (10 mg/kg up to 250 mg orally, 6-hourly for 7 days) is recommended.<sup>13</sup> Treat early to improve symptoms (within 1–2 weeks of start of symptoms) and reduce the infectious period. Patients are seldom infectious after having a cough for longer than three weeks and antibiotics are not recommended at this point.

### **Chronic cough**

The common causes of chronic cough in children differ from those in adults<sup>14</sup> so adult-type management approaches directed at asthma, rhinitis and gastro-oesophageal reflux disease do not apply. In a multicentre study involving 346 new referrals to respiratory paediatricians for chronic cough, the most common diagnoses included protracted bacterial bronchitis (41%), asthma (15.9%) and bronchiectasis (9%). In 13.9% of children, cough resolved without a specific diagnosis.<sup>15</sup>

A detailed respiratory history and examination as well as use of a chronic cough algorithm (see Fig.)<sup>16</sup> assist in the assessment and diagnosis of chronic cough.

## Fig. Simplified paediatric chronic cough algorithm



Adapted from reference 16

#### ARTICLE

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The cough algorithm also significantly improves quality of life and reduces duration of cough.<sup>16</sup> This approach is based on determining the cause of the cough (through systematic history taking and a thorough examination), in addition to spirometry (in a child >5 years of age) and chest X-ray. Indications for referral to a specialist are listed in the Box.

# Box Common indications for specialist referral in chronic childhood cough

Chronic cough (>4 weeks) of unclear aetiology (with or without failure to thrive) Suspected airway malformation e.g. tracheo-oesophageal fistula, vascular ring Cough and feeding difficulties (suspected aspiration disease) Clinical features of chronic lung disease e.g. clubbing Persisting auscultatory findings e.g. crepitations Recurrent pneumonias Abnormalities on chest X-ray or spirometry Failure to respond to treatment e.g. in asthma

### Protracted bacterial bronchitis

Protracted bacterial bronchitis is the most common cause of chronic wet cough in Australian children.<sup>14,16</sup> It is defined as:

- cough lasting more than four weeks
- response to two weeks of antibiotic therapy
- absence of specific pointers indicating an alternative cause.

A history of a preceding viral infection is common. Protracted bacterial bronchitis is more common in boys than girls and in those aged 1–3 years.

Lower airway bacterial infection is frequently found on bronchoalveolar lavage sampling and is usually accompanied by elevated neutrophils suggestive of active airway inflammation. The major bacterial organisms found are *Haemophilus influenzae*, *Moraxella catarrhalis* and *Streptococcus pneumoniae*. After exclusion of other causes of chronic cough, a two-week course of amoxycillin-clavulanate is recommended. Children should receive follow-up after 2–3 weeks to ensure complete resolution of cough. A chest X-ray should be performed in any child with clinical suspicion of an alternative cause of chronic cough or if their cough persists despite antibiotic therapy.

#### Bronchiectasis

Bronchiectasis is another important cause of wet cough to consider, and should be suspected in any child with the following:

- chronic wet cough lasting longer than eight weeks
- two or more episodes of chronic wet cough (lasting ≥4 weeks) per year responding to antibiotics

 chest radiographic changes lasting more than six weeks despite appropriate antibiotic therapy.<sup>17</sup>

Antibiotic therapy is usually started at the onset of wet cough in children known to have bronchiectasis. Antibiotic selection is based upon lower airway culture, local antibiotic susceptibility patterns and clinical severity. If symptoms do not respond promptly or adequately to oral antibiotic therapy patients should be hospitalised for intravenous antibiotics. Regular physiotherapy, physical exercise, avoidance of triggers (for example tobacco smoke) and routine vaccinations are recommended.<sup>17</sup> Aboriginal and Torres Strait Islander children are at increased risk of bronchiectasis and doctors should be aware that cough may be under-reported by those from remote communities.<sup>18</sup>

#### Asthma and chronic cough

While asthma can cause chronic cough, isolated chronic cough without any other symptoms in children is rarely due to asthma.<sup>19,20</sup> Other symptoms usually present in asthma are wheeze, dyspnoea, chest tightness or exercise limitation. Risk factors such as eczema, hay fever, allergies or a family history of asthma in a first-degree relative are often present.

Spirometry and measurements of airway responsiveness (for example exercise challenge) in children aged over five years can help to diagnose asthma. The presence of atopy does not distinguish asthma from other causes of chronic cough. Previous response to asthma therapies may be helpful, however response on a single occasion does not necessarily mean that the child has asthma. Guidelines for the management of asthma are available from the National Asthma Council of Australia (www.nationalasthma.org.au/handbook).

## Conclusion

Accurate diagnosis of cough in children depends upon a thorough clinical history and examination to guide appropriate prescribing. The nature of the cough and its chronicity provide important diagnostic clues as to a specific cause of cough. Cough guidelines and algorithms further enhance diagnostic accuracy and may help to ensure more effective prescribing of cough therapies in children.

