

Proceedings of The Thoracic Society

The Spring Meeting of The Thoracic Society was held on 27 February 1976 at the Royal College of Physicians, London. Summaries of the papers follow:

Contaminated water from a factory machine producing extrinsic allergic alveolitis

J. A. R. FRIEND, J. GADDIE, K. N. V. PALMER, C. A. C. PICKERING, and J. PEPYS Recently, there have been reports of extrinsic allergic alveolitis arising from contamination of domestic air humidifiers with microorganisms (Banaszak *et al.*, 1970). Typical symptoms and signs of this illness developed in 24 employees of a large modern stationery factory in Aberdeen. An aerosol of water was induced by vacuum pumps and distributed through the ventilation system to other areas of the factory. Chest x-rays during attacks were normal, but pulmonary function tests showed significant reductions in vital capacity and single breath carbon monoxide diffusing capacity with hypoxaemia. All these employees, together with five apparently asymptomatic individuals, had abnormal serum precipitins to samples of water obtained from a recirculating cooling system serving air compressors and vacuum pumps. Two of these employees were challenged with an inhalation of extract of this water, and the symptoms and the functional changes of a typical attack developed after several hours. Although a variety of microorganisms were cultured from the water, no single specific organism could be associated with the precipitin reaction. Modifications have now been made to the ventilation system and no further episodes of the illness have occurred. In future factory design the possibility of dispersion of contaminated water into the air should be avoided.

Banaszak, E. F., Thiede, W. H. and Fink, J. N. (1970). Hypersensitivity pneumonitis due to contamination of an air conditioner. *New England Journal of Medicine*, 283, 271–276.

Influenza and parainfluenza virus titres in bird fanciers with acute allergic alveolitis

A. J. NEWMAN TAYLOR, P. TAYLOR, D. BRYANT, JOAN LONGBOTTOM, and J. PEPYS Sera from pigeon fanciers with acute allergic alveolitis commonly have high titre positive complement fixation tests (CFTs) to influenza A and B, and less commonly to influenza C and Sendai virus (parainfluenza). In the absence of avian exposure, a fourfold or greater fall in titre is observed over a period of a few weeks, a finding which would generally be regarded as diagnostic of an acute viral infection. Sera from budgerigar fanciers with acute alveolitis commonly have negative CFTs to these viruses but may occasionally have low titre positive CFTs. The complement fixing activity in pigeon

fanciers is attributable to antibodies produced by these subjects which react with antigens of the chorio-allantoic membrane of chicken eggs in which influenza A and B are grown, and of the allantoic fluid from which influenza C and Sendai virus are harvested. Sera with positive CFTs to influenza A and B give positive CFTs to extracts of chorio-allantoic membrane, and such sera have antibodies to chorio-allantoic membrane antigens demonstrable on immunoelectrophoresis. These sera have negative CFTs to influenza A grown in monkey kidney cell culture, and also negative haemagglutination tests with two recent strains of influenza A2.

It is uncommon for virology laboratories routinely to include chorio-allantoic membrane extracts as a control for influenza A and B CFTs, and allantoic fluid as a control for influenza C and Sendai virus is not generally available. Clinically and radiologically influenza pneumonia and acute allergic alveolitis may have similar features. Our findings indicate that a definite diagnosis of influenza cannot be based in a pigeon fancier on either a single elevated CFT titre or rapidly falling titres in paired specimens, in the absence of appropriate serological controls.

Occupational asthma in workers using epoxy resin systems

I. W. FAWCETT and J. PEPYS Epoxy resins are widely used in industry and are a well recognized cause of contact dermatitis. The addition of a hardening agent such as an amine or acid anhydride to the epoxy resin either at room temperature or in the presence of heat allows complete polymerization of the resin producing a high molecular weight and product. This process, particularly when it occurs at high temperatures, liberates fumes of the hardening agent into the atmosphere.

