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## Bronchitis in Children

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### 1. Introduction

For a paediatrician, children with bronchitis are part of the daily work. Infections of the respiratory system are the most common reason for children presenting at the doctor's practice. Almost all infants and younger school children become sick several times a year with a bronchitis. In most cases with the beginning of day nursery or nursery school there is an abrupt accumulation and many parents have the feeling that their child is permanently ill. That bronchitis occurs much more frequently in winter than in summer, as everyone knows from personal experience. The cold air outside and the dry heated air indoors, increases the vulnerability of the mucosa for pathogens. Whether the clinical course of a bronchitis is uncomplicated or associated with a bronchial obstruction, is partly caused by the genetic predisposition of the child. Depending on family history of bronchial asthma and allergies, the risk may be increased many times over. The health damage due to exposure to tobacco smoke is a major point which should not be underestimated.

The following pages describe in the form of a brief overview symptoms and signs of bronchitis in children. The different types and stages of bronchitis are shown. The most common viruses that cause bronchitis are described, in particular the respiratory syncytial virus. One chapter deals with bronchopulmonary dysplasia, an important risk factor for bronchitis in children. Furthermore, some important differential diagnoses are presented, which can become manifest with the typical symptoms of a bronchitis. The laboratory diagnosis with the aim of differentiating between viral and bacterial bronchitis is discussed. Finally, therapeutic options are mentioned.

### 2. Signs and symptoms of bronchitis in children

#### 2.1 Cough

The main symptom of bronchitis is a cough. At the beginning of the disease it tends to be dry and unproductive. With increasing production of secretion the mucus becomes less viscous, which makes coughing more effective. Some children have such severe coughing attacks that vomiting can be induced. An adequate supply of volume and inhalation therapy with 0.9% NaCl can help to make the mucus more fluid, enabling it to be brought up more easily by coughing. There are medications, usually in the form of so-called cough syrups, which will also assist mucolytic activity. After regression of an acute bronchitis, an

unpleasant dry cough can still remain for several days or weeks. This is caused by a transient hyperreactivity of the bronchial system due to the infection-induced inflammation.

## **2.2 Tachypnoea and dyspnoea**

If secreted mucus, an oedema of the bronchial mucosa or a spasm of the bronchial musculature induce bronchial obstruction, tachypnoea and dyspnoea may belong to the acute disorders. Typical clinical signs for dyspnoea are movement of the nostrils, inter- or subcostal retractions, use of accessory respiratory muscles, an upright upper body position, and in the auscultation wheezing and sometimes also rales. In this situation inhalation therapy with bronchodilatory agents and the systemic administration of steroids may be helpful. Because the expiration is more difficult than the inspiration, an emphysema may be formed due to air trapping. Children with respiratory distress may become anxious and excited, which makes the situation worse. The excitement and anxiety of the parents may also be transferred to the child. In the case of severe respiratory distress, the oxygen saturation in the blood may decrease critically, making oxygen substitution necessary. Measurement of vital parameters and blood gas analyses are standard procedures. The suctioning of secretions and mucus, or the application of respiratory supportive procedures, such as CPAP or intubation and ventilation, should be made immediately possible.

## **2.3 Pain**

Pain in the context of bronchitis can be caused by an inflammatory involvement of the trachea or pleura. In the case of retrosternal pain during coughing, a tracheitis is most probable. Respiratory-dependent, especially in deep inspiration increasing pain, which is localized more laterally in one or both sides of the chest, makes a pleuritis more probable. Especially the dry chafing of inflamed visceral pleura and parietal pleura against each other is very painful. If the child develops shallow breathing to avoid the pain, an insufficient ventilation of the lung may result with the increased risk of a secondary bacterial infection. For this reason, an appropriate analgesia is strongly recommended.

## **2.4 Fever**

Fever is a general clinical sign, which may occur in any infection, including one of the respiratory system. The increase of body temperature is a non-specific symptom and can range from low-grade fever up to hyperpyrexia with acute physical stress for the child. In the case of an infection of the upper respiratory tract, additionally clinical signs (in addition to the cough, tachydyspnea, pain and fever) are sniffing (rhinitis), a sore throat (pharyngitis) and earache (otitis media). Furthermore, swollen and aching cervical lymph nodes are a common local response to the inflammation process.

# **3. Different types of bronchitis in children**

## **3.1 Acute, complicated, chronic, recurrent**

The average duration of an acute bronchitis is about 1 week with the range from ½ week up to 2 weeks. Afterwards a nervous cough may remain for several days or a few weeks. The acute bronchitis has a very high rate of complete recovery; the prognosis is very good. An

exception is an acute bronchitis caused by adenovirus; in this case complications in the clinical course or a chronification of the bronchitis are described.

If the symptoms and signs of an acute bronchitis persist for 4 – 6 weeks, we call it complicated bronchitis. If an acute bronchitis is followed by another one, they can be taken for a complicated bronchitis by mistake. Approximately 20% of acute bronchitis has a complicated course. One possible complication is the secondary bacterial superinfection of a primary viral infection. In this case the child needs to be treated with antibiotics. Another possible complication is the transition from bronchitis into bronchopneumonia. In many cases this is detectable by pulmonary auscultation, but to confirm the diagnosis, a chest X-ray is necessary. A primary bacterial bronchitis usually presents clinically as a complicated bronchitis.

Signs and symptoms of a bronchitis persisting for more than 3 months are called chronic bronchitis.

If children repeat lots of acute bronchitis over months, it is called recurrent bronchitis. Mainly children in day nursery or nursery school are affected quite often, because the risk of infection is particularly high there. In the cold seasons bronchitis occurs more frequently compared to the warm seasons.

### **3.2 Non-obstructive or obstructive**

Bronchitis can be associated more or less with bronchial obstruction. The risk of an obstruction depends on the lumen of the inflamed bronchus; the smaller the lumen, the more likely is a clinically relevant obstruction. For this reason, the terms “obstructive bronchitis” and “bronchiolitis” were sometimes used as synonyms. Bronchial obstruction can be caused by the following pathophysiological alterations:

1. The smooth muscles of the bronchus get contracted, which can lead to an acute shortness of breath.
2. The mucosa of the respiratory epithelium is swollen due to the inflammation, which narrows the bronchial lumen.
3. The increased production of mucus clogs the lumen as well. Furthermore, due to the inflammation in the respiratory epithelium, the function of the cilia is reduced, and mucus cannot be transported adequately.

Auscultation of the lung shows wheezing. A so-called silent lung is typical for a severe bronchial obstruction with air trapping and emphysema. In this case the resting expiratory position is shifted to the inspiration, what may create a circulus vitiosus.

