EDITORIAL REVIEW

Clearance of particles from the human tracheobronchial tree

P. CAMNER

Department of Environmental Hygiene, The Karolinska Institute and the National Environmental Protection Board, Stockholm, Sweden

Introduction

Particles deposited in the tracheobronchial tree are removed by mucociliary transport and, in the larger airways, by coughing. Lucas & Douglas (1934) proposed a model for mucociliary transport in which the fluid covering the epithelium consists of two layers: one layer of a low-viscosity fluid (the sol layer), on which a layer of a highly viscous fluid (gel or mucous layer) is floating. The cilia beat in the sol layer and come in contact with the gel layer only with their tips during active strokes. On the whole, this model is still accepted. There are, however, different opinions regarding the continuity of the mucous layer. Some authors (Iravani & Van As, 1972; Van As & Webster, 1974) claim that the mucous layer is not continuous but consists of droplets and flakes. Others claim that it is continuous (Holma, 1971; Sturgess, 1977). A large number of studies on the effects of various agents on mucociliary transport have been made in animals *in vivo* and *in vitro* (Dalhamn, 1956; Asmundsson & Kilburn, 1973).

Human tracheobronchial clearance has been studied with methods whereby external measurements of inhaled test particles, labelled radioactively, were made (Albert, Lippmann, Spiegelman, Liuzzi & Nelson, 1967; Morrow, Gibb & Gazioglu, 1967; Thomson & Short, 1969; Camner, 1971; Lourenço, Klimek & Barowski, 1971; Sanchis, Dolovich, Chalmers & Newhouse, 1971; Yeates, Aspin, Levison, Jones & Bryan, 1975; Bertrand & Puchelle, 1977). These methods affect the transport mechanism very little and allow studies of physiological variations in transport to be made. Mucociliary transport in the human trachea has been studied by observation of particles through a bronchofibrescope (Sackner, Rosen & Wanner, 1973). In a further development, radiopaque particles are placed in the trachea by the bronchofibrescope and the transport of particles is followed by means of X-rays (Goodman, Yergin, Landa, Golinwaux & Sackner, 1978).

This paper reviews studies of the following: the influence of genetic, physiological and environmental factors on human mucociliary clearance; the importance of mucociliary clearance as a defence mechanism; mucociliary clearance in chronic diseases; clearance by coughing.

Correspondence: Dr Per Camner, Department of Environmental Hygiene, Karolinska Institute, S-104 01 Stockholm, Sweden.

Factors influencing mucociliary clearance

From most studies on mucociliary clearance, it is evident that there are large variations among healthy persons. Studies of clearance in twins indicate that genetic factors are partly responsible for this variation. Camner, Philipson & Friberg (1972) found the clearance rate of inhaled test particles to be fairly similar within pairs of monzygotic twins, but not in dizygotic twins. Bohning, Albert, Lippmann & Foster (1975) also found tracheobronchial clearance to be fairly similar in monozygotic twins.

Physiological factors too are important in mucociliary transport. Older persons have on average a slower rate of transport than younger ones (Goodman *et al.*, 1978; Puchelle, Zahn & Bertrand, 1979). Mucociliary transport also varies within subjects. Bateman, Pavia & Clarke (1978) found the clearance rate of inhaled test particles to be significantly slower in a group of healthy males when they were asleep during the night, than when they were awake during the day. This observation is of special interest because it is well known that asthma attacks often start in the late night or early morning. It is known that the supine position itself causes increased obstruction. Mossberg, Strandberg, Philipson &

0143-5221/80/080079-06$01.50/1 © 1980 The Biochemical Society and the Medical Research Society

Camner (1976a, b) found that the forced expiratory volume in 1 s was significantly decreased in patients with asthma and bronchitis after about 3 h in the supine position. The combination of impaired clearance during sleep and increased obstruction due to the supine position might explain the high frequency of early morning asthma attacks. The reason for decreased mucociliary transport during sleep is not known. A decreased concentration of catecholamines in the blood might be an explanation, since adrenergic compounds can markedly increase mucociliary transport in the lungs (Konietzko, Klopfer, Adam & Matthys, 1975; Yeates *et al.*, 1975; Camner, Strandberg & Philipson, 1976; Foster, Bergofsky, Bohning, Lippmann & Albert, 1976).

