

Chronic cough in children

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SUMMARY

The two most common causes of chronic cough among children are asthma and recurrent viral upper respiratory infection. Awareness of other potential causes of chronic cough is important. A specific diagnosis can usually be made with a thorough history, physical examination, and simple laboratory investigations.

RÉSUMÉ

Les deux causes les plus fréquentes de toux chronique chez les enfants sont l'asthme et l'infection récurrente des voies respiratoires supérieures. Il est important d'être sensible aux autres causes potentielles de toux chronique. Un interrogatoire, un examen clinique détaillé et des épreuves de laboratoire simples permettent généralement d'établir un diagnostic spécifique.

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CHRONIC COUGH CAN BE defined as a persistent or recurrent cough of more than 3 weeks' duration.¹⁻³ Chronic cough is a common problem, for which parents frequently consult their family physicians. The causes of chronic cough are numerous. Although most cases of chronic cough are benign, serious illnesses also present in this fashion. This article reviews the pathophysiology and etiology of chronic cough and offers an approach to manage this problem.

Pathophysiology

Cough is an important defense mechanism that enhances the clearance of abnormal secretions, inflammatory products, and foreign substances from the respiratory tract.^{4,5}

The cough reflex consists of an afferent limb, a central cough centre, and an efferent limb. The afferent limb comprises sensory nerve fibres located in the ciliated

epithelium that covers the airway from the pharynx to the terminal bronchioles.^{3,5} The concentration of these nerve fibres is greatest at the larynx, carina, and bifurcations of the large and medium-sized bronchi.^{1,3} These receptors are sensitive to mechanical stimuli, such as touch, foreign body, inflammation, intrinsic or extrinsic pressure from a tumour or lymph node, and chemical irritation from a noxious gas.⁵⁻⁷

Afferent stimuli travel to the cough centre via the trigeminal, glossopharyngeal, superior laryngeal, or vagus nerves.⁸ The cough centre is located in the upper brainstem and pons.^{1,3,5} Voluntary input to the cough centre can result in the initiation of a voluntary cough or suppression of a cough initiated by stimulation of the afferent limb.^{3,9} Efferent impulses from the cough centre travel via the phrenic, vagus, and spinal motor nerves to the larynx, intercostal muscles, diaphragm, and muscles of the abdominal wall and pelvic floor.^{1,3,9}

Stimulation of the cough reflex results in inspiration and glottic closure followed by contraction of the muscles of the chest wall, diaphragm, abdomen, and pelvic floor, which dramatically increases intrathoracic pressure.^{3,5} The high intrathoracic pressure causes a sudden opening of the glottis and the explosive release of the pressurized air from the lungs.³

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Table 1. Causes of chronic cough

ALLERGY AND REACTIVE AIRWAY DISEASE

- Asthma
- Allergic or vasomotor rhinitis

INFECTIONS

- Recurrent viral respiratory infection
- Pneumonia
- Chlamydial infection
- Mycoplasmal infection
- Pertussis or pertussislike syndrome
- Tuberculosis
- Psittacosis
- Fungal infections (histoplasmosis, blastomycosis, coccidioidomycosis)
- Parasitic infestation (visceral larva migrans, ascariasis)
- Sinusitis

FOREIGN BODY ASPIRATION

IMMUNODEFICIENCY DISORDERS

CONGENITAL MALFORMATIONS

- Tracheoesophageal fistula
- Laryngeal cleft
- Vascular ring
- Bronchiogenic cyst
- Pulmonary sequestration
- Immotile cilia syndrome

CYSTIC FIBROSIS

BRONCHIECTASIS

ENVIRONMENTAL IRRITANTS (cigarette smoke, house dust)

CARDIAC FAILURE

DRUGS

- Angiotensin-converting enzyme inhibitors
- β -Adrenergic antagonists

AIRWAY ENCROACHMENT

- Mediastinal tumours
- Mediastinal adenopathy
- Pulmonary tumours

PSYCHOGENIC COUGH

Etiology

Table 1 lists the causes of chronic cough.