### **3.3 Non-allergic or allergic**

Bronchitis is an inflammatory disease of the bronchial mucosa. In most cases the inflammation is caused by an infection. Also allergens may cause an acute or chronic bronchitis, they act mostly as a trigger. The presence of one or more allergies increases the statistical risk for the development of bronchial asthma. Relevant inhalation allergens are dust mites, animal dander, mould fungus and pollen.

As their zoological name "Dermatophagoides" indicates, dust mites feed on epithelia from the skin, of which one person loses about 1.5 grams per day. They are, depending on the

type, 0.1 - 0.5 mm in size and they live in normal house dust. They are found in carpets, curtains, upholstered furniture, mattresses, duvets and pillows, stuffed animals etc. The allergen comes from the faeces of the mites. In order to avoid exposure, the following protections should be carried out: the use of an encasing such as a mattress cover, monthly washing of duvets and pillows, occasional freezing of soft toys at -20 °C, followed by rinsing, no long carpets, regular vacuuming and avoidance of dust turbulence.

With regard to animal dander, those species which are most relevant and which human beings have close contact with are especially dogs, cats, guinea pigs, hamsters, horses and birds. The allergen concentration varies within a species, depending on the breed. For this reason it could happen that someone tolerates contact with one cat very well, whereas contact with another cat induces an acute bronchial obstruction. In the case of a clinically relevant allergy against an animal, the contact should be avoided.

The spores of mould fungus can also cause an allergic reaction, like bronchial hyperreactivity or bronchial obstruction. If at home the walls are infested with mould fungus, the house has to be renovated.

Among the pollen, early flowering plants (birch, alder, hazel, willow) and grasses are most relevant. The occurrence of pollen-induced disorders, namely rhinoconjunctivitis and bronchial asthma, are strongly season-dependent and time-limited. On the basis of cross-reactions, for example between birch pollen and apple, in the case of an allergy against birch pollen, an allergic reaction against apple in the form of an oral allergy syndrome may occur. In the case of pollen, allergen avoidance is almost impossible. In order to reduce the intensity of pollen-induced allergy symptoms, desensitization is recommended.

### **3.4 Special forms: Bronchitis fibroplastica, bronchiolitis obliterans**

A special form of bronchitis in childhood is the bronchitis fibroplastica. Older synonyms are fibrinous bronchitis, pseudomembranous bronchitis or Hoffmann's bronchitis. It is characterized by obstruction of the bronchi, usually a lobe or segment, consisting of mucin, which forms large endobronchial casts of rubber-like consistency. Pre-existing pathological conditions, such as bronchial asthma or cystic fibrosis, which are attended by hypersecretion of viscous mucus, may act as triggers. Childhood tuberculosis or primary immunodeficiency seem to be associated with a higher incidence of bronchitis fibroplastica as well. However, exact epidemiological data are still missing. Main symptoms are a cough and dyspnoea, and sometimes pleuritic pain and fever occur. In pulmonary auscultation over the affected area of the lung the breath is quiet or absent; sometimes wheezing or rales can be heard. X-rays of the chest typically show an atelectatic area next to an emphysematic one. The therapy consists in the prompt removal of the sticky casts consisting of mucin via rigid bronchoscopy. If they are not removable, administration of N-acetylcysteine or DNase may be helpful. If a child without known pre-existing diseases falls ill with bronchitis fibroplastica, additional diagnostic investigations should be carried out: sweat tests, tuberculin tests, allergy tests.

Another special form of bronchitis in children is the bronchiolitis obliterans. An inflammation of the small airways induces a pathologic tissue remodelling with granulations, which obstruct the lumen of the bronchioles. This process may be triggered by infections, inhalation of toxic agents, autoimmune diseases or a chronic rejection after lung transplantation. In the group of

long-term survivors after lung transplantation, bronchiolitis obliterans is the most frequent cause of death. The clinical signs and symptoms are quite unspecific: a cough and reduced general condition. In pulmonary auscultation the breath is quiet and rales can be heard. The X-ray of the chest eventually shows some infiltration or it looks normal. The disease may begin rapidly or slowly and the clinical course may be progressive or stable. Therapeutic options are a high-dose glucocorticoid administration, and in the case of lung transplantation, an increase in the dosage of the immunosuppressive medication.

#### **4. Different stages of bronchitis in children**

##### **4.1 Bronchial hyperreactivity**

Bronchial hyperreactivity is a chronic inflammation of the bronchial mucosa with recurrent bronchial obstruction, which may be triggered by infections, allergens or nonspecific stimuli, such as cold air, physical or even emotional stress. The inflammatory activity causes a swelling of the bronchial mucosa with a reduction of the bronchial lumen consecutively. The smaller the lumens are physiologically, such as in infants, the more relevant is its reduction regarding clinical symptoms. Furthermore, inflammation of the bronchial mucosa increases the vulnerability to viruses or bacteria.

To make the diagnosis “bronchial hyperreactivity”, an accurate and detailed medical history is the most important step. Additionally, measurement of the lung function may confirm the diagnosis, in particular in the case of a reduced flow in the smaller airways; after administration of a beta-sympathomimetic via inhalation the bronchial obstruction should be reversible, at least partly. The lung function test can be carried out with children who are old enough to participate actively. Furthermore, measurement of the NO-exhalation may be useful to monitor the amount of bronchial inflammation. In some cases it may be helpful to carry out a bronchial provocation test via inhalation of methacholine, histamine or carbachol. Of course, all emergency tools have to be available.

##### **4.2 Bronchitis**

Bronchitis is a clinically apparent inflammation of the bronchi, triggered by a bronchial hyperreactivity, by viruses or bacteria or by allergens. The symptoms (cough, tachypnoea and dyspnoea, pain, fever), the different courses (acute, complicated, chronic, recurrent) and different forms (non-obstructive, obstructive) have been described.

##### **4.3 Bronchiolitis**

Bronchiolitis is an inflammation of the smallest bronchi and bronchioles. Due to the small lumens of these airways, swelling of bronchial mucosa may induce severe obstruction quite rapidly, in most cases associated with pulmonary hyperinflation. This can lead to the phenomenon of the so-called silent obstruction, that means barely wheezing, humming or whistling, but fine bubble rales at the end of inspiration. Bronchiolitis is a typical disease of infancy, the age peak is between 4 and 6 months.

##### **4.4 Bronchopneumonia**

Bronchopneumonia is a possible course of a complicated bronchitis. Whereas a primary pneumonia normally is localized to one segment or lobe of the lung, in the case of a



bronchopneumonia there is a disseminated inflammation from the bronchi down to the alveoli.