Physical exercise produces an increase in the tracheobronchial clearance rate, which cannot be explained by hyperventilation alone (Wolff, Dolovich, Obminski & Newhouse, 1977). The reason for the increase is not known, but it may be caused by an increased concentration of catecholamines in the blood. Alternatively, it may be caused by activation of the vagus nerve. Support for the latter suggestion is that administration of cholinergic compounds increases mucociliary transport (Camner, Strandberg & Philipson, 1974). Some anticholinergic compounds have been found to decrease mucociliary transport (Pavia & Thomson, 1971; Yeates *et al.*, 1975).

Inhalation of particles and gases (e.g. tobacco smoke, carbon dust, sulphur dioxide and sulphuric acid mist) can cause an immediate increase in the mucociliary transport velocity (Camner, Philipson & Arvidsson, 1971; Camner, Hellström & Philipson, 1973b; Albert, Petersson, Bohning & Lippmann, 1975; Wolff, Dolovich, Rossman & Newhouse, 1975; Newhouse, Dolovich, Obminski & Wolff, 1978). It is probable that this increase is reflex in origin, since these agents can activate the vagus nerve and cholinergic compounds are known to increase mucociliary transport velocity. There also exist particles which can decrease mucociliary transport, e.g. hair-spray aerosol (Friedman, Dougherty, Nelson, White, Sackner & Wanner, 1977; Borum, Holten & Loekkegaard, 1979).

It has been shown, both with techniques with radioactively labelled aerosols and techniques in which radiopaque particles are administered through a bronchofibrescope, that long-term smoking impairs mucociliary clearance (Lourenço *et al.*, 1971; Camner & Philipson, 1972; Goodman *et al.*, 1978). In a study by Camner & Philipson (1972), the clearance rate was studied in 10 pairs of monozygotic twins discordant for smoking. They had smoked about 15–30 cigarettes a day for 25–35 years. Although the smokers on average had a significantly slower clearance rate than the non-smokers, clearance was impaired in only five of the 10 smokers.

Impairment of tracheobronchial clearance in healthy smokers is at least partly reversible; a group who had stopped smoking showed a significant improvement in clearance after 3 months (Camner, Philipson & Arvidsson, 1973a).

Certain infectious agents have been found to impair mucociliary transport in the tracheobronchial tree, e.g. influenza A virus and *Mycoplasma pneumoniae* (Camner, Jarstrand & Philipson, 1973c; Jarstrand, Camner & Philipson, 1974). The impaired clearance found in patients infected with influenza A virus appears to be totally reversible. However, patients who had been infected by *Mycoplasma pneumoniae* 1 year before had a slower clearance rate than healthy controls. These results suggest either that some impairment persists or that subjects with a slower clearance rate contract the disease more easily (Jarstrand *et al.*, 1974; Camner, Jarstrand & Philipson, 1978).

Importance of mucociliary clearance

Previously, persons with congenitally immotile cilia have been identified (Camner, Mossberg & Afzelius, 1975; Afzelius, 1976; Pedersen & Mygind, 1976; Eliasson, Mossberg, Camner & Afzelius, 1977; Mossberg, Afzelius, Eliasson & Camner, 1978a; Waite, Steele, Ross, Wakefield, Mackay & Wallace, 1978). The male patients also have immotile sperm tails. The morphology of sperm tails and cilia is usually normal when viewed under the light microscope, but under the electron microscope a partial or total lack of the dynein arms is usually found in both cells. Normal dynein arms have been seen in some patients, but they show instead other ultrastructural defects such as an abnormal central sheath (Afzelius & Eliasson, 1979; Camner, Afzelius, Eliasson & Mossberg, 1979a) and defective radial spokes (Sturgess, Chao, Wong, Aspin & Turner, 1979). Interestingly, nasal cilia that lack dynein arms, from such patients, have shown normal motile activity *in vitro* with added adenosine triphosphate and adenosine triphosphatase (Forrest, Rossman, Newhouse & Ruffin, 1979).