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# Q:

## SELF-TEST QUESTIONS

#### True or false?

1. Aboriginal and Torres Strait Islander children have an increased risk of bronchiectasis.

2. There is evidence for use of steroids in viral bronchiolitis.

Answers on page 143

#### REFERENCES

- Leder K, Sinclair MI, Mitakakis TZ, Hellard ME, Forbes A. A community-based study of respiratory episodes in Melbourne, Australia. Aust N Z J Public Health 2003;27:399-404.
- Chang AB, Landau LI, Van Asperen PP, Glasgow NJ, Robertson CF, Marchant JM, et al. Cough in children: definitions and clinical evaluation. Med J Aust 2006;184:398-403.
- Smith SM, Schroeder K, Fahey T. Over-the-counter medications for acute cough in children and adults in ambulatory settings. Cochrane Database Syst Rev 2012;8:CD001831.
- Therapeutic Goods Administration. OTC cough and cold medicines for children - Final outcomes of TGA review. Canberra: Australian Government Department of Health; 2012.

www.tga.gov.au/industry/otc-notices-cough-cold-reviewoutcomes.htm [cited 2014 Jul 11]

- 5. Cranswick N. Cough and cold remedies for children. Aust Prescr 2013;36:e1.
- Oduwole O, Meremikwu MM, Oyo-Ita A, Udoh EE. Honey for acute cough in children. Cochrane Database Syst Rev 2012;3:CD007094.
- Paul IM, Beiler JS, King TS, Clapp ER, Vallati J, Berlin CM Jr. Vapor rub, petrolatum, and no treatment for children with nocturnal cough and cold symptoms. Pediatrics 2010;126:1092-9.
- Jefferson T, Jones MA, Doshi P, Del Mar CB, Hama R, Thompson MJ, et al. Neuraminidase inhibitors for preventing and treating influenza in healthy adults and children. Cochrane Database Syst Rev 2014;4:CD008965.
- Winther B, Block SL, Reisinger K, Dutkowski R. Impact of oseltamivir treatment on the incidence and course of acute otitis media in children with influenza. Int J Pediatr Otorhinolaryngol 2010;74:684-8.
- 10. Foo H, Dwyer DE. Rapid tests for the diagnosis of influenza. Aust Prescr 2009;32:64-7.

- Harris M, Clark J, Coote N, Fletcher P, Harnden A, McKern M, et al. British Thoracic Society guidelines for the management of community acquired pneumonia in children: update 2011. Thorax 2011;66 Suppl 2:ii1-23.
- Bradley JS, Byington CL, Shah SS, Alverson B, Carter ER, Harrison C, et al. The management of community-acquired pneumonia in infants and children older than 3 months of age: clinical practice guidelines by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America. Clin Infect Dis 2011;53:e25-76.
- Antibiotic Expert Group. eTG complete [internet]. Melbourne: Therapeutic Guidelines Limited; 2010. www.tg.org.au [cited 2014 Jul 11]
- Marchant JM, Masters IB, Taylor SM, Cox NC, Seymour GJ, Chang AB. Evaluation and outcome of young children with chronic cough. Chest 2006;129:1132-41.
- Chang AB, Robertson CF, Van Asperen PP, Glasgow NJ, Mellis CM, Masters IB, et al. A multicenter study on chronic cough in children: burden and etiologies based on a standardized management pathway. Chest 2012;142:943-50.
- Chang AB, Robertson CF, van Asperen PP, Glasgow NJ, Masters IB, Teoh L, et al. A cough algorithm for chronic cough in children: a multicenter, randomized controlled study. Pediatrics 2013;131:e1576-83.
- Chang AB, Bell SC, Byrnes CA, Grimwood K, Holmes PW, King PT, et al. Chronic suppurative lung disease and bronchiectasis in children and adults in Australia and New Zealand. Med J Aust 2010;193:356-65.
- Morey MJ, Cheng AC, McCallum GB, Chang AB. Accuracy of cough reporting by carers of Indigenous children. J Paediatr Child Health 2013;49:E199-203.
- 19. McKenzie S. Cough but is it asthma? Arch Dis Child 1994;70:1-2.
- Wright AL, Holberg CJ, Morgan WJ, Taussig LM, Halonen M, Martinez FD. Recurrent cough in childhood and its relation to asthma. Am J Respir Crit Care Med 1996;153:1259-65.

#### **FURTHER READING**

Centre for Clinical Practice at NICE. Evidence review and recommendations. In: Respiratory Tract Infections - Antibiotic Prescribing: Prescribing of antibiotics for self-limiting respiratory tract infections in adults and children in primary care. NICE Clinical Guidelines 69. London: NICE; 2008.

Chang A. Cough. Pediatr Clin North Am 2009;56:19-31.

Chang AB, Redding GJ, Everard ML. Chronic wet cough: protracted bronchitis, chronic suppurative lung disease and bronchiectasis. Pediatr Pulmonol 2008;43:519-31.

Wurzel DF, Marchant JM, Clark JE, Masters IB, Yerkovich ST, Upham JW, et al. Wet cough in children: infective and inflammatory characteristics in broncho-alveolar lavage fluid. Pediatr Pulmonol 2014:49:561-8.

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