

Proceedings of the Thoracic Society

The Spring Meeting of the Thoracic Society was held on 2-3 March 1973 at the Royal College of Physicians, London. There were eight short papers and three symposia. Summaries follow.

ASTHMA—A LOOK AT THE PAST

R. ELLUL-MICALLEF Asthma has attracted a great deal of attention over the centuries. This is probably because its clinical manifestations of breathlessness and wheezing frequently present themselves in a dramatic manner. The disease which Thomas Willis described as 'asthma morbus maxime terribilis' in 1678 may still be most discouraging to treat.

In this paper some of the original writings on the subject, covering the period from the time of Aretaeus (*circa* 300 AD) to Sir William Osler, are examined. Certain concepts, once established, took a long time to die out, such as the claim that asthma is rarely a cause of death. Other propositions are still remarkably valid today. The clinical description of the disease given by Thomas Willis almost 300 years ago is classical and difficult to improve upon. The contributions of such physicians as Van Helmont, Floyer, Cullen, Laennec, Meltzer, and Osler, among others, have all helped to shed light on the problem of asthma.

We have come a long way since foxes' lungs or smoked amber with tobacco were used for its treatment, but we can have no idea of what future generations will think of modern therapy.

THE RELATIONSHIP OF INSPIRATORY CRACKLES TO THE MECHANICAL EVENTS OF BREATHING

L. H. CAPEL and A. R. NATHOO In patients with airways obstruction inspiratory crackles appear and then disappear early in inspiration. In pulmonary fibrosis, heart failure, and pneumonia the crackles occupy the later part of inspiration and continue to its end. It has been suggested that the crackles are produced by the equalization of pressure that follows the sudden opening of the airways in deflated regions of the lung. One reason advanced in favour of this view is that inspiratory crackles show a repetitive pattern in successive respiratory cycles identifiable by the relative intensity and the time interval between successive crackles. Forgacs (1968) suggested that the timing of crackles was determined by the lung tension required to pull individual airways open and this in turn was linked to inspiratory volume.

This hypothesis was tested by recorded inspiratory lung crackles simultaneously with changes in lung volume, transpulmonary pressure, and volume flow

rate. It was confirmed that inspiratory lung crackles often show a recurrent pattern. It was further shown that individual crackles recur repeatedly at the same lung volume and transpulmonary pressure in consecutive respiratory cycles.

Forgacs, P. (1968) *Thorax*, 23, 328.

CLINICAL APPLICATIONS OF LUNG WATER MEASUREMENTS

W. A. CROSBIE, M. C. CLARKE, V. PARSONS, and P. HUGH-JONES The double indicator dilution technique has now been developed as a method for measuring the volume of water in functional contact with perfused lung capillaries.

We describe how this technique can be used to measure the response of the lung capillary bed to exercise, hypervolaemia, anaemia, and diuretic therapy in human subjects. The correlation with radiological and pulmonary physiological parameters is also described.

PROBLEMS OF UPPER RESPIRATORY DEAD-SPACE

P. HUGH-JONES, C. E. BARTER, and M. HIME A patient is described who presented with an unusual clinical problem related to the size of his anatomical dead-space. The significance of measurement of anatomical dead-space in this patient and the results of measurements of the dead-space/tidal volume ratio in three other similar normal subjects are presented and discussed.

SPUTUM IN CHRONIC LUNG DISEASE

Physical Properties of Sputum

LYNNE REID The two properties of sputum described are viscosity and elasticity: these are responsible for its rheological or flow behaviour.

Sputum has one-fifth the dry weight yield of serum but 10 times the viscosity. It behaves as a visco-elastic solid with non-Newtonian characteristics; i.e., its viscosity is affected by the shear rate at which it is tested. Two instruments have been used—the Weissenberg rheogoniometer that enables oscillation or rotation to be used at pre-selected low shear rate and the Ferranti-Shirley viscometer that tests over a pre-selected range at higher rates.

