

# Proceedings of The Thoracic Society

The Summer Meeting of The Thoracic Society was held on 27–28 June 1974 at Churchill College, Cambridge. Summaries of the papers are given below:

## Wandering pneumonia: some clinical observations

W. M. MACLEOD Pneumonia starts with consolidation. It may resolve; it may persist or become 'chronic', or it may spread to other parts of the lung. The latter developments may be coincident but it is uncommon for resolution in one segment to occur with spreading consolidation in another.

Wandering pneumonia is an uncommon type of lung infection. The pneumonic disease commencing in one part of the lung spreads into neighbouring segments at the same time as it resolves in the first affected area. Wandering through the lung it then passes on to the other side, continuing the same progression and finally ending with complete resolution. It does not recur.

Three patients with such disorder are presented. The clinical problem is illustrated and a short commentary on possible explanations for such strange behaviour is given.

## Intestinal absorption studied in patients with chronic obstructive airways disease

J. S. PRICHARD and D. J. LANE Few studies of gastrointestinal function have been carried out in patients with cardiac failure or chronic hypoxia. Milledge (1972) reported that xylose absorption is impaired in hypoxic patients while, according to Vaughan-Jones (1961), malabsorption of  $^{131}\text{I}$ -triolein occurs in congestive cardiac failure.

A survey has been made of intestinal absorption in 26 patients with severe chronic obstructive airways disease. Among these patients there was a wide range of values of  $\text{Pao}_2$  (42 torr–78 torr),  $\text{Paco}_2$  (35 torr–77 torr), plasma bicarbonate (21–40 mEq/litre), and pH (7.37–7.45). Seven of the patients were in right heart failure at the time of the studies. Twelve patients were not in cardiac failure and the remaining seven were either recovering from it or were to develop cardiac failure within 10 days. Lipid absorption was studied by the proparol test (Keynes and Penfold, 1971), that of xylose by the xylose excretion test, and iron absorption by the use of a total-body counter (Callender and Warner, 1968). No significant relationship was established between hypoxia, hypercapnia, plasma bicarbonate or pH and any of the tests of absorption. However, the seven patients who were in right heart failure showed significantly impaired xylose excretion and proparol absorption when compared with the remaining 19 patients. There was no depression of iron absorption in patients with heart failure. Intestinal biopsies, performed in 12 patients, were all normal.

Plasma levels of vitamin  $\text{B}_{12}$ , folate, iron, iron binding capacity, alkaline phosphatase, calcium, and phosphate were neither related to right heart failure nor to abnormality of the blood gases.

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- Milledge, J. S. (1972). Arterial oxygen desaturation and intestinal absorption of xylose. *British Medical Journal*, 3, 557.
- Vaughan-Jones, R. (1961). Fat malabsorption in congestive cardiac failure. *British Medical Journal*, 1, 1276–1278.

## Assessment of $\text{CO}_2$ sensitivity in airways obstruction

A. W. MATTHEWS and J. B. L. HOWELL The diminished ventilatory response to  $\text{CO}_2$  in subjects with airways obstruction has been attributed to both a loss of central sensitivity to  $\text{CO}_2$  and to the mechanical factors limiting ventilation. The latter make it difficult to study  $\text{CO}_2$  sensitivity in these subjects by means of ventilatory response curves.

A new technique has been developed in which the maximum rate of change of pressure ( $dP/dt$ )<sub>max</sub> is measured at the mouth at the beginning of inspiration against a transient complete obstruction, i.e., before flow occurs. The subject rebreathes 5%  $\text{CO}_2$  in oxygen and the ventilatory and ( $dP/dt$ )<sub>max</sub> responses to  $\text{CO}_2$  are recorded. In normal subjects ( $dP/dt$ )<sub>max</sub> correlates well with ventilation and unlike the ventilatory response it is not reduced by the addition of an external flow resistance. In addition the ( $dP/dt$ )<sub>max</sub> response is not reduced by an increase in lung volume.

In patients with chronic bronchitis the ventilatory responses were uniformly low but the ( $dP/dt$ )<sub>max</sub> responses were below normal range only in those patients with  $\text{CO}_2$  retention. While the ( $dP/dt$ )<sub>max</sub> response is inversely related to  $\text{Paco}_2$ , it is not related to  $\text{FEV}_1$ , indicating that some subjects have a true loss of central sensitivity to  $\text{CO}_2$  which leads to  $\text{CO}_2$  retention when they develop severe airways obstruction. In asthmatic patients with bronchial asthma the ventilatory responses increased with relief of their airways obstruction but the ( $dP/dt$ )<sub>max</sub> response remained relatively unchanged.