The immotile-cilia syndrome includes Kartagener's syndrome (bronchiectasis. chronic sinusitis and situs inversus). However, persons with normal positioning of thoracic and ab-

dominal viscera can also have the syndrome. Their mucociliary clearance rate is slow or absent (Mossberg *et al.*, 1978a). The patients with immotile cilia are only a small fraction of all patients with bronchiectasis, in whom clearance can be impaired or normal (Lourenço, Loddenkemper & Carton, 1972).

Mossberg *et al.* (1978a) described the clinical picture and ventilatory function in 14 patients with the immotile-cilia syndrome (age 25–40 years). From early childhood the patients had chronic or recurrent infections in the upper and lower airways; most had bronchiectasis, several had recurrent pneumonia. As a group, the patients had airflow obstruction, but the obstruction varied considerably, e.g. the forced expiratory volume in 1 s, in percentage of predicted normal values, varied from 27 to 89%, the average was 59%. Most of the patients lived an active life.

Mucociliary transport in chronic diseases

Patients with chronic bronchitis usually have severely impaired mucociliary clearance (Toigo, Imarsio, Murmall & Lepper, 1963; Camner, Mossberg & Philipson, 1973d; Santa Cruz, Landa, Hirsch & Sackner, 1974; Mossberg *et al.*, 1976a; Bertrand & Puchelle, 1977). Considering that patients with the immotile-cilia syndrome have airflow obstruction, although they are usually much younger than patients with chronic bronchitis, and that impaired mucociliary transport can be found in healthy smokers, it is probable that impaired mucociliary transport is a pathogenetic factor in the development of airflow obstruction in patients with chronic bronchitis.

Asthmatic patients may also have impaired mucociliary clearance (Mossberg *et al.*, 1976b; Foster, Langenback, Bohning & Bergofsky, 1978; Mezey, Cohn, Fernandez, Januszkievicz & Wanner, 1978; Bateman, Pavia, Sheanan & Clarke, 1979a). However, the impairment seems on average to be much less in asthmatic patients (Mossberg *et al.*, 1976b) than in patients with mild or severe chronic bronchitis (Camner *et al.*, 1973d; Mossberg *et al.*, 1976a).

Patients with cystic fibrosis usually have mucociliary clearance which is impaired to a varying degree (Sanchis, Dolovich, Rossman, Wilson & Newhouse, 1973; Thomson, Pavia, Short & Norman, 1973; Wood, Wanner, Hirsch & Farrel, 1975; Yeates. Sturgess, Kahn, Levison & Aspin, 1976). Kollberg, Mossberg, Afzelius, Philipson & Camner (1978) compared a group of patients with cystic fibrosis with a group of patients with the immotile-cilia syndrome. Most of the patients with cystic fibrosis had reasonable mucociliary clearance, but they tended to have more airway obstruction and more respiratory disability than the patients with the immotile-cilia syndrome. Impairment of mucociliary clearance in patients with cystic fibrosis does not seem to be the primary pathogenetic factor for respiratory disease in these patients. By the same reasoning, the same seems to be true for patients with emphysema associated with α_1-antitrypsin deficiency (Mossberg, Philipson & Camner, 1978b).

Young (1970) described a syndrome in which infection of the upper and lower respiratory tract and obstructed azoospermia occurred. This lung disease is thus similar to that in the immotile-cilia syndrome, but the ultrastructure of cilia is normal and sperm transport in the epididymis is absent (Hendry, Knight, Whitfield, Stansfeld, Pryse-Davies, Ryder, Pavia, Bateman & Clarke, 1978). On average, these patients have a slower clearance rate than do healthy controls (Hendry *et al.*, 1978).