#### **4.5 Bronchial asthma**

Bronchial asthma is a disease with chronic inflammation of the respiratory system with bronchial hyperreactivity and variable airway obstructions. In many children and adolescents we find a positive family history for asthma and/or allergies. The restriction of the air flow, mainly during the expiration, is caused by spastic contraction of the smooth muscle in the bronchial wall, oedematous swelling of the bronchial mucosa and hypersecretion of viscous mucus. In addition to these pathological mechanisms, a tissue remodelling may take place after bronchial asthma over several years, which makes the airways less elastic. In most cases patients have an allergic bronchial asthma; case of non-allergic asthma and mixed forms are possible as well.

Criteria for the diagnosis of bronchial asthma in children and adolescents are a relative forced ventilation capacity (FEV1/VK) < 75% of age- and gender-related norm and a 15 % increase with prolonged expiratory time, or after inhalation of a short-acting beta-sympathomimetic. A further criterion is a decrease in respiratory resistance (R) > 50% of baseline after inhalation of a short-acting beta-sympathomimetic. If the lung function measurement shows a normal result, but the clinical history is typically for bronchial asthma, then a circadian variability of the measured peak expiratory flow (PEF) > 20% confirms the diagnosis. If the doctor is still in doubt with the diagnosis, a provocation test (for example physical stress or inhalation of metacholine) may be helpful to make the right diagnosis.

The therapy of bronchial asthma is successful if clinical signs and symptoms of the disease are under control, so that the affected children or adolescents feel free from disorders if they are able to partake in sport without any restriction, if there are no side effects of the medications and if no long-term injury will occur. Taken together, if the children or adolescents just have a normal life with this chronic disease. Parts of the therapy are prevention (for example not smoking, either actively or passively, avoidance of allergens, if possible), general procedures (for example participation on training courses of instruction, doing sports, doing physiotherapy), pharmacotherapy and rehabilitation, if it is required. The prescription of drugs should be carried out in accordance with an algorithm, which has various steps depending on the severity of the bronchial asthma and gives the opportunity to step up or step down. Standard drugs in pharmacotherapy of bronchial asthma are low-dose inhaled glucocorticoids and orally administered leukotriene antagonists (additionally or alternatively) for long-term therapy, as well as inhaled short-acting beta-sympathomimetics for acute therapy. Because of this treatment, severe asthma attacks have become very rare incidents.

#### **5. Common viruses causing bronchitis in children**

Acute bronchitis is almost (in approximately 90%) induced by viruses. The most common ones are respiratory syncytial, parainfluenza-, influenza-, adeno-, rhino-, metapneumo- and human bocavirus. Acute bronchitis, which is induced by bacteria primary, is rare (approximately 10%). In 15% of viral bronchitis a secondary bacterial infection will happen.

### 5.1 Respiratory syncytial virus (RSV)

It is a member of the family of paramyxoviridae, has a single-stranded RNA and is enveloped. We distinguish two serological groups A and B from each other. The pathogenicity of the virus depends crucially on two glycoproteins on the viral surface: glycoprotein G enables the docking with the host cell, such as pneumocytes, glycoprotein F is responsible for the endocytosis into the cell. The fact that the affected cell undergoes a fusion with neighbouring cells and form syncytia has given the virus its name. Further details of incubation time, infection and clinical signs and symptoms are in the section "Characteristics of RSV infection."

### 5.2 Parainfluenzavirus

It belongs to the family of paramyxoviridae, has a single-stranded RNA and an envelope. It is (in contrast to the influenza viruses) genetically stable. There are 4 different types. The transmission of the virus proceeds via droplet or smear infection. The incubation period is 3 - 6 days. At the age of 2 years, almost all children have been sick at least once with a parainfluenza infection. In infancy and early childhood parainfluenza virus causes an acute laryngotracheobronchitis with typical croup symptoms.

### 5.3 Influenzavirus

It is assigned to the family of orthomyxoviridae. It is divided into the 3 types A, B and C, of which A and B are most relevant for infections of humans. The genome of influenza viruses type A and B consists of eight single-stranded RNA segments. This creates a high genetic variability of antigenic drift and antigenic shift, in the case of a dual infection. The eight RNA segments contain the genetic information for 11 proteins, of which one is the neuraminidase. Transmission paths of the virus are aerosols and saliva, as well as contact with contaminated surfaces. The incubation period is 1 - 4 days. Typically we see a high incidence of influenza during the winter months. The epidemic often has its origin in the nursery, kindergarten or school. Because of the high contagiousity, pandemics with high lethality may occur, recently caused by the H1N1 subtype, the so-called "swine flu". In contrast to the common cold, the clinical course of the influenza infection is characterized by significantly reduced general condition, high fever and a much higher complication rate. Children with a disease of the respiratory tract, a heart failure or a deficiency of the immune system have an especially high risk for severe complications. The diagnosis of influenza can be made with a rapid test (usually an Elisa) or by RT-PCR, which is more sensitive and specific, from a nasal or throat swab or corresponding rinse water.

In the case of a severe or complicated clinical course, treatment with an antiviral compound is indicated. In childhood, the neuraminidase inhibitors oseltamivir (oral administration, approved from the first year of life) and zanamivir (inhalation, approved from the fifth year of life) are used. Safety studies were carried out in order to extend the approval of oseltamivir on the first year of life. The vaccination against influenza provides the best protection. Because of the high genetic variability of the virus, the vaccination has to be repeated each year with a current antigen mixture. In addition to the self-protection, the collective protection is of great importance.



#### **5.4 Adenovirus**

It is a member of the family of adenoviridae. It is a double-stranded DNA virus with a strong environmental resistance. More than 50 serotypes with various clinical manifestations have been identified so far. The transmission proceeds via droplet or smear infection. The incubation time is between 2 and 10 days. Most adenovirus-induced diseases occur in the age between 6 months and 5 years, usually in the form of a common cold. However, it can lead to complicated clinical courses with severe obstruction, pneumonia or persistent bronchial hyperreactivity for months.

#### **5.5 Rhinovirus**

It belongs to the family of picornaviridae, the RNA is single stranded. We know about 100 subtypes; the genetic variability is large. Rhinovirus is transmitted primarily via aerosol. The incubation period is 2 - 5 days. In the first years of life, the incidence of infection with the virus is around 1 - 2 times per year. Whereas in adults rhinovirus infections usually cause a common cold, in infants and small children obstructive bronchitis appear quite often.

#### **5.6 Metapneumovirus**

It is a member of the paramyxoviridae, a RNA virus and enveloped. We know 2 subtypes A and B, each with two sub-groups A1 and A2, as well as B1 and B2. Droplet and smear infections are the transmission paths. Incubation time is 4 - 6 days. During the first year of life about one quarter of infants become infected with the metapneumovirus; by the time children start school, almost everyone has had an infection with this ubiquitous virus. Most prevalent symptoms are rhinitis and bronchitis.