Asthma in workers exposed to epoxy resins and their hardeners has been reported but not previously studied in detail. The case histories and investigations of three men working with these compounds are described. The epoxy resin systems were being used for different purposes in each case—as an adhesive, as a moulding powder, and as an electrostatic paint spray coating. Careful inhalation testing simulating their exposure at work provoked asthmatic reactions, which were shown to be due to the amine or acid anhydride constituents of the system. In two of the three subjects, reactions occurred at atmospheric concentra-

tions well below that producing irritant effects in other exposed workers, suggesting a hypersensitivity reaction; in the third subject asthma only followed prolonged exposure.

In view of the widespread use of epoxy resin systems in industrial processes and in various domestic products, it seems possible that these substances may be responsible for many cases of asthma whose cause is as yet unrecognized.

Effect of prolonged asbestos exposure on regional lung function

N. N. STANLEY Regional distribution of ventilation was studied in 14 pipe-laggers with more than 20 years' occupational exposure to asbestos dust and in eight healthy control subjects. Chest radiographs showed early evidence of pulmonary fibrosis in four and pleural fibrosis at the lung bases in six of the workers.

Each subject was studied in the seated position. The radioactivity in both lungs was recorded by a gamma camera during the washout of ^{133}Xe which had been breathed to equilibrium in a closed circuit. Activity-time plots were constructed using data obtained from upper, middle, and lower lung zones. In healthy subjects the first 70% of washout was always fastest in the lower zones. In two of the asbestos workers, though, the activity declined more slowly throughout the whole of washout in the lower compared with the middle zones. In 10 others, the fall in activity was initially fastest in the lower zones but soon became slower than in the middle zones, which caused a cross-over of the lower and middle zone curves before washout was 70% complete. No individual had a restrictive or gas transfer defect. However, eight had mild airways obstruction characterized by a reduction in maximum mid-expiratory flow rate and an increase in closing volume, although specific conductance was usually normal. The abnormalities in regional and overall ventilatory function occurred in smokers and non-smokers alike.

The findings are consistent with hypoventilation of a proportion of lung units within the lower zones. Analysis of ^{133}Xe washout may provide a sensitive method for the early detection of pulmonary asbestosis.

Slow reacting substance as a preformed mediator from human lung

A. B. KAY, D. G. JONES, and LESLEY S. TURNBULL Slow reacting substance of anaphylaxis (SRS-A) is considered a primary mediator in allergic (extrinsic) bronchial asthma since it is a potent constrictor of bronchial smooth muscle and is released from IgE-sensitized lung fragments *in vitro* following challenge with specific antigen. It is thought that an antigen-antibody reaction on target cells is essential for the formation and release of SRS-A. We have found that an agent with identical pharmacological and chemical properties to SRS-A can be extracted from human

lung tissue in a preformed state (pSRS). The pattern of contraction on the guinea-pig ileum by pSRS was indistinguishable from that of SRS-A. The activity of pSRS could not be attributed to the presence of K, Na^+ , Ca^{++} , and Mg^{++} ions. As with SRS-A, pSRS could be absorbed onto Amberlite XAD-2 and silicic acid. Both were eluted from the former with 80% ethanol and from the latter with a mixture of n-propanol, ammonia, and water. Both pSRS and SRS-A were resistant to boiling in 0.05N NaOH whereas these activities were destroyed by 0.05N HCl. Arylsulphatase IIB destroyed the activities of both pSRS and SRS-A. An antagonist of SRS-A, FPL 55712, inhibited the action of pSRS at concentrations comparable to that of SRS-A. These studies suggest that pSRS and SRS-A are identical and that, like histamine, SRS is preformed and can be released from lung non-specifically as well as immunologically. The non-immunological release of slow reacting substance from human lung by mechanisms independent of IgE and other tissue sensitizing antibodies suggests that SRS may participate in various forms of asthma including chronic (intrinsic) disease.

Comparison of aminophylline and salbutamol infusion in the treatment of acute attacks of asthma

A. J. JOHNSON, J. PIDGEON, S. BATEMAN, S. G. SPIRO, and J. W. PATERSON Salbutamol has recently become available in a formulation suitable for parenteral use. A study was designed to compare its efficacy with aminophylline when given as an infusion to patients with acute attacks of asthma. In addition, the study allowed an investigation of metabolic consequences of asthma and its treatment, and the results are described in a separate paper.

