Cough in children

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Abstract

Cough is a common problem in children. Acute cough lasts less than 3 weeks, subacute 3–8 weeks and chronic cough more than 8 weeks.

Acute cough is usually caused by common viral upper respiratory tract infection. However, a child should be thoroughly evaluated to rule out a serious underlying condition or disease responsible for the cough.

The commonest cause of subacute cough is viral infection (postinfectious cough) and it usually resolves spontaneously. If the child is otherwise healthy and the cough is dry and there are no specific alerts for a serious disease and the cough is resolving, a period of observation is all that is recommended. If there are any specific pointers in the child's history and examination identified for inhaled foreign body, chronic lung disease or in a case of progressive cough immediate investigations are needed.

Most chronic coughs in childhood are due to viral respiratory infections, but may signify a serious underlying disease too. Chronic cough is subdivided into specific cough (i.e. cough associated with other symptoms and signs suggestive of an associated or underlying problem) and nonspecific cough (i.e. dry cough in the absence of an identifiable respiratory disease of known etiology).

To prevent unnecessary investigations and ineffective treatment and at the same time not to overlook a severe underlying disease cough guidelines have been designed which are based on evidence-based medicine.

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1. Introduction

A cough in children is one of the most common presenting symptoms to pediatricians. It can be very distressing for children and parents as it interferes with sleep, ability to play and school performance (1).

A cough is the most important defensive reflex that enhances clearance of secretions from the airways. Cough receptors are found on the surface cells that line the upper respiratory tract from

larynx to segmental bronchioles and are irritated by chemical and mechanical stimuli.

During childhood, the respiratory tract and nervous system undergo a series of anatomical and physiological maturation processes, which make the cough center in children more sensitive to some stimuli from the environment (2).

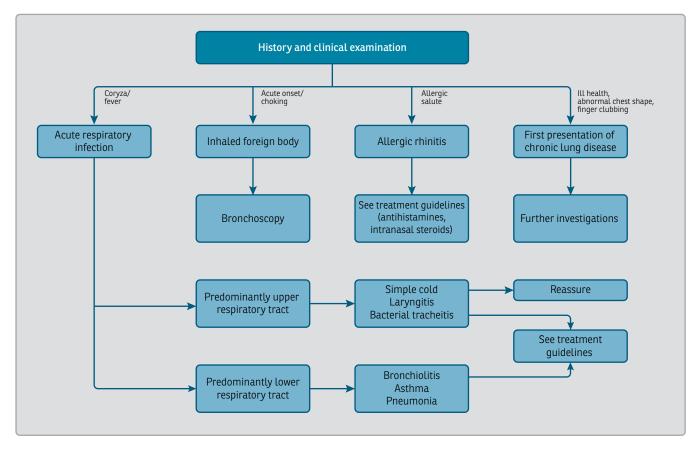


Figure 1: Acute cough algorithm.

Possible underlying etiologies of cough range from common cold to serious causes such as cystic fibrosis (CF), tumor and foreign body aspiration.

An attempt should be made to find the underlying cause of cough and then apply specific treatment. ???Of the underlying cause.

Cough can be classified by different criteria such as the underlying cause, time of onset and characteristics (productive, dry).

From the practical point of view the classification based on the duration of cough is mostly used: acute cough (lasting less than 3 weeks), subacute (lasting 3–8 weeks) and chronic (lasting more than 8 weeks).

Acute cough is usually caused by self limited viral respiratory infections. However, an attempt should be made to exclude serious causes.

Subacute cough is mostly related to acute viral infections (postinfectious

cough) and abates without specific treatment.

If the cough is progressive or if retained inhaled foreign body or chronic lung disease is likely, immediate investigations are required.

Chronic cough is classified into specific and nonspecific.

Specific cough is a cough with symptoms and signs that point to a specific underlying diagnosis; i.e. specific pointers.

Pointers in the child's history: is cough dry or productive, recurrent, chronic, sudden onset, triggering factors, difficulty feeding, presence of associated symptoms.

Pointers in the clinical examination: failure to gain weight, hemopthysis, allergy – nose, skin, eye, finger clubbing, pathologic auscultatory signs, dyspnea:.a cough can be a manifestation of congestive heart disease with pulmonary edema.