#### **5.7 Human bocavirus**

The human bocavirus was discovered only in 2005. It belongs to the Parvoviridae family and has a single-stranded DNA. The transmission of the virus proceeds via droplet or smear infection. Accurate epidemiological data are yet to be collected. Clinically, acute respiratory symptoms are most relevant.

### **6. Characteristics of RSV infection in children**

#### **6.1 Risk factors**

An RSV infection, which occurs in infancy, may have a severe clinical course. Not only in infancy, but until the age of 5 years, RSV infection may cause disorders of clinical relevance. The majority of children undergo one or more RSV infections during the first 2 years of life, usually without a severe or complicated course. Risk factors for a severe or complicated clinical course are small, narrow airways (this is the reason why infants suffer worse than older children). Boys are affected slightly more often than girls. Another risk factor, which should not be underestimated, is the exposure to tobacco smoke. Furthermore, the family history to allergies has an adverse influence. Pre-term birth or chronic diseases of the lung increase the risk for a complicated course of a RSV infection considerably. We see a seasonal accumulation with endemic-like clusters of RSV infections during the cold autumn and

winter months. The transmission occurs by droplet and smear infection. The incubation time is at 3 - 6 days.

### **6.2 Severity of the clinical course**

If the RS virus affects the respiratory epithelium of the smallest bronchi and bronchioles with desquamation of the epithelial cells and oedema of the mucosa, the main symptom is bronchial obstruction. Distal to an obstructed airway, atelectatic areas may be formed, next to emphysematic areas. If this causes a mismatch between ventilation and perfusion, the main symptom is tachydyspnoea with partial or even global respiratory insufficiency. In this case, the infant needs to get hospitalized for oxygen substitution and, if necessary, with respiratory support or even mechanical ventilation. An additional reason for hospitalization is the risk, especially in very young infants, of apnoea and death due to apnoea.

### **6.3 Diagnosis**

The diagnosis can be carried out using a rapid test, which is based on the immunofluorescence method. The inflammation parameters in the blood are only slightly increased. The X-ray of the chest often shows diffuse infiltrations of the lung and a partial reduction of the transmission due to emphysema.

### **6.4 Limitation of therapeutic options**

The therapeutic options are very limited. Because the replication of the RS virus takes place inside the epithelial cells of the lung, bronchodilatory agents show no positive effect. Treatment with steroids has no effect as well, what is confirmed by meta-analysis. An antiviral therapy with the nucleoside analogue ribavirin is not recommended for the following reasons: firstly, there seems to be no relevant effect; secondly, it is teratogenic and has to be administered via aerosol, which could lead to an exposure of pregnant women who are in contact to the child. There is only one agent with a small, but significant benefit in the case of an RSV bronchitis or bronchiolitis; it is the leukotriene receptor antagonist montelukast. Additionally, supportive therapy, such as inhalation with 0.9% NaCl or decongestant nose drops may be helpful.

### **6.5 Indications for palivizumab**

Palivizumab is a monoclonal antibody against the RS virus. It can be used for passive immunization. It binds to the glycoprotein F, the fusion protein, and thereby prevents the virus entering the cell. During the months with high incidence of RSV infections, palivizumab has to be injected every 4 weeks. Palivizumab is indicated for significant prematurity, bronchopulmonary dysplasia and hemodynamic relevant congenital heart failures. The prophylactic immunization with palivizumab reduces severity and duration of the disease significantly; the hospitalization frequency is halved.

### **6.6 Recent research on an active immunization**

Previous research on an active vaccine, already carried out in the 1960s, was not successful. Currently there are new research activities in this area. A live vaccine against RSV and PIV3 (parainfluenza virus type 3) is in phase 1 / 2 study.

## **7. Bronchopulmonary dysplasia as a risk factor for bronchitis in children**

### **7.1 Definition and pathophysiology**

Today bronchopulmonary dysplasia (BPD) is more relevant than ever. Because of the major advances in neonatology with high survival rates of extremely immature preterm infants, there is an increase of diseases and complications, which are typically associated with prematurity, like BPD. If very preterm infants are born, their lungs are not completely developed, neither structurally nor functionally, especially with respect to the synthesis of surfactant. Because of the respiration prior to maturity, the lung tissue undergoes a fibrotic remodelling process of the alveoli. Prenatal and postnatal factors, such as inflammation, infection, hyperoxia and mechanical ventilation, have an additional adverse effect.

Because the morphological alterations are not visible and the radiological ones do not correlate well with the clinical severity, the BPD is defined by the duration of oxygen supplementation for longer than 28 days. Depending on the amount of oxygen supplementation and the requirement of breathing support, we distinguish mild, moderate and severe BPD.

### **7.2 Prophylaxis and therapy**

The following prophylactic procedures may reduce the severity of BPD: the prenatal anti-inflammatory treatment via administration of beta-dexamethasone to the mother, the so-called “lung maturation”, is standard. The application of surfactant as soon as possible is very important. A patent ductus arteriosus with hemodynamic relevance should be treated early, if possible pharmacologically, if necessary via ligation. A protective effect of vitamin A has been demonstrated, although the effect is only minor.

Therapeutic procedures are avoidance of hyperoxia, moderate infusion or even forced diuresis. high-caloric nutrition, gentle ventilation mode, physiotherapy, and in very rare cases, the postnatal application of corticosteroids.

### **7.3 Prognosis**

The BPD also affects the future life of the children: they suffer more frequently with bronchial hyperreactivity and asthma, they have an increased risk for the incidence of respiratory infections, and in the first year of life they are more often hospitalized for acute respiratory problems. Even if they have no symptoms, the measurement of lung function will show worse values.

## **8. Differential diagnoses of bronchitis in children**

### **8.1 Croup**

In distinction from the original diphtheritic croup (which has become very rare thanks to the vaccination), the common croup is a subglottic laryngitis with an inflammatory oedema of the mucosa in the context of a viral infection of the respiratory system. The main prevalence is at the age between 6 months and 6 years. Typically in the late evening or during the night in the cold winter, the affected infants and children get an acute attack with a barking cough, hoarseness, inspiratory stridor and dyspnoea. We divide the croup into 4 different

degrees of severity, from just cough and hoarseness without dyspnoea to dramatic dyspnoea with the feeling of combustion.

What are the urgent measures in the case of a croup attack? The first step is to reassure the anxious and excited child. It should be kept in an upright position, in order to allow the use of the thoracic muscles for breathing. The child should be brought into the fresh and cold air, which may reduce the swelling of the respiratory mucosa. If available, a glucocorticoid suppository can be administered by the parents. Prophylactically, a moistening of the air indoors is recommended. In many cases of a moderate croup episode, these easy measures may stabilize the situation, that the parents are able to manage it at home without any professional help. However, in severe cases or in any cases of doubt, the ambulance should be called immediately. The emergency doctor can initiate an inhalation with adrenaline, an oxygen supplementation and an intravenous application of a glucocorticoid. If necessary, the child can be hospitalized and monitored via pulse oximetry. In very rare cases, the sedation of a child (for example with chloral hydrate) is unavoidable. In extreme severe and complicated clinical courses, the treatment of the child at an intensive care unit is recommended.