**An unusual case of primary hypoventilation**

P. M. S. GILLAM, G. M. STERLING, and A. W. MATTHEWS  
Primary alveolar hypoventilation is a rare condition usually presenting as 'cor pulmonale' in the third decade.

**Clinical features** A 12-year-old boy of normal height and weight was admitted to hospital with bronchopneumonia. He was febrile and cyanosed, with tachypnoea of 40/min and bilateral crepitations. CXR showed patchy bilateral lung shadowing. Over the next two days his breathing became increasingly shallow and cyanosis more marked despite antibiotic treatment. Arterial  $P_{CO_2}$  on oxygen rose to 107 mmHg and he was intubated and artificially ventilated, with clinical and radiological improvement. After extubation, ventilation could be maintained by exhortation or nikethamide but without these he fell asleep and lapsed into respiratory failure. Five days later he was his normal self but had an ambulant  $P_{aCO_2}$  of 60 mmHg. Throughout his life he has been lethargic in the mornings and during minor illnesses, but his parents have learned to counteract this by insisting on vigorous early morning exercise.

**Pulmonary function tests** Spirometric values and airways resistance and lung volumes, measured plethysmographically, were normal. Ventilation increased as predicted in response to exercise on a bicycle ergometer, but there was almost no response to carbon dioxide, ventilation rising only to 15.3 l/min at an end-tidal  $P_{CO_2}$  of 76 mmHg. When he rested quietly in a darkened room,  $P_{etCO_2}$  rose spontaneously to 67 mmHg.

These results confirm that he has primary alveolar hypoventilation, which is rarely detected at this age. The defect in ventilatory control appears to lie on the 'input' side of the respiratory driving centre since the response to exercise is unimpaired.

**Ventilatory adaptations to expiratory airflow obstruction: place of breathing exercises**

D. G. LEAVER and N. B. PRIDE Most patients with chronic airflow obstruction having an  $FEV_1$  below 1 litre use their maximum expiratory flow during tidal breathing at rest. In order to increase their ventilation they may: (1) move the tidal volume to a higher lung volume where, as demonstrated by the maximum flow volume curve, higher expiratory flow can be generated, and/or (2) increase their inspiratory flow disproportionately to their expiratory flow. Both adaptations require an increase in inspiratory work.

We have studied the pattern of ventilation of nine patients during exercise by comparing tidal flow volume curves with their maximum flow volume curves. Although the ratio between their inspiratory and expiratory flow was abnormally high at rest it did not change further with increasing ventilation. The tidal volume moved very close to total lung capacity, and to achieve maximum ventilation the size of the tidal volume was reduced.

In any individual there was a unique relationship between the ventilation, the size of the tidal volume, and the position of the tidal volume within the lung volume.

When such patients are ventilated artificially allowance must be made for this in order to prevent an increase in total lung capacity.

Breathing exercises which require patients to prolong expiration and breathe at a lower lung volume are likely to reduce ventilation. It might be more appropriate to encourage patients to breathe high in their lung volume and to concentrate on inspiration.

**Prediction of response to treatment with corticosteroids and cromoglycate in patients with chronic airways obstruction**

R. A. L. BREWIS, M. D. W. LYE, W. R. DODDS, and D. R. APPLETON Among patients with chronic bronchitis and airways obstruction individuals may be found who show a favourable response to treatment with corticosteroids although they do not conform to the accepted clinical definition of asthma. An attempt has been made to identify features which would best discriminate between individuals who respond favourably and those who do not.

Forty-six patients with chronic bronchitis and airways obstruction were studied using a respiratory questionnaire, measurement of blood and sputum eosinophil leucocytes, chest radiography, and standard tests of pulmonary function including measurement of response to bronchodilator aerosols. The patients then participated in two separate double-blind comparisons of prednisone, 15 mg daily, and placebo and cromoglycate and placebo.

Severity of morning symptoms, a relatively short duration of symptoms, and blood eosinophilia were among the most potent discriminating factors separating those who responded favourably from those who did not. Pulmonary function tests, including measurement of response to bronchodilators, were unhelpful.

It is suggested that less attention should be paid to 'reversibility' of airways obstruction in assessing the likelihood of a favourable response to cromoglycate or corticosteroid therapy and more attention directed to the results of a symptomatic enquiry.