Allergy and reactive airway disease.

Asthma is the most common cause of chronic cough in children.^{1,4,10} The cough is caused by bronchospasm, mucosal inflammation, and excess mucus production.⁶ Although wheezing is generally considered the sine qua non of asthma, chronic cough can be the only symptom.^{4,11}

Allergic or vasomotor rhinitis sometimes causes a chronic cough secondary to postnasal drip and stimulation of cough receptors.¹² Chronic postnasal drip can cause a persistent cough in the absence of disease in the lower respiratory tract.³

Infections. Recurrent viral respiratory infection is the second most common cause of chronic cough. Viral infection is more common than bacterial infection. Although more than 200 different viral agents can cause cough, the usual causative agents are rhinoviruses, coronaviruses, respiratory syncytial virus, parainfluenza viruses, or adenoviruses.² Recurrent viral bronchitis or unresolved pneumonia is an important cause of chronic cough.

The bacteria that cause chronic cough include *Chlamydia*, *Mycoplasma*, *Bordetella pertussis*, and *Mycobacterium tuberculosis*. The pneumonia caused by *Chlamydia* is characteristic. The infection is usually acquired during birth by transmission through an infected birth canal. Affected infants appear well and are afebrile but develop increasing tachypnea and prominent cough at 3 to 16 weeks of age. About half of the infants have a history or evidence of conjunctivitis.

Infection of the lower respiratory tract with *Mycoplasma pneumoniae* can occur at any age and is the leading cause of pneumonia in school-aged children and young adults. The pneumonia is usually interstitial or bronchopneumonic, and the lower lobes are most commonly involved. Pertussis is a particularly contagious disease that is caused by *B pertussis*. *Bordetella paraptussis* and certain adenoviruses can cause a pertussislike syndrome. Pulmonary tuberculosis is caused mainly by *M tuberculosis*. Tuberculosis is common in developing countries and in crowded and poor living conditions. Although most individuals with

pulmonary tuberculosis are asymptomatic, some individuals have chronic cough as the principal respiratory symptom.

Psittacosis (ornithosis), an infectious disease of birds, is caused by *Chlamydia psittaci*. Infection can be transmitted from birds to humans and results in an acute respiratory tract infection associated with fever.

Fungal infections, such as histoplasmosis caused by *Histoplasma capsulatum*, blastomycosis caused by *Blastomyces dermatitidis*, and coccidioidomycosis caused by *Coccidioides immitis*, can cause a respiratory infection and result in a chronic cough. Respiratory infections due to these fungi should be considered in individuals who have resided in areas where these fungi are endemic.

Visceral larva migrans is caused by infestation with larvae of *Toxocara* species, which are common roundworms of dogs and cats. Visceral larva migrans is more common in children 1 to 4 years of age, especially those who put everything in their mouths and have close contact with dogs and cats.¹³ The most common symptoms include fever, cough, and wheezing. Ascariasis occurs when humans are infested with *Ascaris lumbricoides*. Fever, cough, blood-stained sputum, dyspnea, wheezing, eosinophilia, and migratory pulmonary infiltrates (Löffer-like syndrome) can occur as the larvae pass through the lung.¹⁴

The most common bacterial pathogens found in sinusitis are *Streptococcus pneumoniae*, non-typable *Haemophilus influenzae*, *Branhamella catarrhalis*, *Streptococcus pyogenes*, and in chronic cases, *Staphylococcus aureus* and anaerobic bacteria. Cough associated with sinusitis is caused by irritation of the branches of the vagus nerve that innervate the sinuses or by postnasal drip.^{15,16} Children with sinusitis have an increased risk of developing asthma.¹⁶

Foreign body aspiration. Foreign body aspiration is a common cause of chronic cough among preschool children. During infancy, chronic cough can be due to aspiration of milk or formula, which can be secondary to gastroesophageal reflux, tracheoesophageal fistula, or laryngeal cleft.¹⁷ Often there is a history of a choking episode associated with feeding. Chronic cough is sometimes the sole presenting manifestation of gastroesophageal reflux.¹⁸ Toddlers and preschool children

can aspirate a small object, such as a food particle, peanut, candy, or small toy. Foreign body aspiration should be considered when there is a sudden onset of unexplained coughing, wheezing, choking, or cyanosis, which then develops into a chronic cough.¹⁹