In the extremely rare case of a diphtheritic croup, the treatment with diphtheria antitoxin has to start immediately. Also extremely rare (thanks to the haemophilus vaccination), a bacterial epiglottitis occurs. But because of its rarity, the risk of misinterpretation as a normal croup is quite high. In contrast to the croup, the epiglottitis usually is associated with high fever, a very poor general condition, a septic clinical course, an increased salivation and dysphagia. An epiglottitis is always a peracute emergency. Inspection of the pharynx using a spatula is strictly contraindicated, because the slightest mechanical provocation can induce a complete occlusion of the epiglottitis without any possibility for an intubation. Then only cricothyrotomy or tracheostomy can be carried out, to save the life of the child.

## 8.2 Aspiration

Aspiration of gastric juice or of a foreign body causes coughing. Common foreign bodies are small pieces of an apple or a carrot, half or whole peanuts and all sorts of small parts made of plastic or metal, quite often from the toys, the child has played with. We distinguish between the acute and the chronic foreign body aspiration.

In the case of an acute aspiration the child has an abrupt coughing attack and dyspnoea. Because the beginning of the right main bronchus from the trachea is angulated to a lesser extent compared with the left one, it is preferentially affected. Over the affected side the breath is quiet and wheezing can be heard. Radiologically, a mediastinal shift to the healthy side can be seen.

In contrast to an acute aspiration, which is associated with an abrupt coughing attack and dyspnoea, in the case of a chronic aspiration the clinical symptoms are milder and less severe. In most cases the foreign body is smaller compared to those of an acute aspiration, so that it can slide into a segmental bronchus, settle there and maintain an inflammatory response, which occurs as a chronic cough. This is the reason why chronic aspirations quite often get misinterpreted as a chronic bronchitis of infectious or allergic origin.

For treatment the bronchoscopical removal of the foreign body is necessary, almost always in the form of a rigid bronchoscopy.

### 8.3 Tuberculosis

In the case of a chronic cough it is important to take the possibility of a pulmonary tuberculosis as a differential diagnosis into account, especially in children who come from high-incidence countries, or if they have had or still have close contact with people coming from such areas. The mycobacterium tuberculosis is transmitted via the aerosols, which comes from coughing people with an open pulmonary tuberculosis. Children are generally less contagious, even if they have an open pulmonary tuberculosis, because there are only a few bacteria in the sputum. This phenomenon is called paucibacillary tuberculosis.

At the slightest suspicion of a tuberculosis infection, an appropriate diagnostic investigation has to be made: next to an accurate medical history and physical examination, immunological tests have to be carried out. These are an intracutaneously applied tuberculin test and an IGRA (interferon-gamma release assay) from the blood. The combination of both tests results in an optimal specificity. Additionally, an X-ray from the chest at two levels belongs to the standard diagnostic. The microscopical and microbiological analysis is made from induced sputum or from gastric juice, because children younger than 10 years usually are not able to give sputum spontaneously.

If, in the case of an exposure to tuberculosis, all diagnostic investigations have a negative result, a chemoprophylaxis with isoniazid for 3 months is recommended. If the immunological tests are positive, but the clinical course, the X-ray and the analysis of induced sputum or gastric juice show normal results, then a preventive chemotherapy with either isoniazid as monotherapy for 9 months or alternatively with isoniazid and rifampicin as dual therapy for 4 months should be carried out. If a child has signs or symptoms of a tuberculosis, if pulmonary or extra-pulmonary, a combination therapy with at least 3 tuberculostatic drugs has to be initiated, for example with isoniazid, rifampicin and pyrazinamide. In most cases, after 2 months of treatment the medication can be reduced to an isoniazid/rifampicin - dual therapy. The total duration of the treatment depends on the clinical course and the severity of complication and is at least 6 months. Of course the choice of the tuberculostatic drugs has to be adjusted to possible resistances.

### 8.4 Cystic fibrosis (CF)

If infants have recurrent obstructive bronchitis with a chronic cough and problems to dissolve the mucus, one differential diagnosis, which has to be taken into account, is CF. Even though it is a rare disease, it is still one of the most common hereditary diseases. The mode of inheritance is autosomal recessive and caused by a mutation in the CFTR (cystic fibrosis transmembrane conductance regulator) - gene, which encodes a chloride ion channel. More than 1500 mutations have been known. The mutation deltaF508 describes the deletion of 3 base pairs, what causes the lack of phenylalanine at position 508 of the protein chain, and is with 70% by far the most frequent one. Depending on the amount of the CFTR defect, there are milder and more severe clinical courses of the disease. Due to the dysfunction of the chloride ion channel, the epithelial fluid film becomes hyperosmolar and the produced mucus gets dyscrinic.



The clinical course is characterized by this problem. Shortly after birth, due to the viscous intestinal secretion, a meconium ileus can be the first complication of a CF. The same problem may occur in later life as distal intestinal obstruction syndrome (DIOS). The most important focus in the progress of the CF is the respiratory system. The viscous sputum cannot be mobilized and brought out adequately, what gives bacteria a good medium for colonization, unfortunately quite often with mucoid *Pseudomonas aeruginosa* and other multi-resistant bacteria. Also pulmonary mycoses (for example an aspergillosis) may occur. These permanent inflammatory processes lead to an irreversible tissue remodelling of the respiratory tract. At the end, atelectatic areas and emphysematic bullae, insufficient for ventilation or diffusion, replace the normal tissue. Haemoptysis and pneumothoraces are dreaded complications. About 90% of all patients with CF develop an exocrine pancreatic insufficiency with the consequence of an inadequate intestinal absorption of proteins, fats and fat-soluble vitamins, which leads to dystrophy of the affected patients. With further progress of the disease, an endocrine pancreatic insufficiency may occur, which is why about 15% of all patients with CF develop an insulin-dependent diabetes mellitus.

Therapeutical tools are the removal of bronchial secretions by autogenic drainage, physiotherapy, inhalations, mucolysis and ample fluid intake, the antibacterial treatment by intravenous antibiotics, the stimulation of the digestion by dietary fibre enriched food and physical activity, the improvement of the intestinal absorption by replacement of enzymes (porcine pancreas powder) and substitution of vitamins, and the counteraction of dystrophy by high-caloric nutrition.