In most children a detailed history and clinical examination will determine the presence of specific pointers, and consequently the need for further investigations (3-5).

A nonspecific cough is a dry cough in the otherwise healthy child without associated specific pointers that would point to an underlying disease.

In most children with a chronic *dry* cough there is no serious underlying disease, it is a postinfectious cough due to hypersensitivity of cough receptors after a viral infection. In this group of children investigations are mostly not necessary, although a careful follow up until cough disappears is required (3,4).

On the other hand, a chronic wet cough is always the consequence of a serious underlying disease, and further investigations are needed.

All children cough from time to time. As childhood coughing is a common problem and has numerous different causes the management of a child with a cough is a big challenge.

Recommendations for the assessment of cough in children are very helpful to the pediatrician as they enable a highly structured approach to the diagnosis and treatment, avoidance of unnecessary investigations and help diminish the possibility to overlook serious or even lifethreatening conditions (4,5). However, guidelines cannot be a substitute for a personal approach in clinical decisions.

2. Classification of cough

In literature there are different classifications regarding the duration of couhging. Some authors classify cough as acute if it lasts less than three weeks, and chronic if it lasts more than three weeks.

In the recommendations for cough in children by the British Thoracic Society (BTS)(4) and American College of Chest Physicians (ACCP)(5-6) cough is classified as acute, subacute (postinfectious, prolonged acute cough) and chronic. In Slovenia, this classification was used by the Working Group for Pediatric Pulmonology when preparing the national recommendations for the management of cough in children (ref. manjka)

Table 1: Questions to be addressed to arrive at a specific diagnosis of acute cough (4).

Questions and features	Likely diagnoses
Does a child have acute upper respiratory infection?	Tracheitis Bacterial sinusitis
Is stridor accompanying coughing?	Acute laryngitis Bacterial tracheitis
Are there any features to suggest a lower respiratory tract illness: tachypnea, increased work of breathing, crackles/wheeze, fever?	Pneumonia Bronchiolitis Asthma
Is there anything to suggest hay fever?	Asthma – likely
Is there anything to suggest a presentation of a chronic respiratory disorder: failure to thrive, finger clubbing, overinflated chest, atopy?	Cystic fibrosis Primary ciliary dyskinesia Bronchiectasis
Is there anything to suggest an inhaled foreign body: sudden onset or witnessed choking episode?	Inhaled foreign body

2.1. Acute cough

Acute cough lasts less than three weeks and is usually caused by a viral upper respiratory tract infection. The intensity of cough is reduced in the second and third week.

In the absence of fever, tachypnea, chest symptoms and signs of lower respiratory tract infection, cough will most likely abate within 2-3 weeks.

The reason that acute cough has been classified as a cough that lasts up to three weeks is that it may take two to three weeks for most infectious causes of cough to fully resolve (4).

Acute cough is mostly the due to a viral upper respiratory tract infection, but it can also be a sign of serious life-threatening underlying diseases, such as foreign body aspiration, pulmonary embolism, cardiac decompensation, pneumonia or mediastinal neoplasm.

In a child with acute cough an attempt must be made to find whether

the cough is the sign of a serious life-threatening underlying disease

OR

whether it is the sign of a mild disease such as the common cold, asthma, upper airway syndrome.

When a history, clinical examination **2.2. Subacute cough** and investigations point toward a simple viral respiratory infection as the cause of cough, only symptomatic treatment is advised.

The children in whom a serious lifethreatening condition is a likely cause of acute cough should undergo immediate investigations, and specific treatment must be initiated (Figure 1).

When a chest radiograph should be considered in a child with acute cough (4).

possibility of pneumonia:

fever and tachipnea in the absence of wheezing, localized auscultatory sign - dullness, crackles or bronchial breathing, if fever and cough last longer than 4-5 days, unusual course of bronchiolitis.

possibility of foreign body aspira-

sudden onset of coughing, localized auscultation sign - wheezing, hyperinflation; X-ray must be performed in inspiration and expiration, but also normal X-ray does not exclude aspiration; bronchoscopy is the most important diagnostic and therapeutic investigation.

possibility of chronic lung disease: failure to thrive, fingers clubbing, hyperinflation or chest deformity.

