The airways are effectively protected against inhaled particles by the production and subsequently continuous transport of mucus in the airways. However, retention of mucus in the lungs is a wellknown phenomenon in patients with airways disease, such as chronic obstructive pulmonary disease, cystic fibrosis and primary ciliary dyskinesia. Mucus retention may contribute to the development of respiratory tract infections and may also increase airflow obstruction. Retention of mucus is usually treated symptomatically by the application of physiotherapeutic techniques in an attempt to increase mucus transport. Some of these techniques such as manual percussion and postural drainage have been used for years, based upon the clinical impression that they improve mucus transport or make expectoration easier. Manual percussion on the thorax is thought to increase mucus transport in the airways by the externally applied vibrations. In case of postural drainage it is assumed that gravitational force will support transport of mucus. Other more recently introduced techniques, including the forced expiration technique and positive expiratory pressure breathing, are based upon data obtained by physiological knowledge or hypotheses. In case of the forced expiration technique a forced expiration is performed with an open glottis at different lung volumes. This technique is based on the hypothesis that a high expiratory airflow velocity will arise in the airways due to a combination of a high expiratory flow and a small diameter due to a dynamic compression of the airways. Positive expiratory pressure breathing, during which the patient is asked to breath with an expiratory mouth pressure of 10-20 cm H_2O, is based upon the hypothesis that it increases the quantity of air behind mucus plugs and consequently expectoration by coughing or forced expiration will be more effective.

The effect of physiotherapeutic measures is clinically difficult to judge, because often a combination of several techniques is applied and no reliable, easy to handle assessment is available that reflects transport of mucus. In this thesis the effects of several physiotherapeutic measures, applied to improve mucus transport in the airways, are described. In order to investigate mucus transport and the effect of physiotherapeutic measures we developed an objective technique to quantify mucus transport.

Mucus transport in the lower respiratory tract.

Mucus is produced throughout the bronchial tree and is continuously transported in the direction of the oropharynx. The different mechanisms of mucus transport in healthy subjects and in patients with airways disease are discussed in Chapter 2. In healthy subjects mucus transport in the lower respiratory tract is mainly taking place by cilia activity and expiratory airflow. Ciliated cells are found in the airways, from the trachea as far as the terminal bronchioles. The cilia beat continuously and have an effective beat during which mucus is "pushed" in the direction of the oropharynx. The recovery beat takes place in the direction of the alveoli; during this phase no transport takes place. The capacity of transport by cilia activity depends among other factors on the quantity of ciliated cells, which is directly related to the total airway surface at a given level in the bronchial tree. The effectivity of mucus transport by cilia beating, therefore, decreases from the peripheral airways, which have a large total airway surface, to the central airways, which have a much smaller total airway surface. The effectivity of transport by expiratory airflow is mainly dependent on expiratory airflow velocity. Mucus transport by expiratory airflow, therefore, is probably less effective in the peripheral airways, in which the airflow velocity is low due to a large total airway diameter, than in the central airways, in which the airflow velocity is much higher due to a much smaller total airway diameter.

In patients with airways disease i.e. chronic obstructive pulmonary disease, asthma, cystic fibrosis, and primary ciliary dyskinesia, retention of mucus is wellknown and may be caused by hypersecretion in combination with impaired mucus transport. Mucus transport is impaired due to reduced cilia activity as a result of respiratory tract infections and hypersecretion. Although expiratory airflow is often decreased, due to an obstruction of the airways, it is likely that forced expirations and coughing become the most important mechanisms to compensate the decreased mucociliary transport.

Measurement of mucus transport.

The effectivity of measures to improve mucus transport is by some authors investigated using lung function measurements, representing ventilatory parameters, or gas exchange measurements using arterial bloodgas analysis.