In the most patients with CF, the life limiting factor is the global respiratory insufficiency. Often, lung transplantation is the only life-prolonging option. Because of the enormous medical progress, especially in the development of new antibiotics, the life expectancy of people with CF increases steadily and rapidly. CF as a disease which occurs exclusively in childhood is part of medical history.

### **8.5 Primary ciliary dyskinesia**

A primary ciliary dyskinesia often causes recurrent bronchitis. It is a genetically determined (usually autosomal recessive) disorder of the respiratory ciliated epithelium and other ciliated cells, resulting in a reduction in mucociliary clearance. Typical clinical symptoms are chronic rhinitis and sinusitis with much secretion, chronic bronchitis with a productive cough and recurrent pneumonia. Additional possible abnormalities are the formation of a hydrocephalus (due to the lack of ciliary motility of the ependymal cells), infertility in male (due to the lack of motility of the sperms) and in female patients (due to the lack of motility of the cilia of the fallopian tube) or a situs inversus (due to the absence of a directed cilia beat during the embryogenesis). A situs inversus occurs in 50% of the patients who are affected by the primary ciliary dyskinesia and it is called Kartagener's syndrome. In the diagnostic investigation of the primary ciliary dyskinesia the measurement of exhaled NO and the analysis of the ciliary function using a light microscope are purposeful tools. For confirmation of the diagnosis, an analysis via an electron microscope is needed. Therapeutic options are physiotherapy, inhalation and antibiotic treatment in the case of bacterial infections.

### **8.6 Vocal cord dysfunction**

The vocal cord dysfunction (VCD) is a functional disorder with an acute spasm of the vocal cords. In most cases school children are affected. A VCD attack can range from a mild dyspnoea to the feeling of suffocation. Fortunately, such episodes are not life threatening, because despite the vocal cord spasm a small air gap still remains. Possible triggers for a VCD attack are coughing, physical exertion, inhalation of cigarette smoke or reflux of gastric juice, postnasal drip syndrome and general stress.

### **8.7 Gastroesophageal reflux**

In the case of a recurrent or chronic cough, of course at first everybody thinks of a disease of the respiratory system. However, a gastroesophageal reflux may also cause such symptoms. Especially in the first months of life, chyme and gastric juice can flow back into the oesophagus and induce an inflammation of the mucosa there. Clinical symptoms may be heartburn, regurgitation, vomiting, feeding problems and finally dystrophia. Further symptoms may be a cough, hoarseness, bronchial obstruction, episodes with apnoea and cyanosis, as well as pneumonia due to aspiration. In order to avoid the gastroesophageal reflux in infants, the nutrition can be thickened and the feeding portions can be reduced by increasing the feeding frequency. In addition, the upper body should be slightly elevated. Potential drugs are antacids or proton pump blockers.

## **9. Inflammation parameters in the case of bronchitis in children**

### **9.1 C-reactive protein (CRP)**

CRP is an annular pentamer with sub-units composed of 206 amino acids each. It is synthesized in the liver and then secreted into the blood. Its concentration in the blood increases within 6 to 48 h in the case of any systemic inflammation. That can be an infectious disease, an immune reaction of non-infectious etiology or large tissue damage. Thus, CRP is an unspecific marker for inflammation and its increase starts with delay. Depending on the laboratory, a plasma concentration up to 0.1 - 1 mg/dl is in the normal range. Concentrations between 1 - 10 mg/dl are typical for mild to moderate concentrations, > 10 mg/dl for severe inflammation. Because of the reasonably long half-life of approximately 24 h, CRP is ideal for the follow-up monitoring of an inflammatory process which can help to evaluate the effectiveness of a treatment.

### **9.2 Interleukin-6 (IL-6)**

IL-6 is a proinflammatory cytokine consisting of 184 amino acids. It is released primarily by monocytes, but also by T-lymphocytes, as well as endothelial and epithelial cells. Infections, non-infectious immunological reactions, tissue hypoxia and trauma induce the release of IL-6 within 6 h. Thus, IL-6 is an unspecific marker for various forms of inflammation as well, but its increase starts much faster. Depending on the laboratory, a plasma concentration up to 10 - 50 ng/l is in the normal range. The half-life in the blood is just a few minutes. Because of this very short half-life, the kinetics shows a narrow peak with the risk of false negative results in the case of measurements outside this peak.

### 9.3 Complete blood count (CBC)

The CBC may also be helpful in the diagnosis of an inflammation. High increases in the amount of the leucocytes occur in bacterial infections, but also in other inflammatory processes. Like CRP and IL-6, CBC is a non-specific marker of general inflammation. The increase of the leucocytes needs several hours and starts a little bit earlier than the increase of the CRP level. The standard value of the amount of leucocytes depends on the age of life: for adults 4 - 10 / nl, for school children 5 - 15 / nl, for small children 6 - 17,5 / nl and for newborns even 9 - 30 / nl are physiological. The differential blood count shows a reactive shift to the immature leucocytes, because their reinforced presence in the peripheral blood induces an enhanced release of still premature leucocytes from the bone marrow.

### 9.4 Erythrocyte sedimentation rate (ESR)

The ESR is a very non-specific marker for any kind of inflammation. The pathophysiological mechanisms, which lead to a higher ESR, are as follows: in the case of an inflammatory condition, erythrocytes form aggregates, which have a lower flow resistance compared to the sum of each separate erythrocyte. Furthermore, higher concentrations of acute phase proteins (like CRP), of fibrinogen or of immunoglobulins in the plasma, increase the ESR. It takes several weeks, after an inflammation has taken place, until an increased ESR gets normalized again. Standard value for boys or male adolescents is a sedimentation of 15 mm during 1 h, for girls or female adolescents 20 mm during 1 h.

### 9.5 Procalcitonin (PCT)

PCT is a protein which is constructed from 116 amino acids. It is produced mainly in the parafollicular C cells of the thyroid gland and in various neuroendocrine cells. Under physiological conditions, it acts as a prohormone of calcitonin. It is known that the release of PCT increases in the case of an infection, which is caused by bacteria, fungi or parasites. In this special condition, PCT is secreted predominantly in cells other than the thyroid gland, including leukocytes, adipocytes, myocytes and hepatocytes. Stimuli for the synthesis of PCT in these cells are bacterial endotoxins (lipopolysaccharides = LPS) and cytokines (Interleukin - 1 beta, tumour necrosis factor - alpha). The pathophysiological significance of PCT increase has not yet been clarified. Anyway, there is no effect on the thyroid gland.