**Effects of an acute diuresis on cardiopulmonary function in oedematous chronic bronchitic patients**

J. F. RIORDAN, R. W. SILLETT, and M. W. MCNICOL Although diuretics are widely used in cor pulmonale, reports of improvement in gas exchange consequent on their use are few and do not exclude other causes of improvement. We have therefore studied the effects of an acute diuresis on arterial blood gas tensions in 14 stable oedematous chronic bronchitic patients.  $P_{aO_2}$  rose by 3 mmHg ( $p < 0.001$ ) two hours after an intravenous injection of frusemide but returned to baseline at four hours.  $P_{aCO_2}$  did not change while arterial pH rose progressively. Haemodynamic measurements in six of the patients showed a fall in mean pulmonary artery pressure at one hour which persisted, and a fall in cardiac output maximal at two hours which returned towards baseline thereafter. The fall in cardiac output correlated significantly with the rise in  $P_{aO_2}$  ( $p < 0.01$ ).  $P_{\bar{V}O_2}$  and calculated  $\dot{V}O_2$  did not change. Oxygen delivery did not change, suggesting that

the rise in  $PaO_2$  was not accompanied by a net improvement in tissue oxygenation.

The haemodynamic responses are consistent with the known effects of frusemide. It is suggested that the fall in cardiac output led to the improved  $PaO_2$  by a diminution in the venous admixture effect. It is concluded that the effects on cardiac output must be considered when assessing the effects of diuretic therapy on arterial oxygenation in chronic bronchitis.

#### Body water and cor pulmonale

R. H. A. CAMPBELL, J. R. COX, and P. HOWARD The appearance of oedema in chronic cor pulmonale associated with obstructive airways disease surprisingly often occurs without increase of body weight. Yet after treatment with controlled oxygen and diuretics body weight falls substantially. Multiple radioactive tracer techniques were used to measure the distribution of body water in the oedematous phase and again in convalescence. Evidence will be presented to suggest an important redistribution of body water when oedema appears. It is likely that this is a metabolic effect of severe hypoxia. Oedema formation in this disorder is not necessarily due to impairment of cardiac function.

#### Regional lung function in bronchial asthma

C. C. EVANS Regional lung function was studied in 40 carefully selected asthmatic patients using xenon-133 and a supine scanning technique. Heckscher *et al.* (1968) have shown that, as symptoms and overall pulmonary function deteriorate, abnormalities in the distribution of ventilation and perfusion may be encountered. In 15 extrinsic and 13 intrinsic asthmatics, all of whom were symptomatic, abnormalities of ventilation and perfusion distribution were detected and perfusion of hypoventilated zones directly related to hypoxaemia. These patients also had a uniform retention of injected xenon-133, suggesting either main airway obstruction or a uniform peripheral airway narrowing.

In 12 symptom-free extrinsic asthmatics, however, retention of injected xenon-133 was mainly confined to the lower zones in spite of both normal ventilatory capacity and lung volume, and this implies peripheral airway narrowing.

The lower zones were also the principal site for the ventilation and perfusion defects found in symptomatic patients, according with the concept that airway narrowing in the dependent lung zones in the upright patient is the major functional abnormality in bronchial asthma. This is most likely to be due to inspissated mucus.

#### REFERENCE

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#### Bronchial asthma in the savanna of Nigeria

I. FAWCETT, D. WARRELL, B. HARRISON, J. IBU, and J. AGAMAH Over the last three years more than 300 patients have been seen at an asthma clinic in Zaria in the savanna region of northern Nigeria. One hundred and six patients with documented variability of symptoms and airways obstruction were arbitrarily selected from this group of asthmatics for special study.

Eighty-seven per cent showed immediate hypersensitivity on skin testing with various allergens, notably house dust (58%), animal hair (36%), cockroach (32%), and maize (30%). Unlike extrinsic asthmatics in other parts of the world their asthma usually started in adult life (mean age 26.1 years) and, apart from seasonal rhinitis (15%), they showed no other allergic manifestations. There were two seasonal peaks for asthma, during the harmattan in 19% of patients and during the annual rains in 45%. Most of the rainy season asthma was attributed to the house dust mite which was discovered in mattress dust.

Serum IgE levels were significantly lower in the asthmatics than in a control group who showed characteristically high levels. The occurrence of asthma in African populations is discussed in the light of these findings.

The management of asthmatic patients in rural areas of West Africa presents particular problems which are discussed.

#### Late carcinoma of lung associated with 'shrapnel' foreign bodies

J. B. O'MEARA and R. H. F. BRAIN Four cases are presented of carcinoma of the lung developing in close association with metallic intrapulmonary foreign bodies. In each case the injury was sustained as a result of shrapnel or gunshot wound in the 1914-18 war.

The mode of presentation is discussed and an analysis of a piece of German shrapnel from one patient leads to a discussion on 'metal cancers'.

Whereas in no case can the foreign body be proven as the aetiological factor, it seems likely that this, in combination with chronic irritation and scar tissue formation, may have led to a 'syncarcinogenic' situation and neoplastic change.

Particular attention is drawn to the long latent period between the injury and the development of the carcinoma, which makes the previous existence of an underlying neoplasm most unlikely.