• unusual clinical course:

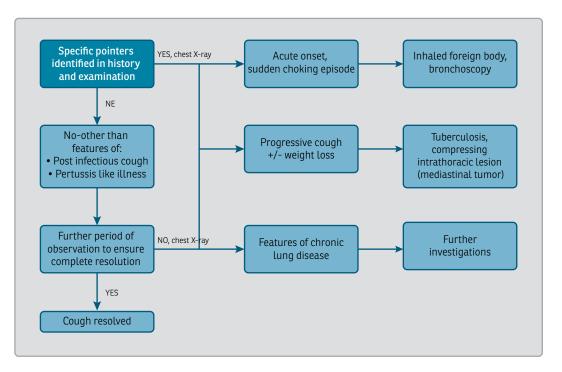
cough is relentlessly progressive beyond 2-3 weeks, or recurrent fever after initial resolution: pneumonia, mediastinal tumor, tuberculosis, foreign body aspiration, atelectasis.

hemoptysis:

indicative of pneumonia or lung abscess, chronic suppurative lung disease such as cystic fibrosis, inhaled foreign body, tuberculosis, pulmonary hemosiderosis, tumor, pulmonary arteriovenous malformation.

Studies and clinical observations show that in the majority of children acute cough with the common cold is associated with bronchitis and cough abates within 2-3 weeks, but 10 % of children will still cough after 4 weeks. Cough gradually improves and a complete resolution is expected within 3-8

Figure 2: Subacute cough algorithm.



weeks (4-6). This data should be known to all health workers and parents to avoid unnecessary visits and investigations. This type of cough is called prolonged acute cough, postinfectious cough or subacute cough. If the child is otherwise well, the cough is dry and specific pointers for a serious disease are absent, only observation of the child is recommended until complete resolution of the cough.

If there is suspicion of a retained inhaled foreign body, or the cough is progressively worsening or there are signs of a chronic disease present, further investigations are needed. Pertussis has been increasingly identified as the cause of prolonged cough even in a previously vaccinated child (10-11).

In a child who coughs for more than three but less than eight weeks (subacute cough), it is necessary to find whether the cough is associated with an acute respiratory infection or not.

A. If subacute cough is due to an acute viral infection in an otherwise healthy child, the cough is dry and gradually

improving, specific pointers for a serious disease are absent, the observation of the child is only required until the complete resolution of the cough; no further tests are needed. Most coughing in the child is related to transient viral infections, i.e. it is postinfectious (postviral). It starts with other symptoms of the common cold and persists after the other cold signs have abated. There are many mechanisms: viral inflammation is related to hypersensitivity of the airways, sputum production and impaired airway clearance, which trigger the cough receptors. In most children this cough resolves spontaneously. A period of 3-8 weeks is needed to determine if further tests are needed. If the cough lasts more than 8 weeks, other causes, not only postinfectious cough, should be considered (4-6).

- B. If subacute cough is not due to an acute respiratory viral infection, the following investigations are required to exclude:
 - retained inhaled foreign body,

- onset,
- pertussis, mediastinal tumor and lung collapse due to mucous plug or pressure due to enlarged lymph node (i.e. tuberculosis) if the cough is progressively worsening (10-11).

2.3. Chronic cough

Chronic cough is by majority of guidelines regarded as a cough, which lasts for more than 8 weeks. In comparison to an acute or subacute cough, a chronic cough is diagnostically more complex, because it could be an effect of several diseases (4,5,12,13).

Management of child with chronic cough

A structured approach is necessary in the treatment of a child with chronic cough. Most important steps are taking an accurate history and a thorough physical examination. In both steps the focus should be on searching for clinical characteristics, the so-called specific indicators that reveal the cause of chronic cough (4,6,12).

The results of both patient history and physical examination help with the decision on the investigations needed (3,4,6,11).

In history taking and in clinical examination the focus should be on specific indicators (information/symptoms/signs), which lead us to further examinations and help with the diagnosis or the cause of cough.