The PCT level in the blood increases within 3 h after stimulation by endotoxins or cytokines. The maximum of the PCT level is reached after 8 - 24 h and will be stable for another 24 h. Then the PCT amount will decrease again with a quite long half-life of 20 - 24 h. In healthy individuals, the physiological PCT level is < 0.5 µg/l. Values from 0.5 to 2.0 µg/l are associated with a mild respective moderate systemic infection, values from 2.0 to 10.0 µg/l with a severe systemic infection and values > 10.0 µg/l are in the majority of cases a sign of a sepsis. The amount of PCT correlates with the severity of the infectious disease and the mortality rate. In other very severe diseases, such as multiple trauma, large-scale burning, cardiogenic shock or multiple organ failure, the PCT level increases as well.

PCT remains nearly unaffected in the case of a localized, a viral, an autoimmunological or an allergic inflammation. For this reason it is an excellent marker for the rapid differentiation between viral and bacterial systemic (= antibiotic-requiring) infections.

Furthermore, PCT is well suited for the monitoring of the course of a systemic bacterial infection.

A big advantage of PCT, compared to CRP, CBC and ESR, is its much faster increase, which allows a very early detection of a systemic bacterial infection. Moreover, its predictive value for prediction of sepsis with 0.93 is much better than that of CRP, which is only 0.68. Furthermore, the interference by a therapy with steroids is much lower. One advantage compared to IL-6 is the better biological stability with a much longer half-life, what reduces the risk of false negative results. Additionally, in contrast to IL-6, autoimmunological inflammations do not interfere with PCT.

The measurement of the PCT level in patients with a febrile infection may be helpful to decide whether or not a patient needs an antibiotic treatment. In a clinical study it has been shown that by using a simple algorithm, the knowledge of the PCT level could reduce the administration of antibiotics from 80% previously to 44%.

On the one hand one wants to avoid the “treatment” of a viral infection with antibiotics, on the other hand one wants to assure the start of a required antibiotic therapy in time. Especially newborns and young infants may undergo fulminant clinical courses in the form of severe sepsis, for which reason this age group is very critical, and it is not acceptable to delay the start of an antibiotic treatment. Generally, it seems to be useful to give the measurement of PCT a higher priority than is currently given.

## **10. Therapeutic concepts for bronchitis in children - pro and contra**

In general, a bronchitis may be treated symptomatically, because in most cases it is caused by a viral infection, and there exists no specific treatment. But the importance of the so-called household remedies should not be underestimated: an adequate fluid intake and inhalation of 0.9% NaCl may help to keep the bronchial mucosa moist and to liquefy the mucus. Sage drops may reduce the tussive irritation. The inhalation of essential oils, which are suitable for children, may also help to reduce discomfort, but it should be noted that there is a small risk of sensitization. In addition, there are a number of drugs (some are available in the pharmacy without prescription, some have to be prescribed), which have a reasonably proficient efficacy.

### **10.1 Sympathomimetic**

For the treatment of an acute bronchial obstruction beta 2 - agonists are used, which have a selective effect on the respiratory system, in order to minimize beta 1 - receptor - mediated adverse effects on the heart. The binding of the drug to its receptor activates the adenylyl cyclase whereby ATP is converted to cAMP. That leads to a relaxation of the smooth musculature via a reduction in calcium ion concentration in the cells, and it leads to an inhibition of the release of mediators from mast cells. Generally, short-acting beta 2 - agonists, such as salbutamol, are used. In most cases salbutamol is applied in the form of inhalation, the common dosage is about ½ drop per kg body weight in about 2 ml 0.9% NaCl, administered with an ultrasonic nebulizer. Alternatively, especially en route, 1 - 2 puffs of a spray via a spacer can be used. The frequency of inhalation depends on the severity of bronchial obstruction. 3 - 6 applications in 24 hours are an average frequency

during an acute obstructive bronchitis, but it can be increased, if necessary. The oral administration of salbutamol is possible, but because of a lower efficacy and an increase of adverse effects due to a higher intake into the blood this is not recommended as a first choice. Common adverse effects are restlessness, heart palpitations and shakiness. These symptoms are induced by an increased sympathetic activity and can be reduced by reduction of the single dosage or the frequency of administration. In pregnant female adolescents, salbutamol can induce tocolysis via the beta 2 - receptor.

### 10.2 Anticholinergic

Anticholinergics inhibit acetylcholine due to competition on the muscarinic acetylcholine receptors and antagonize its bronchoconstrictive effect. They were applied via inhalation. In comparison to the sympathomimetics, their effect is weaker and occurs with a delay. Ipratropium bromide is used most frequently, usually in addition to a beta 2 - agonist, if the sympathomimetic effect is not sufficient. Possible side effects include dry mouth, a bitter taste, tachycardia and arterial hypertension.

### 10.3 Methylxanthine

The exact mechanism of action of methylxanthines, such as theophylline, is not fully known. Several different molecular biological pathways seem to be involved: methylxanthines inhibit the phosphodiesterase, increase intracellular cAMP and antagonize effects on the adenosine receptors. Due to these mechanisms, methylxanthines have bronchodilatory and anti-inflammatory effects and they stimulate the respiratory centre in the brain stem. They are rarely used, mainly as reserve medication for severe asthma - attacks. Theophylline is then usually given as a continuous infusion. The side effects can be serious: tachycardia, extrasystoles, arterial hypertension, restlessness, insomnia, gastrointestinal disorders or increased diuresis.

### 10.4 Glucocorticoid

Glucocorticoids induce the secretion of lipocortin, a glycoprotein which inhibits the phospholipase A2 and thereby reduces the release of arachidonic acid. Due to this mechanism, the cyclooxygenase pathway produces less prostaglandins and the lipoxygenase pathway less leukotrienes. Several cytokines, particularly interleukin-1, interleukin-2 and tumour necrosis factor - alpha, are produced in a reduced amount as well. In the peripheral blood the number of monocytes is decreased and also their bactericidal and chemotactic effects, as well as their migration are reduced. All these changes have a non-specific anti-inflammatory effect. Depending on the half-life, glucocorticoids are divided into short-acting (for example cortisone and cortisol), medium-acting (for example prednisone, prednisolone and methyl prednisolone) and long-acting (for example dexamethasone) substances. The systematic administration of glucocorticoids over a short time period may be necessary in the case of an acute severe bronchial obstruction. In infants and young children the application can be carried out in the form of a suppository, which can be done at home by the parents. If a child with an acute severe bronchial obstruction is brought into the emergency room, the intravenous application is part of the standard therapy. The long-term treatment with a glucocorticoid should be done topically, that is via



inhalation. Commonly used corticosteroids for an inhalation therapy are budesonide, beclomethasone and fluticasone. The dosages are here in the microgram range; that means, they are by a factor of 100 – 1000 lower than the systemically given dosages. Thereby any side effects are reduced to a minimum. Parents who are afraid of the possible adverse effects of corticoids from long-term treatment should have an informative consultation. If they have the relevant knowledge, then their worries should be placated. If there are local side effects, for example the development of an oral thrush these can arise after inhalation if the mouth is not rinsed with water.