Physiological parameters were recorded on admission and, in line with the usual practice of this hospital, the patients were treated with an aminophylline bolus (5 mg/kg) given slowly while the patient received oxygen, followed by two doses of salbutamol (5 mg each) delivered from intermittent positive pressure apparatus (IPPB, Bird). Following each of these treatments the physiology recordings were repeated. At the end of the initial phase, if the clinician in charge decided an infusion of a bronchodilator drug was required, aminophylline or salbutamol was given in random order to successive patients. Physiological parameters were recorded at regular intervals during the infusion, and four hours after cessation. Aminophylline was given in a dose of 1 mg/min and salbutamol at a rate of 10 $\mu\text{g}/\text{min}$, a dose chosen to give bronchodilatation without cardiovascular side effects (May *et al.*, 1975). Blood samples were drawn for the metabolism study on admission, on completion of the initial phase, one and four hours into the infusion, and in a fasting state during the convalescent period.

To date 42 patients between the ages of 16 and 65 years without cardiovascular or renal disease have

entered the study. Seventeen patients improved sufficiently during the initial treatment phase not to require an infusion. On admission these patients' attacks were only marginally less severe, as judged by peak expiratory flow rates, than those of the 25 patients who went on to an infusion, but they showed a greater response to the initial treatment. Of the patients who received an infusion the improvement in airflow obstruction was significantly greater in the aminophylline group. No patient required to be changed from aminophylline, but in 10 patients the response to salbutamol was insufficient and the infusion was changed to aminophylline. However, not all these patients improved on the second infusion. One patient developed marked systemic hypotension which necessitated discontinuation of salbutamol, but no serious side effects were noted with aminophylline.

At this stage in the study it would appear that aminophylline is more effective than salbutamol in the doses given, in acute asthma.

May, C. S., Spiro, S. G., Johnson, A. J., and Paterson, J. W. (1975) *Thorax*, 30, 236.

Lipid changes during acute attacks of severe bronchial asthma and following therapy

T. R. TICKNER, D. G. CRAMP, M. R. WILLS, J. PIDGEON, S. BATEMAN, A. J. JOHNSON, S. G. SPIRO, and S. W. CLARKE Salbutamol has been shown to produce a marked rise of plasma non-esterified fatty acids (NEFA) following its administration by intravenous infusion (Goldberg *et al.*, 1975; Leading article, 1975). In view of this finding it has been suggested that the administration of salbutamol may endanger the myocardium, particularly if anoxia is also present.

During a clinical trial of salbutamol and aminophylline therapy the opportunity was taken to measure plasma NEFA, triglyceride, glucose, and insulin concentrations during an acute asthmatic attack and its subsequent treatment.

A profound metabolic disturbance as assessed by the measured variables was found to be present on admission in nearly all the patients. Furthermore, no further enhancement of the disturbance was seen during the drug administration. The initial gross abnormalities did not persist after the acute phase of the attack had resolved.

These findings suggest that these metabolic disturbances were likely to be due to the stress of the asthmatic attack. The findings also suggest that any contribution to the metabolic disturbances from the drug regimen *per se* was unlikely. It seems, therefore, that neither salbutamol nor aminophylline produce metabolic disturbances greater than those of the condition for which they are used.

Goldberg, R., van As, M., Joffe, B. I., Krut, L., Bersohn, I. and Seftel, H.C. (1975). *Postgrad. med. J.*, 51, 53.
Leading article (1975). *Brit. med. J.*, 4, 65.

Status asthmaticus and death from asthma

RUTH M. CAYTON Since 1970 the number of deaths from asthma occurring annually in England and Wales

has not changed. Status asthmaticus is commonly believed to precede death from asthma, but this may not necessarily be true. A group of 61 asthmatic patients admitted to hospital during 76 attacks of status asthmaticus has been studied. Patients who did not respond to an initial injection of intravenous aminophylline (250 mg) were treated with intravenous injections of hydrocortisone (200 mg) at four-hourly intervals until clinical improvement occurred. Clinical signs and measurements of respiratory function, including arterial blood gases, were documented throughout the acute illness and during convalescence.