The only previous reports of carcinoma in association with metallic intrapulmonary foreign bodies are to be found in the German literature in which one paper (Pomplun, 1970) contains a chemical analysis of a piece of English shrapnel.

#### REFERENCE

Pomplun, S. (1970). Zur Karzinomentstehung durch intrapulmonale Fremdkörper. *Z. für Erkrankungen der Atmungsorgane*, Bd 132, Heft 3.

### Prolonged survival after resection for lung cancer

C. A. JACKSON In a series of 739 patients operated on between 1948 and 1963, 132 survived to live for over 10 and 84 more than 20 years. This represents 17.8% alive at 10 years, 15% at 15 years, and 11.4% over 20 years: for women, a smaller number, the related percentages are 19%, 23%, and 15% respectively. Included are 82 patients with squamous-cell tumours, 24 with oat-cell, 12 with adenocarcinoma, two with small-cell, and two with alveolar-cell tumours. Sixty-seven had a pneumonectomy and 66 a lobectomy.

The study suggests that right-sided resections are more favourable than left, and lower lobes better than upper, and confirms that after 10 years the survival of squamous, oat and other cell types is equal; women fare better than men. The longest interval before death from the primary disease was at 14 years, and no other patient died of lung cancer after this time period. There was a tendency for older patients to come to resection in the later years reviewed and survival in such cases was relatively good. The development of a second primary lung cancer is a real danger 10 years after a successful primary resection and appears to be related to continued smoking. The quality of life in the long survival patient has been generally good and cor pulmonale a rare cause of death. The long-term survivors tend to come from parents who themselves enjoy longevity.

### Long survival after carcinoma lung despite adverse pathology

L. J. TEMPLE A series of patients is described who were either inoperable when first seen, or in whom after operation a very adverse pathology report was given, indicating that not all tumour had been removed. These patients would normally have been expected to have a very poor prognosis. In all the patients described long-term survival has occurred, and factors have been sought to explain this. The predominating common factor in all these patients has been a severe pyogenic infection often in the form of a persisting sinus. No accurate statistical survey is possible owing to the length of follow-up, but the probability of significance here is high.

The implications of this finding are discussed and its possible relationship to the immunotherapy of carcinoma of the lung is explored. A programme for treatment in the future is suggested and the whole problem of carcinoma of the lung is presented from the angle of immunological competence in the individual.

### Auto-antibodies in lung cancers

M. TURNER-WARWICK and M. E. HODSON Whitehouse and Holbrow (1971) have reported an increased prevalence of antinuclear and smooth muscle antibodies in a variety of tumours, including those of the lung. They suggested that the presence of these tissue antibodies might reflect an impaired tolerance and that antibody to smooth muscle might result from stimulation by actomyosin contractile

protein derived from the cell membrane of tumour cells. If this hypothesis is correct, it might be possible to demonstrate a correlation between such antibodies and certain cell types of tumour.

We have studied the prevalence of circulating auto-antibodies in 100 patients with lung cancers of established cell types. The results have been compared with 65 patients with simple and complicated chronic bronchitis (using MRC criteria of symptoms).

All sera were read 'blind' and were studied without knowledge of the clinical or cytological features. Antibodies were only regarded as present if confirmed on two independent occasions. Using our technique, the prevalence of ANA and smooth muscle antibodies was considerably lower than in previous reports but was still significantly greater than in control series.

The prevalence of these auto-antibodies in lung cancer will be reported in relation to (a) cell type, (b) smoking history, and (c) the presence of simple or complicated chronic bronchitis.

### REFERENCE

Whitehouse and Holbrow (1971). *British Medical Journal*, 4, 511.

### Surgical treatment of superior vena caval obstruction

D. R. WALKER, S. HOLGATE, and S. C. LENNOX The commonest cause of superior vena caval obstruction is mediastinal involvement from carcinoma of the lung and is frequently relieved by radiotherapy or chemotherapy. A rare but important cause of obstruction is mediastinal fibrosis. In view of the relatively benign course of this disease, it is important that it is diagnosed and that patients with this condition are not submitted to radiotherapy.

Over the past five years six patients who attended the Brompton Hospital with superior vena caval obstruction have been treated surgically. In five of these, certain features, including length of history and absence of a pulmonary lesion on bronchoscopy and radiography, suggested a diagnosis of mediastinal fibrosis and led to exploration of the mediastinum. In three this diagnosis was confirmed but the remaining two had a scirrhous carcinoma. In the two earlier patients partial relief was obtained by bypassing the obstruction with saphenous vein grafts. In the last three patients full relief was obtained using woven silicone rubber as conduit to bypass the obstruction. A graft was also inserted into the sixth patient who had proven carcinoma and who had had a full course of radiotherapy without relief. The pre-operative studies, operative techniques, and follow-up, including postoperative venograms, will be presented.