### **10.5 Leukotriene antagonist**

Leukotrienes, products of the arachidonic acid metabolism, are synthesized in mast cells, macrophages, eosinophils and basophils. They have a very strong bronchoconstrictive effect (1000-fold more potent than histamine), induce an oedema of the bronchial mucus via increasing the capillary permeability and increase the production of mucus. Additionally, leukotrienes have a chemotactic influence on inflammatory cells, especially the eosinophils, which sensitizes the nerve fibres occurring in the respiratory tract, resulting in a bronchial hyperreactivity. The most common leukotriene antagonist is montelukast. Because its structure is similar to the leukotriene D<sub>4</sub>, it acts as a selective competitor at the receptor without the effects mentioned above. Montelukast is used as a long-term anti-inflammatory therapy, often in combination with a topical corticosteroid. Montelukast is administered orally in the evening. The adverse effects that may occur include headache and abdominal pain.

### **10.6 Mucolytic**

Mucolytic respective secretolytic drugs are expectorants. In contrast to secretomotoric drugs, which increase the activity of the ciliated epithelium, expectorants should cause a liquefaction of the bronchial mucus to make it easier to cough it up. Among the mucolytics are acetylcysteine, bromhexin and ambroxol. Acetylcysteine cleaves the disulfide bonds of the mucopolysaccharides. Furthermore, it has an anti-inflammatory effect due to catching free radicals with its reactive SH group. Bromhexin activates enzymes, which cleave the molecules of the mucus and stimulate the glandular cells to increase the mucus production, reduce the viscosity. Ambroxol is a metabolite of bromhexin. In addition to the effects of bromhexin, it stimulates the synthesis of surfactant. Some herbal substances, such as ivy, also belong to mucolytic drugs. Generally, the therapeutic significance of all these so-called cough syrups should not be overestimated. It is much more important that the children drink enough and make inhalations.

### **10.7 Antitussive**

Antitussives reduce the cough by acting on the brain stem. Opiates, like codeine, dihydrocodeine, hydrocodone or noscapine, are the most common drugs against tussive irritation. There are newer substances, such as pentoxiverin, which have the advantage of lacking a sedative effect or an addiction potential. Pentoxiverin is an agonist at the sigma receptor and also acts antagonistically at the muscarinic M<sub>1</sub> receptor. Potential side effects are nausea, vomiting and diarrhoea. It is contraindicated in children younger than 2 years

because a depressant effect on the respiration cannot be excluded, and in pregnant women because there are no sufficient safety data. However, in childhood antitussives, these should be prescribed only in rare cases with a non-productive cough. Otherwise, if a productive cough is inhibited, the mucus remains in the airways, increasing the risk of secondary bacterial infections with bronchopneumonia.

### 10.8 Antibiotic

In the case of a bacterial infection treatment with antibiotics is recommended. The choice of the appropriate antibiotic depends on the age of the child, because in different age groups there are different spectra of bacteria. After receiving the antibiogram, the antibiotic therapy can be specified in accordance to sensitivities and resistances of the bacterium. Between community-acquired and nosocomial infections, bacterial spectra differ as well. Sometimes it is not possible to distinguish between a viral and a bacterial infection, since the clinical course and the blood parameters can be quite similar. In this situation it may be that a child will be treated with an antibiotic, although it is just a viral infection with high fever.

### 10.9 Oxygen supplementation

In the case of severe bronchial obstruction with spasms of the bronchial musculature, with oedema of the bronchial mucosa and production of viscous secretions, ventilation in the airways and diffusion in the alveoli may be disturbed. This can cause a partial (hypoxia, normocapnia) or global (hypoxia, hypercapnia) respiratory insufficiency. If the transcutaneously measured oxygen saturation in the blood is too low, the supplementation of oxygen is necessary. Usually the oxygen is supplied via nasal prongs. If small children do not tolerate nasal prongs, a mask can be placed in front of the face, especially during sleep.

In the treatment of premature infants with a respiratory distress syndrome, we have different procedures, because there the toxic effect of oxygen on the immature organs has to be taken into account. Complications caused by oxygen can be BPD, the retinopathy of prematurity and an apoptosis-mediated neurodegeneration. The monitoring of the premature infants should contain a capnometric analysis next to the measurement of the oxygen saturation.

### 10.10 Physiotherapy

Physiotherapy is required in the case of chronic diseases of the respiratory system (for example cystic fibrosis or primary ciliary dyskinesia), but also in the case of acute pneumological problems (for example the formation of an atelectasis as a complication of pneumonia). The aims of physiotherapy are to attain effective ventilation of all lung sections and an effective drainage of secretion.

### 10.11 Nasal drops

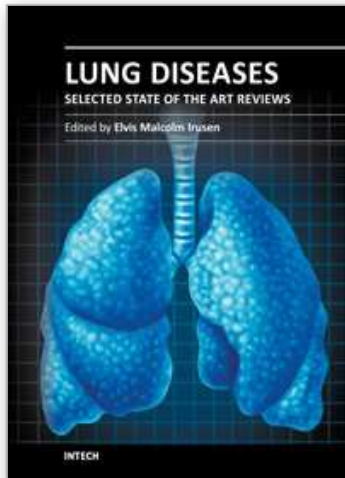
0.9% NaCl - nose drops are used to moisten and clean the nasal mucosa. Decongestant nose drops (dependent on age 0.25%, 0.5% or 1% xylometazoline) should be given, if the eustachian tube is swollen in response to an infection of the upper airways, in order to guarantee the ventilation of the middle ear. These nose drops should not be given for longer

than 7 days, otherwise they could lead to an irreversible damage of the mucosa. A stuffy nose is not a good reason for the application of decongestant nose drops. Depending on the age of the child, a nose spray may be used instead of nose drops.

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## **Lung Diseases - Selected State of the Art Reviews**

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The developments in molecular medicine are transforming respiratory medicine. Leading clinicians and scientists in the world have brought their knowledge and experience in their contributions to this book. Clinicians and researchers will learn about the most recent advances in a variety of lung diseases that will better enable them to understand respiratory disorders. This treatise presents state of the art essays on airways disease, neoplastic diseases, and pediatric respiratory conditions. Additionally, aspects of immune regulation, respiratory infections, acute lung injury/ARDS, pulmonary edema, functional evaluation in respiratory disorders, and a variety of other conditions are also discussed. The book will be invaluable to clinicians who keep up with the current concepts, improve their diagnostic skills, and understand potential new therapeutic applications in lung diseases, while scientists can contemplate a plethora of new research avenues for exploration.

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