The initial assessment of the severity of the attack gave no guide to those patients likely to respond to a single injection of aminophylline or hydrocortisone or to those requiring repeated injections of hydrocortisone for several days. Two patterns of recovery emerged, judged by symptoms, spirometric measurements of respiratory function, and arterial blood gases. In one group of patients (aged 28 years) hydrocortisone in dosages ranging from 200 to 1200 mg for 18 hours was required to treat the acute attack. Rapid relief of symptoms coincided with progressive improvement in the FEV_{0.75} and FVC for five days, not matched by improvement in the PaO₂ which continued for as long as four weeks. The second group of 26 patients (aged 53 years) required dosages of 200 to 8000 mg of hydrocortisone for 63 hours. Further treatment with oral prednisolone was required to maintain the slow improvement which occurred in symptomatology, FEV_{0.75}, FVC, and PaO₂.

It is suggested that asthmatic patients are at risk from sudden death when gross disturbance in respiratory function, especially PaO₂, are not matched by corresponding severe symptoms. This may occur following the treatment of an acute attack of asthma and is especially common to young people.

Pressure studies following high and low oesophagogastrostomy

H. R. MATTHEWS and D. W. WARD Conventional oesophagogastratomy involves an intrathoracic oesophagogastratomy below the aortic arch. This creates an hiatus hernia, and reflux with stricture often results. With anastomoses performed at cervical level, however, these problems are less common. To investigate possible reasons for this, transanastomotic pressures were measured, using open-sided continuously perfused catheters, in 14 patients.

Group 1 comprised seven patients (aged 40-73 years) who were studied one to six years after a thoracic ('low') anastomosis; all operations were for carcinoma. No gradient was demonstrated across any anastomosis. Group 2 comprised seven patients (aged 55-74 years) who were studied eight months to two years after a cervical ('high') anastomosis; five operations were for carcinoma, one for achalasia, and one for peptic stricture. All seven patients had a sphincter zone depicted within 3.5 cm of the anastomosis. Mean maximum sphincter pressure was 29 mmHg (range

9-53) and mean length 2.7 cm (range 1.5-3.5). This compares with a mean pressure of 18 mmHg and mean length of 3.5 cm in seven unoperated subjects.

Two principal conclusions are drawn: (1) that the conventional 'low' anastomosis provides no sphincteric function whatsoever, and (2) that the 'high' anastomosis, rather than destroying the cricopharyngeal sphincter, actually retains it as a functioning unit immediately adjacent to the anastomosis. The implications of these findings with regard to the site of election for oesophagostomy will be discussed.

Selective vagotomy of the oesophagus—a new possibility for treatment of hiatal hernia

M. H. EDWARDS The view that hiatal hernia is aggravated by upward pull from the longitudinal muscle of the oesophagus has led to recent reports of transection of the muscle as an adjunct to the usual repair (Davidson, 1972; Mullard, 1972). Transection of the vagal nerve supply of the oesophagus along all or part of its length would appear to be a logical alternative to this possibly hazardous method of reducing longitudinal muscle strength, especially if vagotomy could be selective, so preserving innervation of more distal organs.

In a canine preparation, dissection of the whole intrathoracic vagus from the oesophagus reduced longitudinal muscle contraction by 88%. This was an effect on striated muscle.

Since striated muscle in man is limited to the upper half of the oesophagus (Arey and Tremaine, 1933), the effects of vagal dissections on this region were studied in the preparation. A highly significant ($P < 0.001$) reduction of longitudinal contraction of the suprahilar oesophagus was obtained by dissecting the vagus from the oesophagus between the hilum and the upper border of the aorta. Lower oesophageal sphincter pressures and pyloric function were unaffected.

Selective oesophageal vagotomy in this region in man may prove a useful adjunct to hiatal hernia repair.

Arey, L. B. and Tremaine, M. J. (1933). The muscle content of the lower oesophagus of man. *Anatomical Record*, 56, 315.

Davidson, J. S. (1972). Circumferential oesophageal myotomy. *British Journal of Surgery*, 59, 938.

