

## Proceedings of the Thoracic Society

The Spring Meeting of the Thoracic Society was held on 3 and 4 March 1967, at the Royal College of Physicians, London. There were 11 short papers and 3 symposia.

### THE RADIOLOGY OF FARMER'S LUNG

J. C. MEEK (introduced by H. M. FOREMAN) said that a retrospective study of the radiographs of 270 patients in West Wales, diagnosed on clinical and serological grounds as farmer's lung, indicated that chest radiology makes an important contribution (1) in the initial diagnosis of the acute stage, by a fine miliary or ground-glass appearance; (2) in the assessment of severity of the acute attack, by additional signs of alveolar exudate or oedema; (3) in confirming recovery by complete clearing, or incomplete recovery by persisting nodular change; (4) in the recognition of recurring acute episodes; and (5) in the assessment of chronic lung damage and cor pulmonale which develop in a minority of cases.

### PULMONARY HYPERTENSION IN CHRONIC BRONCHITIS

J. MILLARD (introduced by G. SIMON) presented the results of a study of a group of patients who died from chronic lung disease. The degree of right ventricular hypertrophy was measured by weighing the ventricles. This is the most accurate method of measuring ventricular hypertrophy and is probably the best way of assessing the severity and duration of pulmonary hypertension. Emphysema was diagnosed from the chest radiographs taken during life and confirmed by examination of the lungs *post mortem*. Almost all the patients had more than one lung disease at the time of death, and this difficulty was discussed.

The results confirmed the findings of other workers that right ventricular hypertrophy and therefore pulmonary hypertension are usually more severe in patients in whom chronic bronchitis is the predominant pulmonary condition. In patients with extensive emphysema right ventricular hypertrophy is less marked or absent. It was also found that secondary polycythaemia was always associated with severe right ventricular hypertrophy. Although polycythaemia may in itself contribute to pulmonary hypertension this finding supports the suggestion that chronic hypoxia is the most important factor in the development of pulmonary hypertension. The ways in which chronic bronchitis may cause chronic hypoxia and therefore lead to pulmonary hypertension were discussed.

### LUNG BIOPSY WITH A HIGH-SPEED AIR-DRILL

S. J. STEEL and D. P. WINSTANLEY (introduced by J. BELCHER) said that during the last four years S. J. S. had carried out 91 biopsies of lung and pleura with a rotating trephine, 2.95 mm. in external diameter, driven at 15,000 r.p.m. by a compressed air drill. Successful biopsies had been obtained in 68 cases (75%). The main value of the method was in obtaining biopsies from patients with diffuse lung disease not diagnosable by standard methods. Examples of such successes included cases of alveolar proteinosis, beryllium granuloma, and allergic vasculitis. Complications (chiefly pneumothorax and slight haemoptysis) occurred in 18 patients (20%) but were never serious.

### EMPHYSEMATOUS BULLAE

COLIN OGILVIE (Convener) said that the main purpose of this symposium was to describe the indications for surgery and its consequences. The case for surgery was summarized in the history of a man with generalized emphysema from whom bullae occupying most of the left hemithorax had been removed. There was a dramatic relief of dyspnoea, reversion to normal of the bronchspirometric pattern, and objective improvement in lung function which had lasted now for nearly 10 years.

Physiological differences relating to the site of the bulla in 30 patients were then described. Patients with apical bullae tend to have a larger total lung capacity and residual volume but less airway obstruction than those with basal bullae. Moreover, the excision of an apical bulla can abolish airway obstruction without correcting the excess of residual volume. It was suggested that airway obstruction was the result of bullous emphysema in the patients with apical bullae and possibly a cause of it in the patients with basal bullae.

### PHYSIOLOGICAL AND CLINICAL ASPECTS

P. HUGH-JONES considered that surgical resection of the lung or deflation of bullae might improve the emphysematous patient either mechanically or by altering the ventilation-perfusion balance. Past experience had shown that both may happen, though mechanical improvement seemed the commoner effect. The clinical problem, therefore, was one of selection.

of patients who have homogeneous areas of the lung with poor blood flow which could be removed or, if bullous, the bullae could be collapsed.

There was the need to select psychologically satisfactory patients and those in whom all medical measures had been given full trial. The importance of radiology and tomography for selection was stressed, as well as the possible significance of the site of the bullae.