### A controlled trial of doxapram in acute respiratory failure

M. W. MCNICOL, R. W. SILLETT, and J. F. RIORDAN Significant carbon dioxide retention may complicate controlled oxygen therapy in chronic bronchitic patients despite

careful clinical control (Warrell *et al.*, 1970). The value of respiratory stimulants in this situation remains controversial (Woolf, 1970; Bickerman and Chusid, 1970). The efficacy of a respiratory stimulant (doxapram) in antagonizing carbon dioxide retention associated with controlled oxygen therapy (28%) in acute-on-chronic respiratory failure was assessed by a double-blind cross-over trial of two three-hour periods in eight patients.  $Paco_2$  rose in every case during the placebo period; this rise was particularly marked in patients who received placebo in the initial treatment period (mean increase 10 mmHg). In those patients receiving doxapram initially,  $Paco_2$  fell in three and rose in one (mean decrease 4 mmHg). All who had shown a rise in  $Paco_2$  during the initial period on placebo showed a fall in the subsequent period on doxapram. In the six patients who completed the study, mean  $Paco_2$  at the end of the doxapram period was significantly lower than at the end of the placebo period (60 mmHg against 67 mmHg;  $P < 0.01$ ). In three patients the rise in  $Paco_2$  was accompanied by significant impairment in the level of consciousness which was reversed during the doxapram period.  $PaO_2$  was not significantly different during either treatment period. No serious unwanted effects were encountered.

It is concluded that doxapram consistently and safely antagonizes the rise in  $Paco_2$  associated with oxygen therapy in acute-on-chronic respiratory failure. Further assessment of its place in the conservative management of such patients is required.

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#### Mortality of Appalachian coal miners, 1963-71

W. K. C. MORGAN During 1963-64, the US Public Health Service conducted a prevalence study of coal worker's pneumoconiosis in Appalachia in which random samples consisting of (a) 2,549 employed miners, and (b) 1,177 ex-miners were examined. The effects of pneumoconiosis, years spent underground, cigarette smoking, and obstructive pulmonary disease on the length of life were examined. The mortality for actively employed miners was 7% less than the expected death rate for all men in the United States. Ex-miners, many of whom had retired because of ill health, had a death rate 24% greater than expected. While simple pneumoconiosis did not affect life expectancy, complicated pneumoconiosis was associated with premature death. Cigarette smoking and airway obstruction led to consistent excesses in mortality.

#### Silicosis in grind-stone cutters in Nigeria

B. D. W. HARRISON, D. A. WARRELL, I. W. FAWCETT, Y. MOHAMMED, W. S. MOHAMMED, HELEN POPE, and BARBARA WATKINS Grind-stone quarrying is the main occupation

of men living along the sandstone escarpment in Dambatta district situated at the southern limit of the area in West Africa currently affected by drought. Since the introduction of metal tools around 1920, many stone cutters have died from chest disease which they attribute to their occupation.

An unselected group of 126 stone cutters was examined during a one-week field survey. Forty-nine had radiographic evidence of silicosis, with progressive massive fibrosis (PMF) in 17. They had been exposed to dust for significantly longer, and had worked significantly harder, than the 77 men with normal radiographs. Thirty had respiratory symptoms; breathlessness on exertion, chest pain, and productive cough were the commonest. Eleven had abandoned stone cutting because of their symptoms. Seventeen had signs of cardiorespiratory disease.

Pulmonary tuberculosis was suggested radiologically in seven cases; acid-fast bacilli were seen in the sputum in three of these and in one other man with PMF.

Ventilatory capacity was indisputably normal in 20 of the 49 men with silicosis. Gross reduction of  $FEV_1/FVC\%$  was found in 10 men (eight silicotics and two without silicosis) and peak expiratory flow was similarly grossly reduced in seven silicotics and three without silicosis.

The prevalence of silicosis in this community is higher than has been found in open-cast sandstone quarrying in Europe and similar to that observed in stone cutters in India (Gupta *et al.*, 1972). This is probably related to the intensity of dust exposure during quarrying and shaping the grindstones in narrow, deep pits.

Reduction of dust exposure is particularly difficult in the dry hot environment of northern Nigeria. On the basis of the survey simple recommendations have been made to try to achieve this and so allow the men in this drought-affected area to continue their traditional livelihood with a reduced risk of developing silicosis.

#### REFERENCE

- Gupta, S. P., Bajaj, A., Jain, A. L., and Vasudeva, Y. L. (1972). *Indian Journal of Medical Research*, **60**, 1309.