Immunodeficiency disorders. A chronic cough can be a symptom of an immunodeficiency disorder. Immune deficiency can be due to failure of antibody production, failure of cell-mediated immunity, or defects in the polymorphonuclear leukocyte, macrophage, or complement systems.²⁰ Combined deficiencies of immunoglobulins and lymphocytes also occur.

Immunodeficiency may be primary or secondary. Secondary immunodeficiencies are caused by malignancy, splenectomy, malnutrition, infection by human immunodeficiency virus, or treatment with cytotoxic drugs or corticosteroids.²⁰ Children with immunodeficiency disorders are prone to recurrent or persistent respiratory tract infections, as well as to infections with opportunistic pathogens, such as *Pneumocystis carinii* and *Legionella pneumophila*.

Congenital malformations. Congenital malformations of the esophagus or airway are uncommon causes of chronic cough. Tracheoesophageal fistula and laryngeal cleft can cause cough due to aspiration. Compression of the trachea or bronchi by a vascular ring can produce stridor and cough.⁵ A bronchiogenic cyst or pulmonary sequestration can lead to a chronic cough due to infection or airway compression.¹² In the immotile cilia syndrome, the mucociliary apparatus is impaired, resulting in recurrent sinusitis, otitis media, and pulmonary infections, with or without bronchiectasis.² Some of these patients also have situs inversus (Kartagener's syndrome).

Cystic fibrosis. Cystic fibrosis is an important cause of chronic cough. It is inherited as an autosomal recessive trait and affects approximately one in 2500 white children.²¹ The disease is characterized by chronic obstruction and infection of the respiratory tract and by intestinal malabsorption.²¹

Bronchiectasis. Bronchiectasis refers to permanent dilation and distortion of the architecture of the bronchi, usually accompanied by inflammation and accumulation of purulent or exudative material in the dependent bronchi. Bronchiectasis can be secondary to cystic fibrosis, foreign body aspiration, immunodeficiency, pertussis, pneumonia, or tuberculosis. Bronchiectasis is an uncommon cause of chronic cough in children.

Environmental irritants. Cigarette smoke, inhaled either actively or passively, can lead to chronic cough due to irritation of the airway.²² Smoking can also trigger asthma.¹⁰

Exposure to a dry, dusty environment sometimes produces an irritative cough because of mucus production, pooling of secretions, and irritation of the airway.²²

Cardiac failure. Cough is a feature of pulmonary edema associated with congestive heart failure. Undiagnosed or inadequately treated congestive heart failure occasionally causes chronic cough in children.

Drugs. Angiotensin-converting enzyme inhibitors, such as captopril and enalapril, produce a chronic cough in about 5% to 10% of individuals.^{23,24} β -Adrenergic antagonists, such as propranolol, can precipitate symptoms of asthma.²⁴

Airway encroachment. Extrinsic masses, such as mediastinal tumours or adenopathy, induce chronic cough by compressing the airway. Pulmonary tumours are rare during childhood.

Psychogenic cough. Chronic cough can be a somatic manifestation of a range of psychological problems.²⁵ School phobia, anxiety, and attention-seeking behaviour are more common among these children.