It has been possible to improve tracheobronchial clearance in patients with chronic disease of the lungs. Both in patients with asthma and chronic bronchitis a β_2-adrenergic compound has increased clearance but not as much as in healthy persons (Konietzko *et al.*, 1975; Mossberg *et al.*, 1976a, b). In patients with chronic bronchitis, a significant improvement in clearance has been produced by administration of an hypertonic saline aerosol, physiotherapy and an expectorant (Thomson, Pavia, Gregg & Start, 1974; Pavia, Thomson & Clarke, 1978; Bateman, Daunt, Newman, Pavia & Clarke, 1979b). Although some anticholinergic compounds have been found to decrease the rate of mucociliary clearance, ipratropium bromide did not do so in patients with airflow obstruction (Pavia, Bateman, Sheanan & Clarke, 1979).

Tracheobronchial clearance by coughing

The efficacy of coughing for elimination of inhaled particles has been studied very little, although there are good reasons to do so. Firstly, it is known that one elimination mechanism in the airways, mucociliary clearance, is necessary for healthy lungs. Secondly, in chronic bronchitis this transport is often severely impaired and coughing is probably the most important elimination mechanism in such patients.

Several authors have described a stepwise decrease in retention of inhaled radioactively labelled particles in the larger airways of patients with disease of the lung (Toigo *et al.*, 1963; Camner *et al.*, 1973d; Yeates *et al.*, 1976;

Oldenburg, Dolovich, Montgomery & Newhouse, 1979). Coughing can thus compensate for impaired mucociliary transport, but only partly, since patients with immotile cilia do not have normal healthy lungs. Mossberg *et al.* (1978a) studied the elimination of inhaled radioactively labelled particles produced by 1–2 min of voluntary coughing in 12 patients with the immotile-cilia syndrome. The percentage eliminated varied widely (from 2 to 48%, with an average of 30%). Camner, Mossberg, Philipson & Strandberg (1979b) studied the effect of voluntary coughing on the elimination of inhaled particles in six healthy subjects and eight patients with lung disease. No substantial elimination of particles was found in 10 tests with the healthy subjects. Six of the patients with lung disease had phlegm, showed expectoration and could eliminate particles from the lung by coughing. The other two patients had no phlegm and did not eliminate particles by coughing. Apparently, an increase in tracheobronchial secretions is necessary for coughing to be effective. Some reproducibility of the effect of coughing was seen in the patients, suggesting that the test model used might be useful for studying the influence of physiological and pharmacological factors on the elimination process.

Conclusions

In recent years our knowledge of clearance of particles from the human tracheobronchial tree has increased rapidly. However, there is still much to learn, e.g. the importance of clearance and clearance in different parts of the tracheobronchial tree.

Studies in subjects with the immotile-cilia syndrome have provided information about the importance of mucociliary transport; it is not known whether partial impairment of mucociliary transport will increase the risk of disease in the lungs. No answer has been given to the question of whether impaired transport will increase the risk of lung cancer. This question might be answered if a relatively large number of subjects with immotile-cilia syndrome can be registered and followed clinically for a long time. Alternatively, studies of clearance in monozygotic twins in whom one partner has contracted lung cancer might supply the answer.

In the studies reviewed above, clearance has been studied in the trachea, the larger bronchi or diffusely over the tracheobronchial tree. More detailed knowledge about clearance in the various parts might be of great value. Experiments in rats (Gore & Patrick, 1978) have shown that particles deposited on the first bifurcation may be retained for several days. Although this is a small fraction of the number of deposited particles, these particles might be the ones which are really hazardous. A knowledge of clearance in smaller airways might also give a better understanding of chronic disease of the lungs.

References

AFZELIUS, B.A. (1976) A human syndrome caused by immotile cilia. *Science*, **193**, 317–319.

AFZELIUS, B.A. & ELIASSON, R. (1979) Flagellar mutants in man: on the heterogeneity of the immotile-cilia syndrome. *Journal of Ultrastructure Research*, **69**, 43–52.

ALBERT, R.E., LIPPMANN, M., SPIEGELMAN, I., LIUZZI, A. & NELSON, N. (1967) The deposition and clearance of radioactive particles in the human lung. *Archives of Environmental Health*, **14**, 10–15.

ALBERT, R.E., PETERSSON, H.T., JR, BOHNING, D.E. & LIPPMANN, M. (1975) Short-term effects of cigarette smoking on bronchial clearance in humans. *Archives of Environmental Health*, **30**, 361–367.