3.1. History

The child's age should be considered when taking the history: the younger the

 chronic lung disease with acute child the higher the probability of anatomic disorders in the upper and lower respiratory tract, or digestive tract, and of aspiration of a foreign body. Specific questions must be asked, such as whether a child has feeding problems. Food aspiration can be a cause of chronic cough. In such cases anatomic disorders in the area of digestive and respiratory tracts(tracheoesophageal fistula, laryngeal cleft,...), and neuromuscular diseases must be excluded.

> The following questions must be asked to obtain a detailed history (4)

- 1. When and how did the cough start? In cases the cough started suddenly, a foreign body aspiration must be assumed.
 - In cases the cough started in the neonatal period, an important disorder or disease is most probably the cause. All newborns who cough, need a special attention when feeded, feeding should be done by an experienced person only!

Probable causes of cough in the neonatal period:

- aspiration due to tracheoesophageal fistula or laryngeal cleft (productive cough after feeding, irritation, moving the head backwards after feeding),
- congenital malformation: compression of the airways or tracheobronchomalacia, cystic fibrosis, primary ciliary dyskinesia, especially if chronic rhinitis persists from the birth,
- infections: in utero (cytomegalovirus), during labor (Chlamydia trachomatis) or after birth (e.g. respiratory syncytial virus).
- 2. Is cough productive or dry? It is important to distinguish between both variations of cough, which helps us find the cause of cough. With pro-

Table 2: Red flag (4).

Sudden onset with choking episode	Neonatal onset
Chronic moist cough with phlegm production	Cough with feeding, choking, vomiting.
Associated night sweats/weight loss	Inspiratory stridor (other than during acute laryngitis)
Hemoptysis	Continuous unremitting or worsening cough
Signs of chronic lung disease – (failure to thrive, clubbing, overinflated chest, atopy)	Abnormalities on respiratory examination and/or chest X-ray

- ductive cough phlegm is present in the respiratory tract.
- Is cough chronic or it occurs with intervals of improvement?
 A detailed history is necessary.
- 4. Is cough an isolated symptom or are there other symptoms present (wheezing, shortness of breath, associated ill health)?

 When cough is isolated in a healthy child, a psychogenic or a recurrent bronchitis could be the cause. When
- heavy breathing and wheezing are associated with the cough, the cause fo coughing could be asthma, inhaled foreign body retained in the respiratory tract, recurrent pulmonary aspiration, airway compression, tracheomalacia, bronchiolitis obliterans or interstitial lung disease.
- What triggers the cough?
 Exercise, cold air, allergens possibility of asthma, when a cough occurs in lying position postnasal drip or

Table 3: Specific pointers in chronic cough (4,13).

Cough characteristics and specific pointers	Likely diagnosis
Dry cough, worse at night; wheezing; atopy	Asthma, GOR
Throat clearing, allergic salute	Allergic rhinitis Upper airway cough syndrome
Wet cough	Chronic suppurative lung disease (bronchiectasis) e.g, CF
Choking	TEF, swallow incoordiataion
brassy, barking cough, stridor.	Acute laryngitis, tracheobronchomalacia, pressure on the airways
Bizarre cough in a child exhibiting "la belle indifference" to the cough,which increases with attention, disappears with sleep	Psychogenic cough
Unremitting cough, losing weight, fever	Tuberculosis
Staccato cough	Chlamydia trachomatis infection
Paroxysmal cough with or without an inspiratory "whoop" and vomit	Bordetella pertussis infection
Dry cough, crackles, restrictive spirometry	ILD

GOR-gastroesophageal reflux; CF-cystic fibrosis; TEF-tracheoesophageal fistula; ILD-interstitial lung disease

- gastro-esophageal reflux, postprandial cough – food aspiration.
- 6. Does anyone else in the family suffer from respiratory disease?
- how do they affect the cough?
- 8. Does the cough disappear when asleep?
- 9. Does the child (teenager) smoke cigarettes or is she/he exposed to environmental smoke?