From results obtained with these instruments variation within a sputum specimen and between

patients is described. At low shear rates sputum shows a characteristic feature, a region of fluctuating viscosity, only recently identified and found in certain other epithelial sites. After minimal shearing a time-related increase in viscosity is seen. The relation between elasticity and shear rate is described. Sputum from patients with bronchorrhoea or pituitous catarrh shows characteristic properties.

The chemical basis for some of the rheological features will be described.

Factors affecting Sputum Clearance

M. T. NEWHOUSE Sputum clearance in health and disease depends primarily upon effective mucociliary transport and secondarily on cough. The secretions produced by airway mucous glands and goblet cells are moved cephalad in metachronal waves as a continuous blanket by the integrated function of rapidly beating cilia.

Many physiological and pathological factors have been shown to affect clearance due to a major effect on either mucus visco-elasticity or ciliary function resulting in depression or failure of mucociliary transport. Among the most important known physiological factors are dehydration, hypoxia, and electrolyte imbalance modified by levels of circulating hormones, particularly catecholamines and serotonin. Cardiac glycosides appear to improve transport depressed by hypoxia. In disease, depression of clearance may result from quantitative or qualitative changes in mucus or ciliary function resulting from acute or chronic infection, squamous metaplasia, and loss of ciliated epithelium or chemical agents and drugs such as cigarette smoke, air pollutants, narcotics, and anaesthetic agents.

Clearance appears to be remarkably well maintained in stable patients, even those with fairly advanced pulmonary disease due to chronic bronchitis, emphysema or cystic fibrosis, but in these cough is often an important adjunct in the maintenance of a patent airway.

Failure of these mechanisms leads in the first instance to disordered pulmonary function and later to progressive respiratory failure and death.

Effects of Sputum on Pulmonary Function

S. W. CLARKE, G. M. COCHRANE, and B. WEBBER Though it is generally agreed that sputum should be cleared from the bronchial tree, its effect on pulmonary function is largely unknown. To investigate this, pulmonary function was measured before and after chest physiotherapy. The measurements of pulmonary function included specific conductance using the body plethysmograph followed by static and dynamic lung volumes in that sequence. Physiotherapy consisted of breathing exercises, chest vibrations, and percussion with the subject in different postures, during which sputum was collected and measured. Patients were selected because they

expectorated copious volumes of sputum and all had airways obstruction ($FEV_1/FVC < 70\%$ predicted); they had either chronic bronchitis, bronchiectasis or cystic fibrosis.

The majority of patients showed improvement in all the measured parameters of pulmonary function after physiotherapy. This was particularly marked with specific conductance in which allowance was made for the change in lung volume consequent upon a fall in airway resistance. However, there was no relationship between improvement in pulmonary function and the volume of sputum expectorated in these patients. Though volume is important the distribution of the sputum within the bronchial tree and its visco-elastic properties may be of greater importance in determining its functional effects.

The present study provides ample support for the value of physiotherapy in helping bronchial clearance and thereby improving pulmonary function.

Relationship between Sputum Rheology and Pulmonary Function

E. E. KEAL In 48 mild chronic bronchitics studied over three years a relationship was shown between the neuraminic acid content of the sputum and a grading of its pourability. This was later shown to correlate well with measured viscosity. The initial impairment of maximal breathing capacity and its subsequent deterioration appeared to be greatest in those subjects with high levels of neuraminic acid in the sputum but the relationship in individual patients using mean levels of neuraminic acid was not significant.

In a recent study of 16 advanced chronic bronchitics, measurements were made at monthly intervals of the ventilatory capacity (PEFR and FEV_1/VC), and the chemical constituents, the volume, and the viscosity of the sputum. The sputum viscosity was inversely related to the volume and for the whole group of 67 specimens there was a highly significant relationship between sputum viscosity and ventilatory capacity. A seasonal variation in viscosity and chemistry was, in some cases, related to changes in the degree of airways obstruction. The fucose and dry weight content of the sputum appears to be of greater importance than neuraminic acid in determining its viscosity.