ASMUNDSSON, T. & KILBURN, K.H. (1973) Mechanisms of respiratory tract clearance. In: *Sputum*, pp. 107–180. C. C. Thomas, Springfield, Illinois.

BATEMAN, J.R.M., DAUNT, K.M., NEWMAN, S.P., PAVIA, D. & CLARKE, S.W. (1979b) Regional lung clearance of excessive bronchial secretions during chest physiotherapy in patients with stable chronic airways obstruction. *Lancet*, **i**, 294–297.

BATEMAN, J.R.M., PAVIA, D. & CLARKE, S.W. (1978) The retention of lung secretion during the night in normal subjects. *Clinical Science and Molecular Medicine*, **55**, 523–527.

BATEMAN, J.R.M., PAVIA, D., SHEANAN, N.F. & CLARKE, S.W. (1979a) Tracheobronchial clearance in asthma. *Thorax*, **34**, 418.

BERTRAND, A. & PUCHELLE, E. (1977) Mésure de la clearance muco-ciliaire des bronches proximales chez le bronchitique chronique. *Pathologie Biologie*, **9**, 623–627.

BOHNING, D.E., ALBERT, R.E., LIPPMANN, M. & FOSTER, W.H. (1975) Tracheobronchial particle deposition and clearance. A study of the effects of cigarette smoking in monozygotic twins. *Archives of Environmental Health*, **30**, 457–462.

BORUM, P., HOLTEN, A. & LOEKKEGAARD, N. (1979) Depression of nasal mucociliary transport by an aerosol hair-spray. *Scandinavian Journal of Respiratory Diseases*, **60**, 253–259.

CAMNER, P. (1971) The production and use of test aerosols for studies of human tracheobronchial clearance. *Environmental Physiology*, **1**, 137–154.

CAMNER, P., AFZELIUS, B., ELIASSON, R. & MOSSBERG, B. (1979a) Relation between abnormalities of human sperm flagella and respiratory tract disease. *International Journal of Andrology*, **2**, 211–224.

CAMNER, P., HELLSTRÖM, P.-Å. & PHILIPSON, K. (1973b) Carbon dust and mucociliary transport. *Archives of Environmental Health*, **26**, 294–296.

CAMNER, P., JARSTRAND, C. & PHILIPSON, K. (1973c) Tracheobronchial clearance in patients with influenza. *American Review of Respiratory Disease*, **108**, 131–135.

CAMNER, P., JARSTRAND, C. & PHILIPSON, K. (1978) Tracheobronchial clearance after infection with *Mycoplasma pneumoniae*. *Scandinavian Journal of Infectious Diseases*, **10**, 33–35.

CAMNER, P., MOSSBERG, B. & AFZELIUS, B. (1975) Evidence for congenitally non-functioning cilia in the tracheobronchial tract in two subjects. *American Review of Respiratory Disease*, **112**, 807–809.

CAMNER, P., MOSSBERG, B. & PHILIPSON, K. (1973d) Tracheobronchial clearance and chronic obstructive lung disease. *Scandinavian Journal of Respiratory Diseases*, **54**, 272–281.

CAMNER, P., MOSSBERG, B., PHILIPSON, K. & STRANDBERG, K. (1979b) Elimination of test particles from the human tracheobronchial tract by voluntary coughing. *Scandinavian Journal of Respiratory Diseases*, **60**, 56–62.

CAMNER, P. & PHILIPSON, K. (1972) Tracheobronchial clearance in smoking-discordant twins. *Archives of Environmental Health*, **25**, 60–63.

CAMNER, P., PHILIPSON, K. & ARVIDSSON, T. (1971) Cigarette smoking in man. Short-term effect on mucociliary transport. *Archives of Environmental Health*, **23**, 421–426.

CAMNER, P., PHILIPSON, K. & ARVIDSSON, T. (1973a) Withdrawal of cigarette smoking. A study on tracheobronchial clearance. *Archives of Environmental Health*, **26**, 90–92.