3.2. Clinical examination

Pointers in the clinical examination

1. Full clinical systematic examination must be done to estimate the

- nutritional status and the area of the ears, nose and throat (foreign body in external auditory meatus may be the cause of chronic cough).
- 7. What medication is the child on and 2. Look for the signs of atopic disease: atopic dermatitis, allergic rhinoconiunctivitis.
 - 3. Look for the signs of chronic lung disorder: failure to thrive, presence of otitis and/or sinusitis, overinflated chest, finger clubbing, wheezing and/ or crackling lung sound.
 - 4. Look for the signs of chronic cardiac disease: especially in infancy a chronic cough can be a sign of congestive heart failure with pulmonary edema.

Table 4: Serious diseases with chronic productive cough as a leading symptom (4).

Condition	Investigations
Cystic fibrosis	Sweat test, assessment of pancreatic function, genotyping
Immune deficiencies	Differential white cell counts, immunoglobulin levels and subsets, functional antibody responses and lymphocyte subset analysis
Primary ciliary disorders	Screening with FeNO, ciliary ultrastructure and function, culture of ciliated epithelium, genetic testing
Protracted bacterial bronchitis	Chest radiography, sputum for culture, exclusion of other causes in this table. Response to 4–6 weeks antibiotic and physiotherapy, CT scan
Recurrent pulmonary aspiration: laryngeal cleft, TEF, neuromuscular or neurodevelopmental disorder, GOR, hiatal hernia	Barium swallow, 24 h pH studies, videolaryngoscopy lipid-laden macrophage index on bronchalveolar lavage if bronchoscopy indicated. There is little evidence that GOR alone is the cause of cough in otherwise healthy children
Retained inhaled foreign body	Chest radiography and CT scan may show focal lung disease Rigid bronchoscopy is both diagnostic and therapeutic; indicated almost always if the history is suggestive of inhaled retained foreign body
Tuberculosis	Chest radiography, Mantoux test, early morning gastric aspirates and gamma interferon tests
Anatomical disorder (e.g.bronchomalacia) or lung malformation (e.g. cystic congenital thoracic malformation)	Bronchoscopy and CT scan
Interstitial lung disease	Spirometry (restrictive defect), chest radiography and CT scan, open lung biopsy

FeNO-fraction of exhaled nitric oxide; CT-computer tomography; TEF-tracheoesophageal fistula, GOR-gastroesophageal reflux.

3.3. Investigations

On the first examination it is recommended to perform the following examinations:

- 1. Chest radiograph
- 2. **Spirometry** (only if the child is old enough to perform the maneuvres): provides information on lung volumes and airway caliber.
- 3. Sample of sputum for microbiological assessment in productive cough.
- 4. **Allergy testing:** positive allergen tests increase the likelihood of asthma to be the cause of coughing.
- 5. Otorhinolaryngologic examination in the presence of specific indicators: throat clearing type of cough, allergic salute (Table 3).

IMPORTANT: When examining a child with a cough we must not ignore the warning signs indicating the cough to result from a serious underlying disease or condition – red flag.

Chronic cough can be divided into a specific and non-specific cough, based on the presence or absence of specific pointers in the history and on clinical examination. An Australian study supports this division because the presence of clinical pointers suggests which children with chronic cough are at a higher risk of an important underlying disease and need immediate targeted intervention, whereas the children without specific pointers are at a low risk of an underlying disease not needing detailed investigations on first examination. Regular follow-up is sufficient. The authors have concluded that chronic productive cough is the most accurate indicator reliably predicting the presence of an underlying serious chronic lung disease (14).

A recent study showed that the most common symptom in more than 80% of children with primary ciliary dyskinesia who visited a doctor for the first time was chronic or recurrent cough (15).

In order to avoid antibiotic overuse we recommend performing diagnostic management and treatment of children with suspected protracted bacterial bronchitis in a tertiary level unit for pulmonary diseases.

In an **otherwise healthy** child with **chronic dry cough** only the basic investigations are performe at the primary care level (Table 4). However, the child should be regularly followed-up in order not to overlook the development of a potentially serious disease (4,6).

The most common causes of chronic dry cough (recurrent upper respiratory tract infections and bronchitis, postviral cough, upper airway cough syndrome, allergic rhinitis and psychogenic cough) are listed in Table 5 and apply only to healthy children WITHOUT any sign of a chronic lung disease.