The effect of sputum volume alone on ventilatory function can be illustrated in bronchorrhoea treated with steroids when reduction in volume may lead to improvement in ventilation without alteration of viscosity.

Role of Mucolytic Agents in Sputum Clearance

K. N. V. PALMER In the past, oral expectorants were widely prescribed, but when controlled trials showed that those commonly given did not increase sputum volume¹ their popularity waned. Instead, attempts

were made to use substances which, when given by aerosol inhalation, might reduce sputum viscosity and increase sputum volume by a direct physical or enzymatic action. Many used were too irritative or appeared to act simply by hydrating viscid sputum. Ascorbic acid, sodium percarbonate, and copper sulphate (ascoxal)^{2,3} and n-acetyl cystein⁴ by aerosol have been shown to increase sputum volume and decrease sputum viscosity. But ascoxal is acidic and n-acetyl cystein is alkaline so that both probably impair mucociliary clearance. Bromhexine by mouth has been shown to increase sputum volume and decrease sputum viscosity⁵ but only those patients with slight to moderate airway obstruction show improvement on spirometry when having the drug. Sulphur-containing amino acids (methyl cystein) by mouth have been shown by controlled trial to reduce cough and sputum in outpatient bronchitics⁶.

Large therapeutic benefit cannot be expected from mucolytic agents in patients with advanced respiratory disease, but in those with less severe disease some therapeutic benefit may be seen, particularly when the drugs are used in combination with physiotherapy and bronchodilators.

1. Alstead, S. (1941). *Lancet*, 1, 308.
2. Palmer, K. N. V. (1961). *Lancet*, 2, 802.
3. Dulfano, M. J., and Glass, P. (1969). *J. Amer. med. Ass.*, 207, 1310.
4. Kory, R. C., Hirsch, S. B., and Giraldo (1968). *Dis. Chest*, 54, 504.
5. Hamilton, W. F. D., Palmer, K. N. V., and Gent, M. (1970). *Brit. med. J.*, 3, 260.
6. Palmer, K. N. V., Geake, M. R., and Brass, W. (1962). *Brit. med. J.*, 1, 280.

NON-INVASIVE TECHNIQUES OF MONITORING TIDAL VOLUME AND RESPIRATORY PATTERN

J. M. BEELEY and G. E. WHITTAKER An accurate non-invasive method for monitoring breathing pattern and tidal volume is required because techniques which entail insertion of a tube into the airway and nasal occlusion modify breathing. In recent years a number of workers have reported favourably on experience with impedance pneumographs (see references). However, scant attention has been given to testing the stability of the relationship between tidal volume and impedance changes during monitoring periods.

The tidal volume measured using an impedance pneumograph and using simple cuirasses have been compared with that recorded using a pneumotachograph or spirometer. When the subject was maintained in a static position and breathing within a normal tidal volume range the non-invasive methods produced errors in tidal volume estimation of up to 50%. The errors were increased by minor body movements.

These observations provide further evidence that thoracic impedance changes are partly determined by an alteration of thoracic geometry and are not simply due to aeration of the lungs. However, despite these shortcomings, impedance pneumography

remains at present the most convenient and least disturbing method for monitoring respiratory patterns. In suitable patients its accuracy compares with that of other non-invasive techniques. Examples of success and failure of the impedance pneumograph are given.

- Tanser, A. R. (1967). *Thorax*, 22, 550-554.
 Farman, J. N., and Juett, D. A. (1967). *Brit. med. J.*, 4, 27-29.
 Baker, L. E., and Hill, D. W. (1969). *Brit. J. Anaesth.*, 41, 2.
 North, J. B., and Jennett, S. (1972). *Lancet*, 2, 212-213.