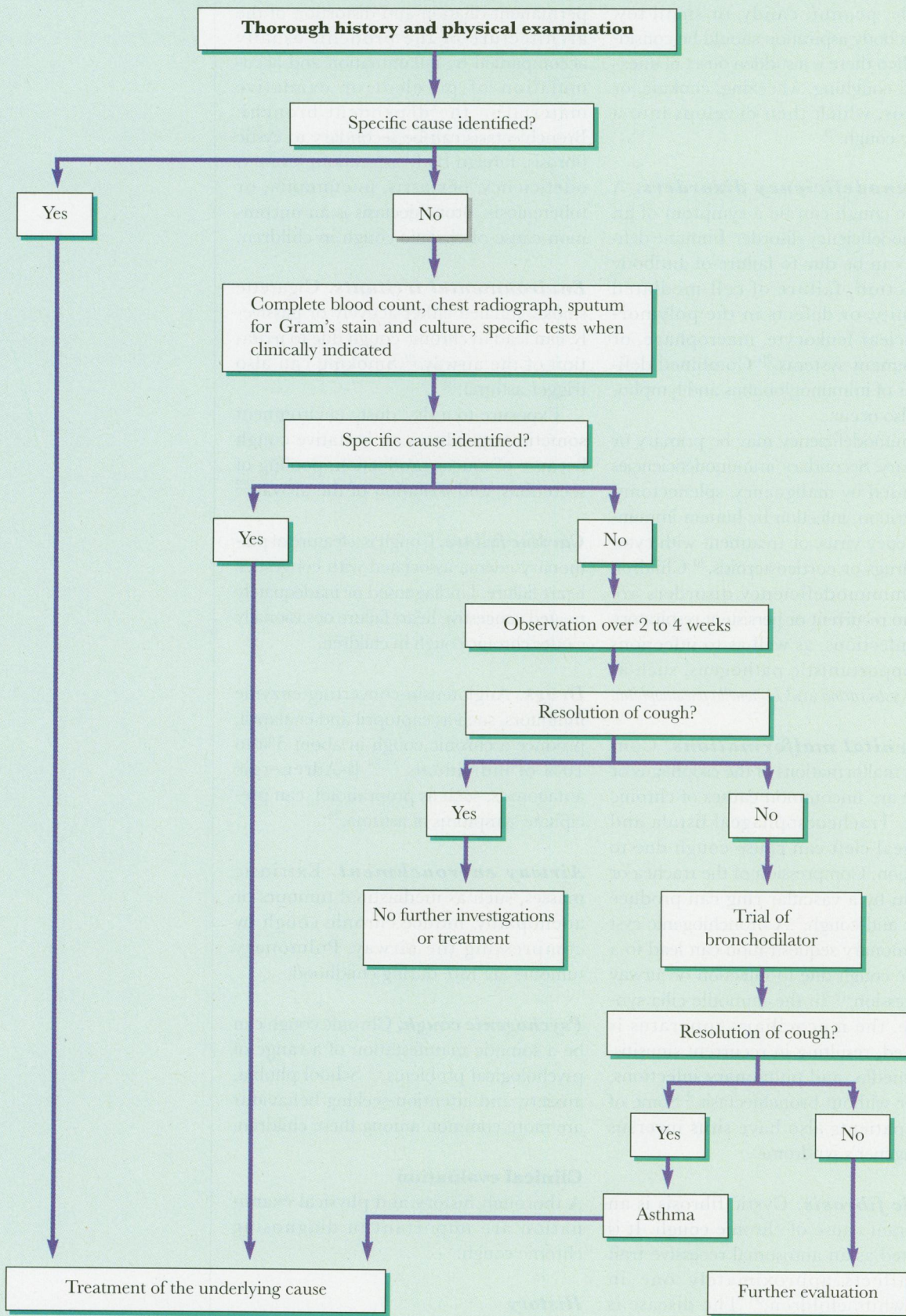
Clinical evaluation

A thorough history and physical examination are important in diagnosing chronic cough.

History

Age of onset: A chronic cough within the first month of life suggests a congenital malformation or infection, or aspiration of breast

Figure 1. Algorithm for evaluating chronic cough



Adapted from Kamei.²

milk or formula. Preschool children are at greatest risk for foreign body aspiration. Pertussis is common among preschool children and can develop among children who are immunized for pertussis. Infections with *M pneumoniae* and psychogenic cough are more common among school-age children than among younger children. Recurrent viral infection and asthma are common in all age groups.