Mullard, K. S. (1972). The surgical treatment of diaphragmatic oesophageal hiatal hernia. *Annals of the Royal College of Surgeons of England*, 50, 73.

Diagnosis of recent viral infection from single serum samples

J. V. COLLINS, Y. BUCHNER, J. R. PATTISON, and R. B. HEATH Conventional methods for identifying a recent viral infection require the isolation of the virus from the patient or the demonstration of a rise in titre of antibodies in consecutive serum samples taken at intervals after the onset of illness. Both methods are dependent upon the presentation of the patient soon after the onset of the illness which is uncommon in

hospital practice. If it were possible to identify recent infection from a single serum sample this would have obvious practical advantages. The presence in the serum of high titres of complement-fixing antibodies against soluble influenza antigens is suggestive of recent infection but methods for their detection are unreliable.

We have developed a method of sucrose-density gradient ultracentrifugation for fractionating sera which separates immunoglobulins of the IgM and IgG classes. We have been able to detect specific IgM and IgG antibodies in the sera of patients recovering from infection with influenza viruses. Our results show that in more than 90% of patients specific IgM and IgG antibodies are detectable in the serum by about 14 days from the onset of symptoms, and IgM class antibodies persist for a further 20-70 days. Conversely, in patients with no recent history of influenza infection or in whom infection is known to have occurred more than 100 days previously, antibodies are exclusively of the IgG class, and no specific IgM antibodies are detectable.

From our results we conclude that the demonstration in the serum of specific IgM antibodies against influenza viruses is a suitable method for identifying recent infection using single serum samples. The usefulness of this technique in identifying the role of influenza infections in precipitating various respiratory illness is illustrated.

A study of methods and results of treatment of pulmonary tuberculosis in Scotland

JOAN F. HEFFERNAN, A. J. NUNN, J. PETO, and W. FOX A survey of a 50% random sample of all patients newly notified as having pulmonary tuberculosis in Scotland in 1968 was undertaken to study methods of treatment and management in the routine services; results achieved up to two years are reported. The estimated notification rates were higher in the males, rising to 90 per 100 000 at 55 or more (Heffernan *et al.*, 1975). After exclusions, 770 patients were eligible for follow-up. The deaths are based on 795 patients, including 20 diagnosed post mortem and five other inadequate records. There were 106 (13.3%) deaths, 34 (4.3%) from tuberculosis, the rest from non-tuberculous causes. Bacteriological failures totalled 4.5% and non-bacteriological failures (eg, regimen changed for drug toxicity, long-term defaulters) 11.4%.

For the study of methods of treatment and management patients have been classified as initially bacteriologically positive (372) or negative (309). Of these, 87% positive and 65% negative were admitted to hospital for an average of 18.0 and 10.7 weeks respectively; in 80% and 57% the initial chemotherapy was streptomycin/PAS/isoniazid, and the total duration of chemotherapy averaged 22.2 and 19.1 months. An analysis of time off work showed that 4% positive and 24% negative patients never stopped work, 41% and 19% were off work for more than six months, and 18% and 8% never returned. An analysis of four

groups of patients classified according to pretreatment bacteriological status and radiological classification at an independent assessment showed that the proportion of patients admitted to hospital was higher, streptomycin was more frequently used and for longer, and total duration of chemotherapy was longest in the bacteriologically positive/radiographically active group. Nevertheless, at the other extreme, the bacteriologically negative/radiographically inactive group received substantial therapy.

The survey provides a useful basis for evaluating tuberculosis programmes.

Heffernan, J. F., Nunn, A. J., Peto, J., and Fox, W. (1975). Pulmonary tuberculosis in Scotland—a national survey and follow-up. The characteristics of the cases notified in 1968. *Tubercle, Lond.*, in press.