#### Cigarette smoking, emphysema and bronchitis in the Caribbean

G. J. MILLER Two community surveys and a clinical study were undertaken in the Caribbean to investigate the relationships between smoking, respiratory symptoms, and lung function in the absence of other factors associated with airways obstruction (atmospheric pollution, damp climate, industrial hazards). Allowing for differences in age and smoking habits, less bronchitis and airways obstruction was found than has been reported for industrial regions of the United Kingdom. In survey subjects cigarette smoking was associated with increased phlegm, airways obstruction, an increased total lung capacity, and reductions in the transfer coefficient and alveolar blood volume.

All 47 hospital patients with chronic obstructive

airways disease were smokers or ex-smokers, apart from six asthmatics. Smoking in patients was associated with a similar, but more severe, pattern of lung function disturbance to that found in the community with, in addition, reductions in vital capacity and the diffusion capacity of the alveolar membrane. Bronchitis and hypercapnia occurred less frequently than among UK patients, and emphysema was present in all six patients who died and came to necropsy.

The results suggested that emphysema contributed more than bronchitis to airways obstruction among smokers in the Caribbean. Africans appeared less susceptible to the emphysema effect of cigarettes than other ethnic groups.

#### Course and prognosis of sarcoidosis around the world

L. E. SILTZBACH, E. NEVILLE, J. TURIAF, J. P. BATTISTI, O. P. SHARMA, Y. HOSODA, R. MIKAMI, M. ODAKA, and D. G. JAMES A retrospective comparison of large series of patients with sarcoidosis in London, New York, Paris, Los Angeles, and Tokyo reveals an extraordinary parallelism, despite differing races and culture. There is no particular sex predilection; 70% of patients are less than 40 years of age at presentation. A routine chest x-ray discloses the disorder in one-third of patients; and alternative presentations include erythema nodosum and other skin lesions or ocular symptoms. The prognosis of intrathoracic sarcoidosis depends upon the stage at discovery; stage 1 has a resolution rate of about 60%, stage 2 about 46%, and stage 3 has an expected incidence of resolution of only about 12%. Frequency of involvement of various systems was also similar with peripheral lymphadenopathy in 28%, ocular involvement in 22%, skin lesions in 18%, splenomegaly in 10%, parotid enlargement in 6%, nervous system in 5%, and bone cysts in 4%. The Kveim-Siltzbach test was positive in 79% and the tuberculin skin test was negative in 66%. The overall mortality was about 6%, of whom the great majority died as a direct result of sarcoidosis and the remainder (1%) due to unrelated diseases.

#### Diffuse smooth muscle hyperplasia in the lung

C. S. DARKE, P. G. I. STOVIN, L. C. LUM, and C. D. R. FLOWER Lymphangiomyomatosis affecting the lungs is a rare but distinctive form of diffuse lung disease (Miller *et al.*, 1971) which has a number of features both clinical, radiological, and functionally similar to cases of tuberous sclerosis with pulmonary involvement (Harris *et al.*, 1969).

One case of pulmonary lymphangiomyomatosis and one of tuberous sclerosis, each of which came to necropsy examination, will be presented. Both were women and both ran a course of progressive respiratory failure culminating in death after three and five years. Both showed a reticular nodular radiological pattern. Both showed reduction in vital capacity, FEV<sub>1</sub>, and increased physiological dead space. The spectrum of pulmonary function reports in the literature will be presented.

Despite these major similarities, points of difference are reported in the incidence of chylothorax and pneumothorax, in the distribution of other lesions in the body, in the presence of other cases in the family, and in the anatomical site of the smooth muscle hyperplasia in the lungs.

We wish to draw attention to the need for more detailed studies of both these conditions so that our tentative conclusion that these are two separate conditions can be confirmed or refuted.

#### REFERENCES

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#### Pulmonary lymphangiomyomatosis

B. CORRIN, A. A. LIEBOW, and P. J. FRIEDMAN The lymphangiomyomatosis syndrome represents an unusual tumour-like proliferation of smooth muscle affecting lymphatic vessels and lymph nodes. In most cases the lungs are involved and pulmonary symptoms then dominate the clinical picture. The principal complaint is shortness of breath, frequently complicated by repeated spontaneous pneumothoraces, chylous effusions, and haemoptysis. Tests of lung function generally show an obstructive pattern while radiologically there is a fine mottling, worse towards the bases. The course is variable but the ultimate prognosis is uniformly poor. At necropsy there is diffuse 'honeycombing' of the lungs. The aetiology is uncertain but it is of interest that the disease is confined to women in the reproductive years; other features, however, suggest a relationship to tuberous sclerosis. Clinical, radiological, and pathological data derived from 28 cases studied at the University of California, San Diego will be presented.