THE ALVEOLAR-CAPILLARY WALL IN MITRAL STENOSIS

J. M. KAY and F. R. EDWARDS The effect of chronic pulmonary venous hypertension on the alveolar-capillary wall was studied in lung biopsy specimens obtained at mitral valvulotomy from four women. Light microscopy showed signs of hypertensive pulmonary vascular disease, cuboidal cell metaplasia of the alveolar epithelium, and a proliferation of cells in the alveolar spaces in all cases. In three cases, some of the proliferated intra-alveolar cells contained haemosiderin and resembled so-called 'heart failure cells'. The alveolar septa were obviously thickened in two cases. Electron microscopy revealed changes in the capillary endothelial cells, interstitial tissue, and alveolar epithelium. The capillary endothelial cells were thickened and oedematous. Their cytoplasm contained many large and small vacuoles. Occasionally, endothelial vacuoles formed polypoid protrusions within the capillary lumen. The capillary basement membrane was thickened and sometimes split to enclose fragmenting extravasated erythrocytes. In some areas, the alveolar septa were thickened by a proliferation of collagen and elastic fibres. The membranous pneumocytes lining the alveolar spaces contained occasional small vacuoles but were not grossly thickened. In areas of cuboidal cell metaplasia, the thin membranous pneumocytes were replaced by thick granular pneumocytes possessing lamellar bodies and surface microvilli. The proliferated intra-alveolar cells consisted of a mixture of granular pneumocytes and macrophages.

REGIONAL LUNG FUNCTION AFTER LUNG RESECTION FOR CARCINOMA

RUSSELL HALL Overall and regional lung function has been studied in 60 patients with bronchial carcinoma. Measurements were made of lung volume, ventilatory capacity, transfer factor, arterial blood gas tensions, and regional ventilation and perfusion by profile scanning with xenon-133. These investigations were repeated in 14 patients between three and six months after lung resection.

The distribution of regional ventilation and perfusion in the residual lung when compared with the pre-operative state was unchanged after pneumonectomy, even in elderly patients.

The effects of the carcinoma upon regional function in the ipsilateral lung were also recorded.

PANCREATITIS AND BASAL EMPHYSEMA

C. OGILVIE, J. B. RIDYARD, and G. MURRAY
Deficiency of the enzyme α_1 -antitrypsin is known to be associated with a severe form of basal emphysema. It has been postulated that lung damage is due to the unopposed action of trypsin or other proteolytic enzymes circulating in the blood. It is impossible to prove this hypothesis in man, but it would receive some support if basal emphysema were to occur in patients with raised blood levels of digestive enzymes, as in chronic relapsing pancreatitis. We now report such a case in the hope that others will be encouraged to look for further examples.

PSEUDOMONAS INFECTIONS OF THE LUNG

Clinical Aspects of Pseudomonas Infections

N. OSWALD In the years 1970 and 1971, *Ps. aeruginosa* was isolated from 86 patients at Brompton Hospital. Of 56 patients with chronic pulmonary disease, eight were given specific antibacterial treatment, including six with cystic fibrosis. Of 30 surgical patients, seven had specific therapy, all of whom had cardiac surgery or tracheostomy or both.

Of 68 inpatients with pseudomonas in the sputum, only 15 (22%) had positive sputum when first tested. Bacterial resistance was noted in 14 patients to carbenicillin and in two each to gentamicin and colomycin.

Examples of pseudomonas pneumonia, lung abscess, and empyema are shown.

Characteristics and Antibiotic Sensitivity of Pseudomonas aeruginosa

E. J. L. LOWBURY *Pseudomonas aeruginosa* is a Gram-negative bacillus which produces characteristic pigments, grows well in water with minimal nutrient additives, and survives well in moist but not in dry environments. It produces a variety of enzymes and diffusible toxic products. Its pathogenic role is that of an opportunist, being virtually harmless on the surfaces of healthy individuals but more prone than some pathogens to cause clinical infection in patients or in tissues with poor natural resistance. In consequence *Ps. aeruginosa* is almost exclusively an agent of hospital acquired infection in patients with severe burns, with immunodeficient disease or receiving immunosuppressive therapy, also in infants, and in organs (e.g., the anterior chamber of the eye and the urinary tract) which offer no humoral or cellular resistance to infective agents.