Nature of the cough: A productive cough usually indicates an underlying inflammatory process. A dry, brassy, croupy, or hoarse cough suggests a disorder of the upper airway. A throat-clearing noise is typical of a postnasal drip. Paroxysms of cough suggest pertussis or a pertussislike syndrome, but are also seen in some children with cystic fibrosis or chlamydial infection.⁹ A paroxysmal cough with a "whoop" is characteristic of pertussis or a pertussislike syndrome. The characteristic whoop is often absent in young children. In psychogenic cough, the cough is nonproductive, isolated, explosive, often bizarre in quality, and characteristically described as "barking" or "honking."⁹

Timing of the cough: A cough that occurs with feeding suggests aspiration, which can be secondary to a tracheoesophageal fistula or gastroesophageal reflux. An exercise-induced cough is typical of asthma.²⁶ Exacerbation of cough on exposure to dusts, pollens, or animals suggests asthma. Nocturnal cough is suggestive of asthma, postnasal drip, or congestive heart failure. A cough that is more noticeable upon awakening in the morning suggests a suppurative lung disease or sinusitis with a postnasal drip.^{2,3} The complete disappearance of a cough during sleep suggests that the cough is psychogenic. Psychogenic cough is more noticeable when people are around.

Seasonal effects: An exacerbation of cough during spring and summer or with changes in the weather suggests asthma. Viral respiratory tract infections are more common during the winter months.

Nature of the sputum: Clear or mucoid sputum is common with asthma. Purulent sputum indicates suppurative lung disease. Bloody sputum or hemoptysis suggests an aspirated foreign body, tuberculosis, cystic fibrosis, or bronchiectasis.^{6,27} Pink, foamy sputum indicates pulmonary edema.⁸

Stridor or wheezing: Cough with stridor indicates a lesion in the larynx or trachea.

Cough with wheezing suggests obstruction in the small airways, as occurs in asthma.

Exposure to infection: A child who attends a day-care centre is more likely to have recurrent viral respiratory infection. Exposure to children with pertussis, mycoplasmal infection, or tuberculosis suggests the corresponding disease.

Immunization history: Children who are not fully immunized against pertussis are at increased risk for the disease.

Functional inquiry: Posttussive vomiting in association with paroxysms of cough is characteristic of pertussis and, less commonly, asthma. Bulky, greasy stools in a child with failure to thrive suggests cystic fibrosis. Recurrent regurgitation or choking suggests that aspiration is the cause. Prolonged fever and weight loss indicate a chronic suppurative lung disease. Low-grade fever, night sweats, and weight loss suggest tuberculosis.

Past health: Any previous hospitalization or important illness should be noted. The response to previous treatment can be a helpful guide. A good response to antibiotic treatment suggests a bacterial infection. A good response to a bronchodilator suggests asthma. However, lack of response to a medication could be related to inadequate dose, incorrect choice of medication, or improper use of a bronchodilator.

A detailed drug history could reveal an angiotensin-converting enzyme inhibitor or a β -adrenergic antagonist as the cause of chronic cough. Treatment with corticosteroids or cytotoxic drugs suggests immunodeficiency.

Family history: A personal or family history of atopy suggests asthma as the cause of chronic cough. A family history of immunodeficiency or cystic fibrosis suggests the corresponding disease.

Psychosocial history: Any psychosocial stress should be noted as a potential cause of psychogenic cough. The living environment of the child should also be noted, as overcrowding can predispose a child to recurrent infection. The presence of active or passive cigarette smoking should be noted.

Physical examination

General: Weight, height, and head circumference should be plotted on standard growth charts. Malnutrition and failure to thrive mark the presence of a chronic disease, such as cystic fibrosis, bronchiectasis,

tuberculosis, immunodeficiency, or severe chronic asthma. Fever indicates an underlying infection. Clubbing of the fingers indicates a suppurative lung disease, such as cystic fibrosis or bronchiectasis, or congenital cyanotic heart disease. Eczematous lesions suggest atopy.