Sarcoidosis of the upper respiratory tract (SURT) and its relationship to lupus pernio

E. NEVILLE, R. G. S. MILLS, D. JASH, D. MCKINNON, and D. GERAINT JAMES Sarcoidosis of the upper respiratory tract (SURT) is an uncommon but disabling manifestation involving the nose, nasopharyngeal mucosa, and larynx. Involvement of the nose may also include the nasal bone and cartilage and overlying skin. Long-term follow-up suggests that SURT sometimes progresses inexorably to lupus pernio with which it is closely linked. We report a series of 32 patients with clinical and histological evidence of multisystem sarcoidosis comprising seven patients with SURT alone, another eight with the transition stage of SURT and lupus pernio, and 17 patients with irreversible lupus pernio. The series has a female preponderance of 7 : 1, and one-quarter of the patients were negro. Patients with mucosal disease presented in the third decade and patients with lupus pernio in the fourth and fifth decades. SURT and lupus pernio are chronic fibrotic manifestations of sarcoidosis and are frequently accompanied by similar fibrotic lesions, including bone cysts, chronic uveitis, and lymphadenopathy. SURT was accompanied by laryngeal sarcoidosis in five instances so it should be sought by examination of the larynx at bronchoscopy.

SURT frequently presents to the nose and throat surgeon who may perform submucous resection to overcome the symptom of longstanding nasal stuffiness. This may have disastrous consequences, such as nasal septal perforation, so it is important to recognize SURT early and treat it without surgical intervention.

Aerosolized lignocaine and irritable airways

P. HOWARD, S. R. BRENNAN, P. B. ANDERSON, and RUTH M. CAYTON Intrapulmonary afferent receptors may be concerned with the control of breathing and with the sensation of breathlessness. The sensation of breathlessness in patients with obstructive airways disease is not closely related to mechanical limitation of air flow judged by simple spirometric tests. It is possible that airways disease increases the sensitivity of afferent

terminals, giving rise to inappropriate reflex stimulation of higher nervous centres. Lignocaine in doses of 150–400 mg was instilled into the airways of 15 patients with obstructive airways disease. Eleven patients derived no benefit but four patients improved, largely due to the prolonged suppression of a persistent irritating cough. Compared with saline, aerosols of lignocaine often increased airways resistance, but, despite this, the cough was suppressed for many days or weeks beyond the time when all local anaesthetic effects on taste or numbness had disappeared. One patient has returned to work as a miner after two years' absence but continues to attend for lignocaine aerosolization every six weeks. An increased sensitivity of tracheal cough receptors is suggested as the mechanism for the persistent irritating cough and will be discussed.

Airway responses to inhaled bronchodilators in patients with reversible airflow obstruction

O. M. P. JOLOBE, J. S. PRICHARD, and D. J. LANE Airway responses to inhaled atropine methonitrate 0.2% followed after 60 minutes by an inhaled β -adrenergic agonist (isoprenaline or salbutamol) have been followed in patients with reversible airflow obstruction (Altounyan, 1964).

Tests were performed on subjects who had not received bronchodilator drugs for at least 12 hours. Results were expressed as an index giving the percentage response to atropine seen in relation to the total response to both agents. Using conventional spirometric indices, 200 patients were tested.

The results showed a bimodal distribution of the index with one peak at 20–30% and a second peak at 90–100%. These two peaks corresponded in clinical terms to patients who could be classified as asthmatics and bronchitics respectively.

In 30 patients, additional measurements were made of airways resistance and specific conductance using a whole body constant volume plethysmograph, and flow volume curves were recorded breathing air and a helium/oxygen mixture. In general, the changes in spirometric flow volume and plethysmographic indices were similar in magnitude and direction, but in six instances FEV_1 and S_{GAW} changed in opposite directions following administration of the β -agonist.

Particular attention will be drawn to a group of bronchitic subjects who, following maximal bronchodilation with atropine, showed deterioration in airways function, by whatever index that was assessed, with a β -agonist.

Altounyan, R. E. C. (1964). Variation of drug action on airway obstruction in man. *Thorax*, 19, 406–415.

Pulmonary artery pressure in severe thoracic deformity

J. M. SHNEERSON For many years it has been known that patients with severe thoracic deformities frequently die in middle age with right ventricular failure

due to pulmonary hypertension. The cause of the latter is, however, still uncertain. Studies on 32 patients, mainly young adults, have helped to resolve this question.