The organism can be isolated with ease, and this is facilitated by the use of a selective medium containing cetrimide and nalidixic acid and by examination of cultures on agar media under ultraviolet irradiation. Treatment for pseudomonas infection presents difficulties because only three antibiotics are

active against the organism; of these the polymyxins (including colistin) are always active *in vitro* but disappointing in therapy (except in urinary tract infection); the other two antibiotics, gentamicin and carbenicillin, are clinically more useful, but resistance to each can emerge, and carbenicillin-resistance transferable between *Ps. aeruginosa* and Enterobacteria has appeared in some hospitals; carbenicillin dosage must be high for effective action and gentamicin dosage must be low for safety. Good immunity can be produced in animals by vaccines, and this method promises to be useful in the protection of severely burned patients and others especially prone to pseudomonas infection.

Control of Pseudomonas Infection

R. W. RIDDELL The limitation of spread of pseudomonas infection is discussed under the following headings:

- (a) Decontamination procedures
 - (1) Anaesthetic equipment including respirators and other apparatus
 - (2) Surfaces of all equipment in the vicinity of patients (e.g., horizontal surfaces, sinks, sluices, and drains)
 - (3) Regular checking of humidifier temperatures (60–65° C)
 - (4) Disinfection of hospital rooms by the use of appropriate bactericidal agents in aerosols
 - (5) Removal and destruction of infected dressings
- (b) Environmental studies
 - (1) Use of piped sterile air for operating ventilators and removal of expired air from the environment of patients
 - (2) Regular bacteriological checking of all possible sources of infection in the region of susceptible patients
 - (3) Nasal swabbing of medical and nursing staff appointed to surgical units and of patients
 - (4) Bacteriological air sampling when indicated
 - (5) The role of 'air change' units in intensive care wards
- (c) Control of infection
 - (1) Determination of significant pseudomonas infection
 - (2) Isolation of infected patients and, where possible, their removal from the intensive care unit
 - (3) Institution of an antibiotic policy designed to reduce the risk of pseudomonas infection
 - (4) Rapid identification and reporting of infecting organisms with their drug sensitivity patterns
 - (5) Effective treatment of local and systemic infection by drug-resistant Gram-negative bacilli.

Treatment of Pseudomonas Infections

- A. PERCIVAL The main problems are:
1. deciding when to treat because isolation of pseudomonas may not be clinically significant;

2. selection of correct dosage, since the margin between effective and toxic doses of appropriate antibiotics is narrow ;
3. limitation of penetration of antibiotics into diseased bronchi because sputum levels are much lower than those in serum ;
4. prevention of infection requires adequate disinfection of ventilatory equipment and exclusion of pseudomonas during use.

Choice of antibiotic is between gentamicin, polymyxins, and carbenicillin or combinations of these. In severe infections, polymyxins appear to be less effective than gentamicin, although there are no proper comparative studies. Carbenicillin is much less active *in vitro* than the others and high intravenous dosage is needed. Though not toxic, this is expensive and causes thrombophlebitis. In some units resistant strains have emerged.

With gentamicin, good results have been obtained even in severe bacteraemic infections, including pneumonia in patients with impaired body defences. Treatment must be controlled by measuring serum levels to ensure that these are inhibitory but not toxic and failure has commonly been due to insufficient dosage. In contrast, eradication of pseudomonas from bronchiectatic cavities is rarely achieved even when systemic treatment is combined with administration by aerosol. The new antibiotic, tobramycin, is slightly more active than gentamicin *in vitro*, but early results do not suggest that tobramycin will be any more effective therapeutically.