CAMNER, P., PHILIPSON, K. & FRIBERG, L. (1972) Tracheobronchial clearance in twins. *Archives of Environmental Health*, **24**, 82–87.

CAMNER, P., STRANDBERG, K. & PHILIPSON, K. (1974) Increased mucociliary transport by cholinergic stimulation. *Archives of Environmental Health*, **29**, 220–224.

CAMNER, P., STRANDBERG, K. & PHILIPSON, K. (1976) Increased mucociliary transport by adrenergic stimulation. *Archives of Environmental Health*, **31**, 79–82.

DALHAMN, T. (1956) Mucous flow and ciliary activity in the trachea of healthy rats and rats exposed to respiratory irritant gases. *Acta Physiologica Scandinavica*, **36** (Suppl. 123).

ELIASSON, R., MOSSBERG, B., CAMNER, P. & AFZELIUS, B. (1977) The immotile cilia syndrome: a congenital ciliary abnormality as an etiological factor in chronic airway infection and male sterility. *New England Journal of Medicine*, **297**, 1–6.

FORREST, J.B., ROSSMAN, C.M., NEWHOUSE, T. & RUFFIN, R. (1979) Activation of nasal cilia in immotile cilia syndrome. *American Review of Respiratory Disease*, **120**, 511–515.

FOSTER, W.M., BERGOFSKY, E.H., BOHNING, D.E., LIPPMANN, H. & ALBERT, R.E. (1976) Effects of adrenergic agents and their mode of action on mucociliary clearance in man. *Journal of Applied Physiology*, **41**, 146–152.

FOSTER, W.M., LANGENBACK, E., BOHNING, D.E. & BERGOFSKY, E.H. (1978) Quantitation of mucous clearance in peripheral lung and comparison with tracheal and bronchial mucus transport velocities in man: adrenergics return depressed clearance and transport velocities in asthmatics to normal. *American Review of Respiratory Disease*, **117**, 337.

FRIEDMAN, M., DOUGHERTY, R., NELSON, S.R., WHITE, R.P., SACKNER, M.A. & WANNER, A. (1977) Acute effects of an aerosol hair-spray on tracheal mucociliary transport. *American Review of Respiratory Disease*, **116**, 281–286.

GOODMAN, R.M., YERGIN, B.M., LANDA, J.F., GOLINWAUX, M.H. & SACKNER, M.A. (1978) Relationship of smoking history and pulmonary function tests to tracheal mucous velocity in non-smokers, young smokers, ex-smokers and patients with chronic bronchitis. *American Review of Respiratory Disease*, **117**, 205–214.

GORE, D.J. & PATRICK, G. (1978) The distribution and clearance of inhaled UO_2 particles on the first bifurcation and trachea of rats. *Physics in Medicine and Biology*, **23**, 730–737.

HENDRY, W.F., KNIGHT, R.K., WHITFIELD, H.N., STANSFIELD, A.G., PRYSE-DAVIES, J., RYDER, T.A., PAVIA, D., BATEMAN, J.R.M. & CLARKE, S.W. (1978) Obstructive azoospermia: respiratory function tests, electron microscopy and the results of surgery. *British Journal of Urology*, **50**, 598–604.

HOLMA, B. (1971) Pathophysiology of the clearing mechanism of the lung. *Progress in Respiration Research*, vol. 6, pp. 51–65. Karger, Basel.

IRAVANI, J. & VAN AS, A. (1972) Mucus transport in the tracheobronchial tree of normal and bronchitic rats. *Journal of Pathology*, **106**, 81–93.

JARSTRAND, C., CAMNER, P. & PHILIPSON, K. (1974) *Mycoplasma pneumoniae* and tracheobronchial clearance. *American Review of Respiratory Disease*, **110**, 415–419.

KOLLBERG, H., MOSSBERG, B., AFZELIUS, B., PHILIPSON, K. & CAMNER, P. (1978) Cystic fibrosis compared with the immotile cilia syndrome: a study of mucociliary clearance, ciliary ultrastructure, clinical picture and ventilatory function. *Scandinavian Journal of Respiratory Diseases*, **59**, 297–306.