Tests of lung function included (1) overall assessment, including mechanical measurements and exercise testing, and (2) regional assessment, scanning with radioactive gases, and subsequent use of lobar function at bronchoscopy.

The possible future outlook included the role of afferent nerves in breathless patients with emphysema.

#### PATHOLOGY

LYNNE REID thought it was still not clear which patients with bullae benefit from surgical excision. One aspect which might be expected to affect the prognosis was the amount of lung tissue represented by the bulla. According to the amount of lung the bulla represents, three pathological types could be recognized: each type had characteristic radiological features.

#### POST-OPERATIVE ASSESSMENT

G. DAVIES said that the pre- and post-operative state of 60 patients from whom bullae had been removed had been compared on the basis of clinical story of cough and sputum, shortness of breath and its degree, and limited respiratory function tests. These were correlated with the type of bulla diagnosed radiographically and pathologically and with the presence of lung compression and of widespread emphysema on the radiograph.

Certain facts with a bearing on prognosis emerge, and this way of describing patients was a satisfactory basis for the assessment of post-operative results.

#### SURGICAL TECHNIQUES

A. MACARTHUR said that surgical technique has remained virtually unchanged during the last 30 years. The advances made by the respiratory physiologist and the pathologist in the understanding of this disease have not been matched by the surgeon. He can still only treat the patient by obliterating the emphysematous cyst. This can be achieved by excision, plication, pulmonary resection, or two-stage decompression.

A few technical details were discussed and the results achieved by these methods in the past 15 years were mentioned.

#### SURGICAL FOLLOW-UP

J. BELCHER delivered a paper based on the study of 90 patients who had had emphysematous or epithelial

cysts operated on. The first was operated on in 1951: 18 had been followed up for more than 10 years, 48 for more than five years.

The indication for surgery was dyspnoea, not the mere presence of a cyst. Each cyst was treated on its merits in bilateral cases, and no patient was thought to be too disabled to have an operation, one having recently been done after a cardiac arrest.

The operative mortality was 12%. Thirty-five per cent had died since their operation, two-thirds from respiratory failure, but more than half the survivors still have excellent subjective results. All the seven patients with epithelial cysts have done well.

The factors affecting the results had been looked at, and it seemed that advancing age, the necessity for a lobectomy rather than a cystectomy, and the severity of residual emphysema have an adverse effect on the results, but that in general the bigger the cyst the better the result, and lastly that bilateral disease does not appear to have such dire consequences as might be expected.

#### A METHOD OF TREATING RECURRENT MALIGNANT PLEURAL EFFUSIONS

GLYNNE R. JONES said that recurrent malignant pleural effusions constitute a problem for both patient and physician. The conventional methods of treatment are not entirely satisfactory. He described a series of 15 patients treated for recurrent malignant pleural effusion with iodized talc pleurodesis.

The underlying diagnoses, the survival time of the patient post-operatively, the final chest radiographic appearances compared to the pre-operative film, and the number of chest aspirations in the series before and after operation were shown.

There was a total of 66 chest aspirations before, and only one aspiration after, pleurodesis.

Two illustrative cases were mentioned briefly by showing their pre- and post-operative chest radiographs.

#### RESULTS OF SURGERY FOR BRONCHIAL CARCINOMA IN PATIENTS AGED 70 AND OVER

M. BATES said that between August 1950 and 31 December 1966, 81 men and five women of this age group (74 between 70 and 75, and 12 between 76 and 81) had been operated on for bronchial carcinoma.

A man of 70 can expect to live a further nine years. In an ageing population many patients are quite fit at the age of 70; hence the justification for resecting their carcinomas so that they may enjoy the years which they could otherwise expect to live. The majority of these patients presented with thoracic symptoms, but five of them had hypertrophic pulmonary osteoarthropathy, which in itself is sufficient justification for a thoracotomy.

The histological distribution of growths in this age group is the same as in the younger age groups,

and they do not all suffer from slowly growing squamous carcinomas. In this group there were 53 squamous, 21 undifferentiated, 7 oat-cell, and 5 adenocarcinomas. Of the 12 inoperable cases at thoracotomy, six were undifferentiated and two were oat-cell carcinomas. Where these histological types are found on bronchial biopsy, then probably operation should not be advised.