There is however no direct relationship between mucus transport and these parameters. Therefore these parameters are in fact not suitable to evaluate methods to improve mucus transport. In Chapter 3 different methods which directly or indirectly reflect mucus transport are discussed. Measurement of mucus transport by a radioactive aerosol tracer technique is probably the best method to investigate the effectivity of physiotherapeutic measures applied to increase mucus transport. In our investigations we used ^{99m}Tc-tin colloid as tracer, which was nebulised by an intermittent positive pressure respirator. The tracer was subsequently inhaled by the subjects. Deposition of the tracer in the airways, and clearance from the airways was recorded using a gamma camera.

Mucus transport, measured by registration of the clearance of the radioactive aerosol tracer, and the repeatability of this method, was investigated in a group of healthy volunteers, and described in chapter 3. Mucus transport, measured for 45 minutes using this method, was about 5 % of the initial amount of tracer, which is lower than usually described in the literature. This can be explained by a more peripheral deposition of the tracer we used. It may also be explained by the fact that our data were not corrected for alveolar deposition; the initial amount of deposition in the peripheral lung region is therefore higher, and as a consequence the decrease in percentage of the initial amount is smaller.

Effect of manual percussion.

Manual percussion is a wellknown part of physiotherapy and is based upon the assumption that percussion on the thorax will produce vibrations in the lung supporting mucus transport. In Chapter 4 the results of a study on the effect of manual percussion on mucus transport are described in patients with chronic obstructive pulmonary disease and excessive tracheobronchial secretions. The effect of manual percussion as a single procedure and in combination with postural drainage, breathing exercises and coughing was compared to a treatment that consisted of postural drainage, breathing exercises and coughing, but without manual percussion. Manual percussion as a single procedure resulted in a small but statistically significant increase of mucus transport. Manual percussion in combination with postural drainage, coughing, and breathing exercises, however, resulted in a much greater improvement of mucus transport, which was similar to the effect of a combination of postural drainage,

coughing and breathing exercises but without manual percussion. It is therefore concluded that the most effective part of a physiotherapeutic treatment is a combination of coughing, breathing exercises and postural drainage. Manual percussion apparently does not enhance the effectiveness of a combination of coughing, breathing exercises and postural drainage. Only when these methods can not be effectively applied it should be considered to apply manual percussion.

Influence of elastic recoil pressure on the effect of forced expirations.

Forced expirations and coughing are probably the most important physiotherapeutic measures to increase mucus transport. During forced expirations or coughing mucus is transported in the direction of the oropharynx by the high expiratory airflow velocity, which is the result of a high airflow and a dynamic compression of the airways. Patients with pulmonary emphysema have a loss of elastic recoil pressure of the lung tissue. In these circumstances the dynamic compression of the airways during forced expiration may result in a complete airway collapse and thereby limit the effectiveness of the forced expirations and coughing. In Chapter 5 the results of a study on the influence of elastic recoil pressure on spontaneous mucus clearance and the effectiveness of forced expirations and coughing are described. In patients with decreased elastic recoil pressure spontaneous mucus clearance appeared to be higher as compared to patients with normal elastic recoil pressure with comparable level of airflow obstruction as measured by FEV_1. Mucus transport data in these patients, however, may not be completely comparable with those of healthy subjects, because of differences in deposition pattern of the tracer. Patients with reduced elastic recoil pressure may have normal mucus transport rates, in contrast to patients with normal elastic recoil pressure. It is not known why in patients with emphysema mucus transport is better preserved than in patients with chronic bronchitis. In patients with normal elastic recoil pressure, but not in those with decreased elastic recoil pressure, mucus clearance could be enhanced by forced expirations and coughing. The bronchial collapse that arises in patients with decreased elastic recoil pressure during a forced expiration is likely to be responsible for the limited effect of forced expirations in these patients.

Effect of expiratory resistance on airway collapse.

The results of earlier studies suggest that patients with pulmonary emphysema may have normal or slightly reduced mucus transport in a stable phase of their disease. Mucus transport during a pulmonary infection, however, may be severely reduced by inhibition of ciliary activity and by hypersecretion. As shown in Chapter 5, forced expirations are ineffective in compensating the reduced mucus transport in case of a collapse of the airways during a forced expiration. This collapse is visible in the maximal expiratory flow volume (MEFV)-curve as a sharp bend convex to the volume axis at relatively high lung volume.