Pathogenicity of *Pseudomonas aeruginosa* in Chronic Bronchopulmonary Disease

J. R. MAY Assessment of the pathogenic significance of pseudomonas in the sputum can be facilitated by testing for precipitins in the serum. In a survey of 904 subjects, precipitins were absent in the serum of 110 controls but were present in 2% of 320 chronic bronchitics, 10% of 279 bronchiectatics, and 35% of 195 patients with cystic fibrosis. Serum precipitins are almost invariably associated with strains which give a mucoid colony in culture. These mucoid strains seem to be the most virulent ones in chronic respiratory disease. Their occurrence in patients with cystic fibrosis is a bad prognostic sign.

SMALL AIRWAY ABNORMALITY

Structure of the Airways

K. HORSFIELD The bronchial tree is a dichotomously branching structure arising from a single stem, the trachea, and ending in a quarter of a million distal respiratory bronchioles. When this structure is ordered by the method described by Horsfield and Cumming, starting with the most peripheral branches as order 1, the trachea is found to be order 31. The diameters of bronchi increase with increasing order, and several aspects of the physiology of airflow are related to both diameter and

order. The longitudinal distributions of the constituent tissues of the walls of the airways are described in relation to their diameter and order, and the properties and effects of each are considered in relation to the physiology and pathophysiology of airflow at different levels.

Contributions of Large and Small Airways to Total Airways Resistance and Tests of Forced Expiration

N. B. PRIDE In normal subjects 40 to 50% of the total airways resistance during quiet breathing lies in the upper airway (larynx, pharynx, and mouth or nose). Three-quarters of the lower (sublaryngeal) airways resistance lies between the trachea and airways of 2 mm diameter or more. Airways less than 2 mm diameter account for only 10 to 15% of the normal total airways resistance, so that changes confined to these airways have to be severe before they cause an obvious rise in total airways resistance. Some improvement in sensitivity to changes in the small airways can be obtained by using the panting technique of DuBois to reduce upper airways resistance or by measuring lower airways resistance directly by a tracheal needle or catheter.

Tests of forced expiration are potentially more sensitive than measurements of resistance to changes in the smaller airways, at least in the lower three-quarters of the vital capacity where maximum flow is relatively independent of the force applied by the expiratory muscles. According to the analysis of Mead *et al.* (1967), at these volumes maximum flow rates reflect the dimensions of the airways between the alveoli and the points in the airways where lateral airway pressure during forced expiration equals pleural pressure ('equal pressure points'). Between 75% and 25% of the vital capacity these 'equal pressure points' are in lobar or segmental bronchi and as residual volume is approached they move into smaller bronchi. Hence maximum flow rates in the lower part of the vital capacity should be the most sensitive to disease of the small airways. Unfortunately, flow rates in the lower part of the vital capacity may well show more inter-individual variation than the FEV₁ and are susceptible to small errors in delivering the vital capacity. Tests detecting abnormalities in the distribution of ventilation are likely to be more reliable indicators of patchy small airways disease than measurements of resistance or maximum flow rate.

REFERENCE

Mead, J., Turner, J. M., Macklem, P. T., and Little, J. B. (1967). *J. appl. Physiol.*, 22, 95.

Can Frequency Dependence of Compliance detect Disease of Small Airways?

D. C. FLENLEY, A. R. GUYATT, J. A. SIDDORN, H. M. BRASH, P. K. WRAITH and M. F. SUDLOW If some airways are obstructed, yet others patent, the time constants for ventilation of alveoli served by such airways will

differ. Rapid breathing will then make the lungs appear to become stiffer than on slow breathing (Otis *et al.*, 1956). If the overall airways resistance and elastic properties of the lungs are normal, this phenomenon suggests that there is variation in the calibre of airways of less than 2 mm in diameter and that inspired gas is thus distributed unequally to alveoli. Woolcock, Vincent and Macklem (1969) have used such measurements to detect disease of small airways in patients when conventional tests of lung function were normal. We have found this a tedious, difficult, and technically demanding measurement, with poor reproducibility between repeated measurements in the same 15 normal subjects. These problems include an adequate frequency response of the equipment, the cardiac artefact on oesophageal pressure records, and maintenance of relatively constant tidal volume and functional residual capacity during breathing up to 90 breaths/minute. Examination of published results reveals a similar variability in response. We are currently evaluating on-line reduction of data with a PDP-11 computer to improve precision and speed up the analysis. We seek to correlate frequency dependence with other simpler methods of detecting small airways disease, such as partial expiratory flow volume curves (Bouhuys *et al.*, 1969; Vincent *et al.*, 1970) and 'closing volume' (Dolfuss *et al.*, 1967; McCarthy *et al.*, 1972).