Often, the child's age help us clarify the cause of cough. Some causes of cough are more common in a certain age group. The most common causes of cough by age are listed in Table 6.

3.4. Treatment of cough

• None of the studies has yet proved that symptomatic treatment with antitussives and mucolytics is effective despite large amounts of money being spent on various over-the-counter medications (4,6,22). Some medications have important side effects (23). Unnecessary and ineffective symp-

Table 5: Causes, patterns and potential investigations of chronic cough in otherwise healthy children (4).

Cause	Pattern	Potential investigations
Frequently recurring viral bronchitis	Crowded living conditions, and attendance in child care nursery in winter months. Parents report that the child coughs "all the time". On detailed history they recall that periods of resolution are between episodes of cough. Those children are basically healthy. Rhinovirus, RSV, ADV, B. pertussis, M. pneumoniae and C. pneumoniae. The incidence of upper respiratory infections (with cough) in children < 4 years is 5 to 8 episodes, in children 10–14 years 2 to 5 episodes per year.	 None Consider chest radiography Examine during the symptom-free period
Postinfectious cough	Troublesome cough (day and night) following respiratory infection, it lasts mostly to three weeks, in 5 % of children it resolves slowly over next 2–3 months. Viral respiratory infections, <i>C. pneumoniae</i> and <i>M. pneumoniae</i> .	 None, chest radiography. On rare occasions consider trial of asthma therapy as some mild asthmatics have prolonged recovery from each viral infection
Pertussis	Troublesome spasmodic cough after infection with <i>B. pertussis</i> which slowly resolves over 3–6 months, but it can last up to 1 year. Vomiting of clear tenacious mucus.	 None. Consider chest radiography. Positive serology or culture may be helpful in reducing requirements for further investigations. If pertussis has been diagnosed, macrolide antibiotics given in the first 2 weeks in the course of the disease can slightly alter the clinical course but their main role is to reduce the period of infectivity.
Allergic rhinitis, upper airway cough syndrome – UACS (formerly called postnasal drip syndrome)	Postnasal drip syndrome is now called UACS because it is unclear whether the mechanism of cough is postnasal drip, direct irritation, or inflammation of the cough receptors in the upper airway. Not fully accepted as the cause of cough. Children with allergic rhinitis may have Dennie-Morgan lines and transverse nasal crease of "allergic salute" from frequent nose rubbing.	 ENT examination, chest radiography, allergy tests
Psychogenic cough ("Somatic cough syndrome")	Usually in an older child/adolescent. Dry, tic-like cough persisting after head cold or during times of stress. Child does not look ill. Cough goes away with concentration and sleep. Child is exhibiting "la belle indifference".	It is important to do investigations to assure the doctor and parent that no major disease is being overlooked. It is important not to keep performing futile investigations that may reinforce the underlying problem.