#### Successful local sterilization of *Pseudomonas*-infected lung cavities

S. W. B. NEWSOME and J. STARK *Pseudomonas* infections of the lung are difficult to treat; indeed, lung abscess has been considered incurable. Two patients have been treated successfully at Papworth by direct instillation of antibiotics into the abscess. Both lesions were of short duration—one followed influenza and the second an operation of wedge osteotomy. Cultures from the first patient became sterile within three days of starting daily instillations through an indwelling cannula. His urine contained antibiotic, although none had been given systemically. Chest x-rays suggested total disappearance of the lesion but four years later he developed a mycetoma in the same place.

The second patient had a large abscess from which

150 ml of pus were removed; the cannula was, however, wrongly sited, the antibiotic went into the pleura, and she developed bacteraemia and a pneumothorax. These complications were treated and the pus was re-collected. A cannula was re-inserted into the abscess and carbenicillin and gentamicin were instilled for a week. The abscess became sterile and has resolved, and the patient remains well nine months later.

Direct instillation of antibiotics into a lung abscess should be considered where this is peripheral and presumptively stuck to the pleura. Neither case developed a fistula and the progress of the second case showed that if complications occur they can be overcome.

#### Use of radioactive gold to detect allergy to tuberculin *in vitro*

C. J. MEADE, P. J. LACHMANN, and S. BRENNER The uptake of radioactive colloidal gold by macrophages can easily be measured. The possibility of using such uptake as a basis for measurement of allergy to tuberculin *in vitro* has therefore been investigated and compared with the measurement of allergy by the macrophage migration inhibition assay. Radioactive colloidal gold is taken up by a process different in several important respects (including failure to be inhibited by cytochalasin B) from phagocytosis.

The uptake of radioactive colloidal gold by peritoneal exudate cells from guinea-pigs sensitized against tuberculin (with BCG) or ovalbumin (using ovalbumin-anti ovalbumin complexes) was enhanced by specific antigen. Comparison of the gold uptake and migration inhibition assays on identical populations of sensitive exudate cells showed in terms of minimum effective antigen dose that the gold uptake assay was considerably more sensitive.

The effect was mediated by a soluble material produced by lymphocytes and acting upon macrophages. Activity appeared in supernatants within the first 18 hours of culture and required 24 hours' contact maximally to stimulate normal peritoneal exudate cells. This material could also be obtained from lymph node lymphocytes. Supernatants of cultures of PPD with lymph node lymphocytes from BCG-immunized animals were able to stimulate gold uptake at about 64-fold greater dilution than they would inhibit migration of a population of normal exudate cells.

At low concentrations of the mediator, a log-linear dose response relationship held, but at high concentrations gold uptake levelled off or even fell, and this was true for concentrations of antigen greater than optimal when added to sensitive exudate cells. Some other properties of the mediator will also be discussed.

As a control for indirect effects of antigen on gold uptake by changes in cell viability or proliferation rather than by changes in rate of pinocytosis chromium uptake was simultaneously measured in all experiments. It varied little at the concentrations of antigen and supernatant factors tested.

It was therefore concluded that measurement of gold uptake may provide a useful assay method either for detecting allergy or for a lymphokine.

#### Candidiasis due to steroid aerosol

M. K. MCALLEN A 12-month follow-up study of 120 asthmatic patients using steroid aerosols (beclomethasone dipropionate or betamethasone valerate) is reported. The results indicated that a daily maintenance dose of 200 µg per day of either drug is adequate in most patients and that tolerance does not develop. Temporary lack of response was seen during episodes of sputum production or heavy exposure to antigen.

There were no observed side effects other than fungal infections of the respiratory tract. However, the incidence of candidiasis of the pharynx (13%) and particularly of the larynx (5%) in apparently immunologically normal patients was disturbing. The development of these infections may be dose-related, as they were not seen in any patients taking less than 400 µg/day. Further studies are in progress.

#### Recent advances in antifungal therapy

Y. M. CLAYTON, H. WINGFIELD, and R. W. RIDDELL Until recent years, amphotericin B has been the only antifungal antibiotic available for the treatment of pulmonary and systemic infections; to be effective and relatively non-toxic it has to be administered by the intravenous route. Since the discovery of 5-fluorocytosine and clotrimazole the prospects for therapy have improved. Unlike amphotericin B, both 5-fluorocytosine and clotrimazole are effective when taken by mouth.

5-Fluorocytosine is a pyrimidine derivative used primarily for the treatment of cases of pulmonary and meningeal cryptococcosis and also disseminated candidiasis. Oral administration of the recommended dosage (200 mg/kg body weight) is well tolerated and gives very adequate antifungal concentrations in blood, tissues, and cerebrospinal fluid. However, before the start of treatment the drug sensitivity of the fungal strain isolated from the patient should be ascertained. Drug-resistant strains have been encountered many times, and resistance to the drug may develop during therapy.