KONIETZKO, N., KLOPFER, M., ADAM, W.E. & MATTHYS, H. (1975) Die mukociliare Klarfunktion der Lunge unter adrenerger Stimulation. *Pneumonologie*, **152**, 203–208.

LOURENÇO, R.V., KLIMEK, M.F. & BAROWSKI, C.J. (1971) Deposition and clearance of 2μ particles in the tracheobronchial tree of normal subjects: smokers and non-smokers. *Journal of Clinical Investigation*, **50**, 1411–1419.

LOURENÇO, R.V., LODDENKEMPER, R. & CARTON, R.W. (1972) Patterns of distribution and clearance of aerosols in patients with bronchiectasis. *American Review of Respiratory Disease*, **106**, 857–866.

LUCAS, A. & DOUGLAS, L. (1934) Principles underlying ciliary activity in the respiratory tract. II. A comparison of nasal clearance in man, monkey and other animals. *Archives of Otolaryngology*, **20**, 518–541.

MEZEY, R., COHN, M.A., FERNANDEZ, R.J., JANUSZKIEVICZ, A.J. & WANNER, A. (1978) Mucociliary transport in allergic patients with antigen-induced bronchospasm. *American Review of Respiratory Disease*, **118**, 677–684.

MORROW, P.E., GIBB, F.R. & GAZIOGLU, K.M. (1967) A study of particulate clearance from the human lungs. *American Review of Respiratory Disease*, **96**, 1209–1221.

MOSSBERG, B., AFZELIUS, B.A., ELIASSON, R. & CAMNER, P. (1978a) On the pathogenesis of obstructive lung disease. A study on the immotile-cilia syndrome. *Scandinavian Journal of Respiratory Diseases*, **59**, 55–65.

MOSSBERG, B., PHILIPSON. K. & CAMNER, P. (1978b) Tracheobronchial clearance in patients with emphysema associated with alpha$_1$-antitrypsin deficiency. *Scandinavian Journal of Respiratory Diseases*, **59**, 1–7.

MOSSBERG, B., STRANDBERG, K., PHILIPSON, K. & CAMNER, P. (1976a) Tracheobronchial clearance and beta-adrenoceptor stimulation in patients with chronic bronchitis. *Scandinavian Journal of Respiratory Diseases*, **57**, 281–289.

MOSSBERG, B., STRANDBERG, K., PHILIPSON, K. & CAMNER, P. (1976b) Tracheobronchial clearance in bronchial asthma. Response to beta-adrenoceptor stimulation. *Scandinavian Journal of Respiratory Diseases*, **57**, 119–128.

NEWHOUSE, M.T., DOLOVICH, M., OBMINSKI, G. & WOLFF, R.K. (1978) Effect of TLV levels of SO_2 and H_2SO_4 on bronchial clearance in exercising man. *Archives of Environmental Health*, **33**, 24–32.

OLDENBURG, F.A., DOLOVICH, M.B., MONTGOMERY, J.M. & NEWHOUSE, M.T. (1979) Effects of postural drainage, exercise, and cough on mucus clearance in chronic bronchitis. *American Review of Respiratory Disease*, **120**, 739–745.

PAVIA, D., BATEMAN, J.R., SHEANAN, N.F. & CLARKE, S.W. (1979) Effect of ipratropium bromide on mucociliary clearance and pulmonary function in reversible airways obstruction. *Thorax*, **34**, 501–507.

PAVIA, D. & THOMSON, M.L. (1971) Inhibition of mucociliary clearance from the human lung by hyoscine. *Lancet*, **i**, 449–450.

PAVIA, D., THOMSON, M.L. & CLARKE, S.W. (1978) Enhanced clearance of secretions from the human lung after the administration of hypertonic saline aerosol. *American Review of Respiratory Disease*, **117**, 199–203.

PEDERSEN, H. & MYGIND, N. (1976) Absence of axonemal arms in nasal mucosa cilia Kartagener's syndrome. *Nature (London)*, **262**, 494–495.

PUCHELLE, E., ZAHN, J.-M. & BERTRAND, A. (1979) Influence of age on bronchial mucociliary transport. *Scandinavian Journal of Respiratory Diseases*, **60**, 307–313.