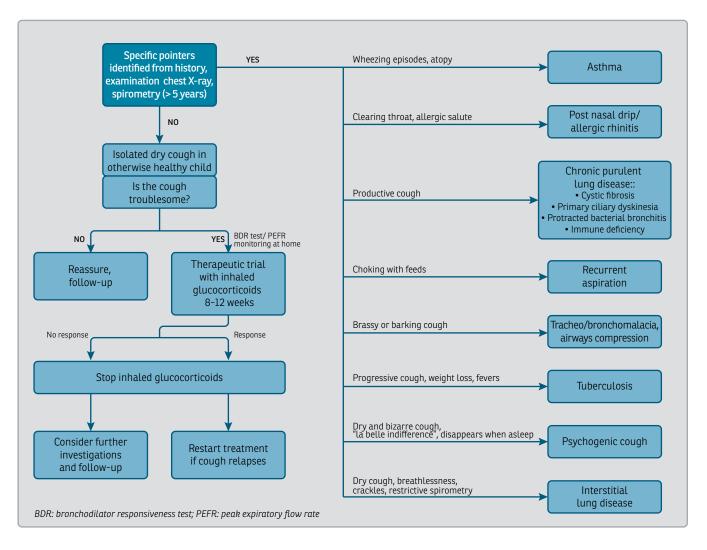


Figure 3: Algorithm for the management of child with chronic cough

- tomatic cough treatment can extend the time to diagnosis and increase the possibility of complications.
- The treatment of cough should be targeted according to the cause. The management of cough relates to making an accurate underlying diagnosis first, and then applying a specific treatment for that condition according to the guidelines.
- The most common diseases that present primary with coughing and have specific guidelines for the treatment are asthma, cystic fibrosis, immune deficiencies, primary ciliary dyskinesia and tuberculosis. We use antibiotics to treat early infection with B. Pertussis and in a hospital protracted bacterial bronchitis, but only after ex-

- clusion of other causes and underlying diseases.
- In an otherwise healthy child with dry cough and without specific pointers the treatment is often empirical with anti-asthma medications (inhaled corticosteroids), medications for allergic rhinitis and gastroesophageal reflux. However, the results show that these medications are generally not effective (4,6). In younger children it is usually impossible to exclude the diagnosis of asthma with certainty, therefore it is recommended to consider a trial of anti-asthma therapy with inhaled corticosteroids in some of them. The duration of therapy needs to be accurately defined (8-12 weeks) together with predefined

Table 6: The most common causes of cough by age (3,21).

<1year	1-6 years	> 6 years
 GOR Anatomical disorders (double aortic arch, bronchogenic cysts) or lung malformation (e.g. cystic congenital thoracic malformations, TEF) Congenital heart disease Neonatal infections Cystic fibrosis Passive smoking Environmental pollution 	 Respiratory infections—postinfectious cough Asthma GOR Inhaled foreign body Anatomical disorders (tracheobronchomalacia, bronchogenic cysts, lung sequester) Immune deficiency Bronchiectasis Passive smoking 	 Asthma Upper airway cough syndrome Psychogenic cough GOR Bronchiectasis Anatomical disorders (bronchogenic cysts, lung sequester) Tumors

TEF- tracheoesophageal fistula, GOR- gastroesophageal reflux.

goals of therapy. Strict criteria need to be met in order to prevent unnecessary and long-term treatment of children with recurrent viral bronchitis or subacute (postviral) cough with inhaled corticosteroids (4,24).

4. Conclusion

Cough is one of the most common symptoms for which patients seek medical attention. It is usually caused by viral respiratory tract infections and resolves spontaneously. However, sometimes it is caused by a serious and life-threatening disease. This is why the treatment of cough in children can be challenging.

The recommendations for the management of children with cough include a structured approach that can prevent overlooking an underlying potentially serious disease and at the same time help to avoid unnecessary investigations and ineffective cough treatment.

Acute cough is mostly due to an acute viral respiratory tract infection. Nevertheless, it can also be caused by a serious and life-threatening disease. At the first visit we need to evaluate the possible causes and decide if there is any need for immediate further investigations or follow-up. The absence of fever, tachypnea

and normal auscultatory lung examination exclude the possibility of complications with high probability.

Many studies and clinical observations show that in most children a cough related to acute viral respiratory tract infection resolves after 2–3 weeks, but in 10 % of children it can last for more than 4 weeks (subacute cough). The most common cause of subacute cough is respiratory tract infection (mostly with B. Pertussis) that needs follow-up only. If there is a risk of an overlooked foreign body aspiration, if there are any signs suggesting a chronic lung disease or if the cough intensifies, immediate diagnostic evaluation and treatment are needed.

Unlike acute and subacute cough, chronic cough is the most difficult to diagnose, because it can be caused by many diseases. Considering the presence of certain clinical characteristics or pointers in the history and on clinical examination that suggest a possible cause, we distinguish specific and non-specific cough. The presence of specific pointers (e..g. productive cough) suggests an underlying disease and requires immediate diagnostic management and treatment.

On the contrary, the absence of specific pointers in an otherwise healthy

child with chronic dry cough excludes a potentially serious disease with high probability. In these children it is unnecessary to perform extended diagnostics, but instead regular follow-up suffices until coughing resolves. In every child with cough we need to carefully look for signs that suggest a potentially serious underlying disease – for the so-called "red flag" signs.

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