A Bradley microcatheter was passed into the pulmonary artery, and pressure readings were obtained at rest and during and after a progressive exercise test on a bicycle ergometer.

The results show that the resting pressure is inversely proportional to the resting PaO_2 and that the rate of rise of pressure during exercise is closely related to the VC, FRC, and TLC. Breathing pure oxygen at rest led to a fall in pressure which was proportional to the degree of pre-existing hypoxaemia. However, breathing oxygen during exercise had no effect on the rate of rise of pressure.

A rat model for long-term oxygen therapy

E. LEACH, P. HOWARD, and G. BARER Chronically hypoxic rats were subjected to different recovery régimes in an attempt to mimic long-term oxygen therapy in chronic bronchitis.

Rats kept for three weeks in a 10% O_2 chamber ('hypoxic rats') developed muscularization of pulmonary arterioles, right ventricular hypertrophy (RVH), and polycythaemia (Hunter *et al.*, 1974). Some 'hypoxic rats' were compared immediately with littermate controls, others were allowed to recover in air for six weeks ('recovery rats') while still others spent 8 or 16 hours daily in air and the rest of the day in 10% O_2 for six weeks ('intermittent-normoxic rats'). During 'intermittent-normoxia' PaO_2 is higher than in bronchitic patients on oxygen therapy.

Right ventricle/left ventricle weight ratio in 'hypoxic', control, 'recovery', 8 and 16-hour 'intermittent-normoxic' rats was, respectively, 0.61 ± 0.02 (SEM), 0.33 ± 0.02 , 0.36 ± 0.01 , 0.50 ± 0.02 , 0.48 ± 0.02 . The ratio in 'hypoxic rats' was significantly different from that in controls and in 16-hour 'intermittent-normoxic' rats ($P < 0.001$) but the latter was still significantly different from controls. The ratio was similar in control and 'recovery' rats. In eight-hour 'intermittent-normoxic rats' it was reduced compared with 'hypoxic rats' but not significantly. Thus 16-hour 'intermittent-normoxia' was required to reduce RVH but did not allow complete resolution.

Muscularization of vessels, assessed by counting the proportion of peripheral vessels with thick walls, resolved even more slowly. The percentage of these vessels in 'hypoxic', control, 'recovery', and 8-hour 'intermittent-normoxic' rats was, respectively, 23 ± 0.9 (SEM), 12 ± 1.1 , 18 ± 1.1 , 20.7 ± 2.3 . Thus vessels were still thickened after six weeks' recovery in air and were not changed by the 'intermittent-normoxic' régime. The vessel changes compared qualitatively and quantitatively with those in patients with chronic obstructive lung disease.

The haematocrit was 64 ± 1.5 (SEM) in 'hypoxic' and $43 \pm 0.9\%$ in control rats. Recovery was complete in air and non-existent after 'intermittent-normoxia'.

The rat model indicates some problems facing long-term oxygen therapy.

Hunter, C., Barer, G. R., Shaw, J. W. and E. J. Clegg (1974). Growth of the heart and lungs in hypoxic rodents; a model of human hypoxic disease. *Clinical Science and Molecular Medicine*, 46, 375-391.

Pattern of stimulated breathing in patients with chronic airflow obstruction

C. S. GARRARD and D. J. LANE We have previously shown that in normal subjects the pattern of breathing during CO_2 stimulation can be adversely influenced by the introduction of an expiratory non-elastic resistance at the mouth (Garrard and Lane, 1975). Tidal volume response was diminished compared with the unloaded state and there was a progressive rise in functional residual capacity (FRC).

In this communication we report an analysis of the pattern of breathing during CO_2 stimulation in 12 patients with chronic airflow obstruction. The pattern was expressed in terms of a plot of tidal volume against breath duration. At all levels of CO_2 , breath duration was shorter than would be anticipated, and tidal volume response was small.

Intermittent estimations of thoracic gas obtained approximately every tenth breath using a whole body constant volume plethysmograph showed a progressive rise in FRC during CO_2 stimulation in 10 of the 12 subjects. Maximum tidal volumes attained approached and in some instances exceeded the inspiratory capacity of the subject (taking into consideration the increase in FRC).