Clotrimazole is a tritylimidazole derivative with a very broad spectrum of antifungal activity against not only yeasts (e.g., *Candida albicans* and *Cryptococcus neoformans*) but also filamentous fungi such as *Aspergillus fumigatus* and *Histoplasma capsulatum*. Unfortunately, oral therapy has given rise to side effects and possibly disruption of certain hepatic enzyme activities so that its potential clinical value remains uncertain. Other imidazole derivatives which are now being studied may prove of clinical value and could enlarge what is still a small list of antifungal drugs effective in the treatment of important fungal infections.

#### Clinical aspects of apical lung tumours

R. ROWLANDSON It is the problem of pain down the arm that is the hallmark of apical lung tumours, making them different from all other lung tumours.

The treatment of this pain and these cancers is under review. Five years ago the feeling among surgeons was that lobectomy with resection of the involved ribs was all one could offer. The majority of patients were relieved of the pain, but the ultimate prognosis was little affected, except in rather rare cases.

Figures will be produced to show the magnitude of the problem. These also show that the possibility of operation is not widely appreciated. The results of operations performed by a group of surgeons (The London Society of Thoracic Surgeons) are also discussed and compared with similar figures obtained five years ago. It appears that the belief current among surgeons in the fifties and sixties that radiotherapy alone had no benefit and often made the pain even more severe is no longer tenable. Finally, the value of a combined attack will be discussed.

#### High anterolateral tractotomy

**J. C. M. CURRIE** Pain caused by neoplastic involvement of peripheral nerves is rarely amenable to direct surgical treatment, and radiotherapy or other conservative measures may not give relief.

Tumours invading the pleura are frequently slow growing and it may be some time before more widespread disease becomes apparent. Should such tumours involve peripheral nerves, especially the brachial plexus, severe pain in a relatively fit patient can be the main clinical feature. In such cases, if medication fails to control the symptoms, surgical treatment of the intractable pain should be considered, especially so as neurosurgical procedures to relieve pain are more effective when due to malignant disease than to other causes. For brachial plexus pain, provided there is no contra-indication, a high cervical spinothalamic tractotomy is advocated.

When the pain is strictly unilateral, expected relief of pain is excellent with minimal side effects. Poor results are obtained if the disease is more widespread and there is diffuse spread of pain to the spine or opposite side.

#### Intrathecal phenol for pain relief in apical tumours of the lung

**P. F. KNIGHT** The pain in shoulder, arm, and chest wall which is frequently associated with apical lung tumours often proves refractory to irradiation and other forms of therapy, and is commonly so severe that a patient who is otherwise well and capable of continuing a fairly normal

life for some months or even longer is quite incapacitated by pain or by the excessive side effects of powerful narcotic analgesics. Treatment of pain in this context, therefore, assumes great importance in the total care of the patient, particularly as palliation when the nature of the tumour precludes more effective primary treatment.

Some 20 years ago Maher introduced the technique of intrathecal injections of phenol in an oily conveying medium as a means of treating the intractable pain of many forms of malignant disease, and this form of therapy has now been used at St. Mary's Hospital for the past 13 years with encouraging success in this special problem of the apical lung tumour. The procedure involves hospitalization of patients for only three to four days, while the technique of injection, although requiring meticulous care, is rapidly and simply carried out with a minimum of equipment and with little discomfort to the patient. Relief, produced in an encouragingly high proportion of patients, is quite often dramatic, and adverse sequelae are rare. Analgesia is long lasting and usually adequate for the natural history of these tumours.

Optimum results, however, are only achieved when phenol block is performed early in the course of the disease, and waiting to observe the success of other therapy may render the method ineffectual.

#### Radiotherapy in the treatment of apical lung tumours

**T. J. DEELEY** Radiation therapy may be used to treat tumours of the apex of the lung in three ways—to attempt cure of inoperable tumours, as a preoperative measure, and palliatively to relieve distressing symptoms. Few lesions at this site can be completely resected and the majority are either inoperable because of clinical evidence of local spread, found to be fixed at thoracotomy, or can be partially removed only. In these patients a radical course of treatment is given using megavoltage therapy. The majority of tumours are differentiated, either squamous carcinoma or adenocarcinoma, and so relatively large doses of radiation are required to the whole apex. There is, as yet, no clear indication that preoperative radiotherapy increases the resectability rate or the survival after surgery, and some workers have reported an increase in the number of complications. However, it is possible that the doses given have been too high. Pain, due to bone destruction or to nerve or pleural involvement, is the most distressing symptom and can be relieved in a proportion of patients.