- Bouhuys, A., Hunt, V. R., Kim, B. M., and Zapletal, A. (1969). *J. clin. Invest.*, **48**, 1159-1168.
 Dolfuss, R. E., Milic-Emili, J., Bates, D. V. (1967). *Resp. Physiol.*, **2**, 234.
 McCarthy, D. S., Spencer, R., Greene, R., Milic-Emili, J. (1972). *Amer. J. Med.*, **52**, 747.
 Otis, A. B., McKerrow, C. B., Bartlett, R. A., Mead, J., McIlroy, M. B., Selvenstone, N. J., and Radford, E. P., Jr. (1956). *J. appl. Physiol.*, **8**, 427-443.
 Vincent, N. J., Kindson, R., Leith, D. E., Macklem, P. T., and Mead, J. (1970). *J. appl. Physiol.*, **29**, 236-243.
 Woolcock, A. J., Vincent, N. J., and Macklem, P. T. (1969). *J. clin. Invest.*, **48**, 1097-1106.

Correlation between Methods of Measuring Small Airways Behaviour

G. M. COCHRANE, S. R. BENATAR, J. DAVIS, T. J. H. CLARK and J. V. COLLINS The main site of obstruction to air flow in diseases characterized by airways obstruction is now thought to be in airways of less than 2-3 mm diameter and it appears that substantial abnormalities can occur in these airways before conventional tests of lung function become abnormal. Recently a number of indirect physiological measurements have been proposed to look specifically at small airways behaviour, and these include dynamic compliance at different breathing frequencies and measurement of closing volume, at a time when routine lung volume determination, lung elastic recoil pressure, and airways resistance are all within the normal range.

We have studied healthy non-smoking subjects with no previous history of lung disease and have made measurements of various aspects of lung

mechanics, including those designed to look at small airway behaviour. We have extended this study to a group of patients whose asthma is in remission and who had normal lung volumes and airway resistance.

These studies have allowed us to relate the test to each other and have provided further insight into their usefulness as tests of airways obstruction.

Small Airway Disease in Asthma

D. BAINBRIDGE, R. C. BORTHWICK, R. ELLUL-MICALLEF, M. J. B. FAREBROTHER and G. J. R. MCHARDY We have studied patients with stable chronic asthma in an attempt to determine the extent of small airway involvement in this condition.

Bronchodilator drugs and corticosteroids have been used to alter airway calibre and changes in ventilatory capacity, airway conductance, lung and thoracic gas volume, flow-volume curves, 'closing volume' and pulmonary gas exchange have been followed.

These studies allow us to conclude that both large and small airways may be involved and can respond to treatment. Precise division of responsibility for any change between airways of different sizes is made difficult, both because of the complexity and inadequacy of present-day methods and because of the great variability in asthma itself.

Our results are compared and contrasted with the published work of others.

Airway Closure in Pulmonary Congestion and Pulmonary Oedema

A. L. MUIR, M. F. SUDLOW, B. J. KIRBY, A. R. GUYATT, H. M. BRASH, and D. C. FLENLEY In pulmonary oedema the earliest histological change is the accumulation of fluid around the small airways (Staub *et al.*, 1967). Although changes in total airway resistance in pulmonary oedema are inconsistent until the oedema is marked, in experimental pulmonary congestion peripheral airway resistance increases with increasing left atrial pressure, indicating early abnormalities of the small airways (Hogg *et al.*, 1972). In man, measurement of abnormalities of small airways must rely on indirect methods and we have studied this by examination of the phenomenon of airway closure.