It is suggested that the changes in FRC may be an important component in the genesis of dyspnoea during stimulated breathing in these patients.

Garrard, C. S. and Lane, D. J. (1975). The pattern of stimulated breathing in man during non-elastic expiratory loading. *Journal of Physiology*, 251, 40-41.

Pulmonary mechanics in respiratory muscle weakness

G. J. GIBSON, N. B. PRIDE, and J. NEWSOM DAVIS If full expansion of the lungs of normal subjects is limited by strapping the chest wall, secondary changes in the elastic properties of the lungs occur (Caro *et al.*, 1960). Weakness of the respiratory muscles similarly restricts lung expansion, but information on the lung distensibility of such patients is limited to measurements of dynamic compliance which are difficult to interpret. We have investigated the static pressure volume characteristics of the lungs in a series of patients with respiratory muscle weakness due to various neuromuscular diseases. The results were similar to those obtained acutely in strapping experiments, with a low value of lung recoil pressure at full inflation but also a reduction in the slope of the pressure volume curve, indicating that secondary changes in lung distensibility occur. These might be due to diffuse microatelectasis or to a generalized alteration in alveolar elastic properties. The implications of these findings are:

1. The restricted vital capacity of these patients may be due not only directly to the loss of distending pressure but also to secondary changes in the lungs themselves.
2. A single measurement of pulmonary compliance (static or dynamic) may not differentiate between primary intrapulmonary disease and changes secondary to extrapulmonary restriction.
3. Reduced distensibility of the lungs may be relevant to the breathing pattern of such patients.

Caro, C. G., Butler, J. and Du Bois, A. B. (1960). Some effects of restriction of chest cage expansion on pulmonary function in man. An experimental study. *Journal of Clinical Investigation*, 39, 573-583.

Use of radioactive N₂ in demonstrating localized disease in children believed to have asthma

S. GODFREY, G. HAMILTON, N. FREEDMAN, and P. WINLOVE We have recently developed the technique of radioisotope scanning to measure total and regional lung function in children of all ages (Ronchetti *et al.*, 1975; Godfrey *et al.*, 1975) and now present the use of the method to help make the correct diagnosis in children erroneously thought to have bronchial asthma.

The technique consists of administering a bolus of ¹⁵N by inhalation and perfusion while the child lies over a gamma camera linked to a computer system which processes the data. For the inhalation study

the gas is given through a nasal catheter at end expiration and for the perfusion study it is dissolved in saline and injected intravenously. The technique requires no active co-operation from the child, and it is painless apart from the injection and carries a negligible radiation hazard. The computer system enables the investigator to divide the lung fields into regions and provides a record of the arrival and washout of ¹⁵N for each region from which information about ventilation and perfusion is obtained.

Wheezing is extremely common in infancy and childhood and, while the commonest cause of severe and persistent wheezing is bronchial asthma, it is recognized that other lesions may mimic asthma. Over a relatively short period several children have been referred to the asthma clinic with apparently intractable asthma which had failed to respond to treatment including steroids in some cases. Certain atypical features suggested that the diagnosis might be incorrect and ¹⁵N gamma scans were carried out. In each case the scan revealed disease confined to one lung, the other being entirely normal, the characteristic change in the scan being diminished ventilation and perfusion of the affected lung with gas trapping. Illustrative cases will be discussed and the value of the new technique will be considered.

Godfrey, S., Ronchetti, R., Stocks, J. and Hallidie-Smith, K. (1975). Generalised pulmonary hyperinflation and Fallot's tetralogy in a neonate investigated by pulmonary physiological and radioisotopic methods. *Thorax*, 30, 456-460.

Ronchetti, R., Stocks, J., Freedman, N., Glass, H. and Godfrey, S. (1975). The clinical application of regional lung function studies in infants and small children using ¹⁵N. *Archives of Disease in Childhood*, 50, 595-603.

CORRECTION

In the October 1975 issue of *Thorax* on p. 594, line 8 of the right-hand column should read as follows:

R. C. GODFREY Epidemiological evidence suggests