Head and neck: Dark periorbital edema ("allergic shiner"), wrinkles beneath the lower eyelid (Dennie's lines), a transverse crease across the lower third of the nose, and mouth breathing ("allergic gape") indicate allergies in a child. Nasal polyps suggest cystic fibrosis or immotile cilia syndrome.²⁷ Postnasal drip suggests sinusitis or rhinitis. A clear nasal discharge indicates a common cold or vasomotor rhinitis. A purulent nasal discharge suggests bacterial sinusitis. The presence of conjunctivitis in the first few weeks of life suggests chlamydial infection.

Chest: An increase in respiratory rate suggests asthma, bronchopulmonary infection, or congestive heart failure. An increase in the anteroposterior diameter of the chest indicates chronic airway obstruction, which appears in patients with cystic fibrosis or chronic severe asthma. Generalized wheezing or expiratory rhonchi suggest asthma, whereas localized wheezing suggests an inhaled foreign body. Decreased air entry suggests bronchial obstruction. Inspiratory crepitations (crackles or rales) suggest pneumonia or pulmonary edema. Hyperresonance of the chest suggests air trapping, which can occur with asthma. Dullness to percussion suggests pneumonia or pleural effusion.

Laboratory evaluation. Some basic laboratory screening studies are worthwhile in most cases and include a complete blood count, sputum for Gram's stain and culture, and a chest radiograph.

A CBC is often helpful. Neutrophilia and increased numbers of band forms or toxic granulations suggest bacterial infection. Neutropenia is seen in some immunodeficiency disorders.²⁰ Marked lymphocytosis is seen in pertussis. Eosinophilia can be seen in allergic disease, parasitic infestation, or chlamydial infection. An elevated erythrocyte sedimentation rate suggests active infection or inflammation.

Sputum, if present, should be sent for Gram's stain, microscopy, and culture.²⁷

Eosinophilia in the sputum suggests asthma, whereas neutrophilia suggests infection.

A chest radiograph can show underlying pneumonia, foreign body, cystic fibrosis, tuberculosis, or bronchiectasis. A film taken during expiration could suggest the presence of a foreign body.

Pulmonary function tests should be done if the diagnosis is not obvious.^{10,23,24} Asthma is diagnosed if airway obstruction is present and if treatment with a bronchodilator reverses the airway obstruction and improves the pulmonary function. Bronchial provocation tests, such as exercises or inhalation of methacholine or histamine, can be useful to identify "hidden asthma" in older children.³

Other tests should be done when indicated, such as a nasopharyngeal swab for culture of *B pertussis*, serology for mycoplasma infection, serum immunoglobulins for immunodeficiency, Mantoux test for tuberculosis, sweat chloride test for cystic fibrosis, upper gastrointestinal series for tracheoesophageal fistula or gastroesophageal reflux, and bronchoscopy for foreign body aspiration.

Figure 1 shows an algorithm helpful for evaluating chronic cough in children.²

Complications

The high intrathoracic pressure generated during a cough can result in complications, including vomiting, exhaustion, headache, insomnia, facial petechiae, subconjunctival hemorrhage, pneumothorax, pneumomediastinum, pulmonary emphysema, muscle pain, rib fracture, and loss of consciousness.^{6,28}

Treatment

Treatment should be directed at the underlying cause whenever possible. Physical and chemical airborne irritants should be removed. Bacterial infections should be treated with appropriate antibiotics. Asthma should be treated with a combination of an inhalation bronchodilator and an anti-inflammatory medication. Postnasal drip sometimes responds to a decongestant or an antihistamine.³ Psychogenic cough could require psychological counseling.

Nonspecific symptomatic therapy is indicated when the cough is dry and irritating, distressing, keeps the child up at night, or otherwise interferes with the

child's quality of life.^{3,6,27} Codeine is a good cough-suppressing medication.^{2,4,9} Codeine is well tolerated and does not lead to addiction with short-term use.^{6,27} Nonnarcotic cough suppressants, such as dextromethorphan, are less effective.^{3,6,27} The efficacy of expectorants and mucolytic agents is doubtful, and their use for children is not generally indicated.^{2,3,6,27} ■

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