In three normal subjects we rapidly infused litres of saline (100 ml/min). Cardiac output and pulmonary arterial pressure nearly doubled without any change in heart rate or systemic arterial pressure. In all three subjects TLC and VC was reduced during the period of infusion but returned to normal after the infusion had ceased. There was an increase in the closing volume and in two subjects the volume at which small airway closure began occurred during normal tidal ventilation. At this time in these two subjects there was a significant decrease in arterial oxygen tensions.

We have also measured closing volumes in patients

with pulmonary congestion or oedema following acute myocardial infarction and during their convalescence. We were often unable to measure closing volume because of abnormal gas distribution but the slope of the alveolar plateau which was steep in the acute phase decreased in the convalescent period.

Our results suggest that there are abnormalities of the small airways in pulmonary congestion and pulmonary oedema.

- Hogg, J. C., Agarawal, J. B., Gardiner, A. J. S., Palmer, W. H., and Macklem, P. T. (1972). Distribution of airway resistance with developing pulmonary oedema in dogs. *J. appl. Physiol.*, **32**, 20-24.
- Staub, N. C., Nagano, H., and Pearce, M. L. (1967). Acute pulmonary oedema in dogs, especially the sequence of fluid accumulation in lungs. *J. appl. Physiol.*, **22**, 227-240.

Cigarette Smoking and Disease of Small Airways

S. FREEDMAN In recent years, several abnormalities of pulmonary function have been demonstrated in asymptomatic cigarette smokers in whom measurements of airway resistance and FEV_{1.0} were normal. These abnormalities include an increased 'closing volume', abnormal patterns of distribution of inspired gas, frequency dependence of compliance, and abnormally low maximum expiratory flow rates at lower lung volumes. Because they can occur in the presence of a normal total airway resistance they have been related to disease of the small airways, although a direct correlation between functional and morbid anatomical abnormalities has yet to be demonstrated. One would predict that widespread disease of small airways would lead to abnormalities of gas exchange, and arterial hypoxaemia and a slight reduction in transfer factor for carbon monoxide have been demonstrated in smokers. Several of these tests, especially 'closing volume' and maximum mid-expiratory flow rate, are being widely promoted as tests which will pick out a pre-symptomatic stage those smokers who are liable to develop disabling airway obstruction and thus provide the possibility of arresting or even of reversing the disease by therapy. Before this view can be accepted several questions need to be answered.

There is as yet little evidence about the reversibility of the functional abnormalities, but two groups of workers have reported that frequency dependence of compliance is diminished or disappears when people stop smoking, while in one of these studies 'closing volume' was unaffected. There is also little information about reproducibility and seasonal variation, particularly of 'closing volume' while maximum mid-expiratory flow rate has an enormously wide normal range. Most important, we do not know whether the presence of one of these functional abnormalities necessarily implies the development of disabling airway obstruction. For example, 'closing volume' is abnormally high in 30 to 50% of smokers, but only 5 to 10% will develop significant airway obstruction. Finally, there is some evidence that the FEV_{1.0}/VC ratio may have as much prognostic significance as some of the newer tests.

Small Airways Disease in Coalworkers' Pneumoconiosis

A. SEATON Abnormalities of gas exchange and increases in residual volume have been demonstrated in coalminers in the USA. In order to investigate the cause of this, lung mechanics, including frequency-dependence of compliance and maximal flow-pressure relationships, were studied in 25 selected coalminers and six comparable controls. The coalminers had category 2 or 3 simple pneumoconiosis, were non-smokers, and had normal overall airways resistance and static pressure-volume curves.

Seventeen miners demonstrated frequency-dependence of compliance, unaffected by bronchodilators and unrelated to history of bronchitis or the type of radiographic opacity. The miners as a group showed lower maximal flow rates, corrected for transpulmonary pressure, at all lung volumes than the controls and these flow rates were significantly lower in the miners who showed frequency-dependence of compliance than in those who did not. It is suggested that this is evidence of obstruction to small airways in these subjects.