SACKNER, M.A., ROSEN, M.J. & WANNER, A. (1973) Estimation of tracheal mucous velocity by bronchofiberscopy. *Journal of Applied Physiology*, **23**, 495–499.

SANCHIS, J., DOLOVICH, M., CHALMERS, R. & NEWHOUSE, M. (1971) Regional distribution and lung clearance mechanisms in smokers and non-smokers. In: *Inhaled Particles III*, pp. 183–188. Ed. Walton, W.H. Unwin Bros, Surrey.

SANCHIS, J., DOLOVICH, M., ROSSMAN, C., WILSON, W. & NEWHOUSE, M. (1973) Pulmonary mucociliary clearance in cystic fibrosis. *New England Journal of Medicine*, **288**, 651–654.

SANTA CRUZ, R., LANDA, J., HIRSCH, J. & SACKNER, M.A. (1974) Tracheal mucous velocity in normal man and patients with obstructive lung disease, effects of terbutaline. *American Review of Respiratory Disease*, **109**, 458–463.

STURGESS, J. (1977) The mucous lining of major bronchi in the rabbit lung. *American Review of Respiratory Disease*, **115**, 819–827.

STURGESS, J., CHAO, J., WONG, J., ASPIN, N. & TURNER, P. (1979) Cilia with defective radial spokes. A cause of human respiratory disease. *New England Journal of Medicine*, **300**, 53–56.

THOMSON, M.L., PAVIA, D., GREGG, I. & START, J.E. (1974) Broxhexine and mucociliary clearance in chronic bronchitis. *British Journal of Diseases of the Chest*, **68**, 21–27.

THOMSON, M.L., PAVIA, D., SHORT, M.D. & NORMAN, A.P. (1973) Lung clearance in two patients with cystic fibrosis. *New England Journal of Medicine*, **289**, 749–750.

THOMSON, M.L. & SHORT, M.D. (1969) Mucociliary function in

health, chronic obstructive airway disease and asbestosis. *Journal of Applied Physiology*, **26**, 535–539.

TOIGO, A., IMARSIO, J.J., MURMALL, H. & LEPPER, M.N. (1963) Clearance of large carbon particles from the human tracheobronchial tree. *American Review of Respiratory Disease*, **87**, 487–492.

VAN AS, A. & WEBSTER, J. (1974) The morphology of mucus in mammalian pulmonary airways. *Environmental Research*, **7**, 1–12.

WAITE, D., STEELE, R., ROSS, I., WAKEFIELD, J.ST J., MACKAY, J. & WALLACE, J. (1978) Cilia and sperm tail abnormalities in Polynesian bronchiectatics. *Lancet*, **ii**, 132–133.

WOLFF, R.K., DOLOVICH, M.B., OBMINSKI, G. & NEWHOUSE, M.T. (1977) Effects of exercise and eucapnic hyperventilation on bronchial clearance in man. *Journal of Applied Physiology*, **43**, 46–50.

WOLFF, R.K., DOLOVICH, M., ROSSMAN, C.M. & NEWHOUSE, M.T. (1975) Sulfur dioxide and tracheobronchial clearance in man. *Archives of Environmental Health*, **30**, 521–527.

WOOD, P., WANNER, A., HIRSCH, J. & FARREL, P. (1975) Tracheal mucociliary transport in patients with cystic fibrosis and its stimulation by terbutaline. *American Review of Respiratory Disease*, **111**, 733–738.

YEATES, D.B., ASPIN, N., LEVISON, H., JONES, M.T. & BRYAN, A.C. (1975) Mucociliary tracheal transport rates in man. *Journal of Applied Physiology*, **39**, 487–495.

YEATES, D., STURGESS, J., KAHN, S., LEVISON, H. & ASPIN, N. (1976) Mucociliary transport in trachea of patients with cystic fibrosis. *Archives of Disease in Childhood*, **51**, 28–33.

YOUNG, D. (1970) Surgical treatment of male infertility. *Journal of Reproduction and Fertility*, **23**, 541–542.