Many patients with emphysema spontaneously use a form of positive expiratory pressure breathing, i.e. pursed lips breathing. They often claim an immediate subjective benefit. It has been hypothesized that positive expiratory pressure breathing reduces airway collapse by an increase of the intra-bronchial pressure. A reduction of airway collapse should be visible in the configuration of the MEFV curve. In Chapter 6 a study on the effect of positive expiratory pressure breathing on the configuration of the MEFV curve in patients with emphysema is described. Positive expiratory pressure breathing was shown to change the configuration of the MEFV-curve in some patients in the sense that the collapse phenomenen was diminished. This indicates that the airway resistance at high lung volumes was reduced, resulting in an increased flow at these lung volumes. This effect was inversely correlated to the predicted total lung capacity. In patients with a severely increased total lung capacity positive expiratory pressure breathing did not reduce the collapse phenomenen. At lower lung volumes no effect was seen on the configuration of the MEFV-curve. An expiratory resistance during forced expiration is to be advised for patients with airway collapse but without severe chronic hyperinflation.

Effect of positive expiratory pressure breathing on pulmonary function and mucus clearance in patients with cystic fibrosis.

In patients with cystic fibrosis tenacious respiratory tract secretions often obstruct small peripheral airways. Mucus mobilisation is very difficult in these airways as local airflow velocity is low due to the huge total airway diameter. Velocity of airflow may be further reduced by the development of atelectasis,

as a result of obstruction by mucus plugs. It has been hypothesized that an increase of expiratory mouth pressure will increase the volume of air behind mucus plugs. Mucus plugs may be subsequently mobilised by a forced expiration. Breathing with an expiratory pressure may increase the pressure gradient between open and closed alveoli. It may also reduce airway resistance in peripheral and collateral airways by an increase of functional residual capacity. Both mechanisms may lead to an increase of air volume in closed alveoli. An increase of air volume in closed alveoli should be visible as an increased thoracic gas volume (TGV). In Chapter 7 the results of a study on the effect of positive expiratory pressure breathing on pulmonary function and mucus clearance in patients with cystic fibrosis are presented. During positive expiratory pressure breathing TGV increased significantly. However, after discontinuation of the positive expiratory pressure TGV returned rapidly to the baseline value. Positive expiratory pressure appeared to have no influence on spontaneous mucus transport or mucus transport by coughing. Positive expiratory pressure breathing can therefore not be recommended as a therapy to improve mucus transport, but may be useful in case of acute atelectasis.

CONCLUSION.

The use of physiotherapeutic techniques may increase mucus transport in patients with airways disease including COPD, asthma, cystic fibrosis and primary ciliary dyskinesia. The most effective parts of the treatment are probably forced expirations with open glottis and coughing. However, in patients with decreased elastic recoil pressure of the lung tissue the effect of these measures is limited as a result of bronchial collapse. In these patients the bronchial collapse can be reduced by a positive expiratory pressure breathing. It should be considered to apply manual percussion only when postural drainage, breathing exercises and forced expirations are ineffective. Positive expiratory pressure breathing in patients with cystic fibrosis is shown to increase lung volume and may therefore be useful in case of acute atelectasis. It had, however, no influence on mucus transport in these patients.

The choice of physiotherapeutic techniques should be dependent on the pathophysiological mechanisms in the airways of the patient. A referral to a

physiotherapist, therefore, should contain sufficient information about the airway mechanics. Physiotherapists should be capable to interpret this information.

Further studies are needed to investigate the physiological effects of physiotherapeutic measures, aiming an increase in mucus transport, in different pathophysiological conditions contributing to the development of mucus retention. Understanding of the relationship between physiotherapeutic techniques, in the treatment of mucus retention, and pathophysiological mechanisms present in the airways may increase the effectiveness of physiotherapy as it provides a base for an individual choice and application of therapy. In this thesis short-term effects of physiotherapeutic treatment have been investigated. However, long-term effects of these techniques on the prognosis of the disease and the frequency of exacerbations still remains to be studied.