The following operations were performed: pneumonectomy 24 (9 intrapericardial, 15 extrapericardial), lobectomy 47, and segmentectomy 4.

Hospital deaths occurred as follows: 3 from 9 intrapericardial pneumonectomies, 3 from 15 extrapericardial pneumonectomies, 8 from 47 lobectomies, 0 from 4 segmental resections.

A low mortality rate must be aimed at to justify resection in this age group, and pneumonectomy should only be performed for very strict criteria, such as the expectation of a malignant abscess or the presence of hypertrophic pulmonary osteoarthropathy. No deaths have occurred in the last 21 cases.

Of the 59 patients who had had resections two or more years ago there were nine two-year survivors (6 alive and well), seven four-year survivors (all alive and well), and five six-year survivors (3 alive and well).

It is justified to operate on fit patients in this age group provided one aims at a high resectability rate and a low mortality rate. In most cases this means that one can foresee a lobectomy as a near certainty, and pneumonectomy in the presence of a positive biopsy of oat-cell or undifferentiated carcinoma should not be advised except in a very few circumstances.

### THE LUNGS IN CYSTIC FIBROSIS

JOHN BATTEN (Convener) said that a brief symposium on 'The Lung in Cystic Fibrosis' was timely because increasing numbers of patients with cystic fibrosis are reaching adolescence and adult life as the result of adequate treatment in special centres.

The history of the syndrome with present views on genetics was outlined. The difficulties to be encountered in diagnosis were explained, with particular reference to the analysis of sweat electrolyte concentrations. The use of this and other methods to differentiate the homozygous and heterozygous state was discussed. The significance of the heterozygote state in adult chest disease was clarified.

### CONSIDERATION OF BASIC MECHANISMS

G. J. BARBERO said that the site of dysfunction in cystic fibrosis had not yet been delineated. The studies in his laboratory had shown that the submaxillary gland offers a unique opportunity to study a seromucoid secretion in a dynamic state in a quantitative manner. These studies had shown that the submaxillary secretion from a patient with cystic fibrosis shows a consistent presence of turbidity as contrasted to a clear transparent saliva from well children. The turbidity is a reflection of an increase

in organic constituents. Analyses had revealed high total nitrogen, fucose, sialic acid, hexosamine, and calcium content when compared to the saliva of normal children. In addition, there had been an increase in submaxillary amylase and acid and alkaline ribonuclease in the cystic fibrosis group. Such evidence suggested that there was a generalized increase in the secretion of all organic constituents associated with the seromucoid excretory glands of patients with cystic fibrosis.

Other studies had shown that there is derangement in pupillary reactivity as a measure of autonomic nervous system function in patients with cystic fibrosis. It was demonstrated that there seemed to be diminished dilatation of the pupil in darkness under conditions of rest, stress, and almost static recovery from stress. Utilizing an adrenergic blocking agent, guanethidine, it had been possible to diminish the turbidity of the submaxillary saliva in patients with cystic fibrosis. It was not possible to produce this effect with other adrenergic blocking agents, so that the current impression is that this is not related to this pharmacological action but to some other non-identified effect. The studies with other pharmacological agents which had been carried out had not made it possible to explain this effect on the basis of vascular changes or interference with the adrenergic side of glandular stimulation at various selected points. The effect of guanethidine in reversing the insolubility associated with submaxillary secretion seemed to indicate that the secretory abnormality in cystic fibrosis is not of an irreversible type.

### EARLY PATHOLOGICAL CHANGES

LYNNE REID said that hypertrophy of the bronchial mucous glands, extension of goblet cells along the bronchial tree, and a change in the histochemical type of the mucus are features of chronic bronchitis as seen in the adult. These same changes are seen in the lungs of patients with cystic fibrosis who die after many months of recurrent infections.

Her report concerned the investigation of the mucus-secreting structures in patients with cystic fibrosis who had not suffered from pulmonary infection (as well as similar preliminary studies in foetal and newborn lungs) to find whether these changes are a necessary part of the pattern of cystic fibrosis. It seemed that by present methods of study no abnormality could be detected in the lungs of the child with cystic fibrosis without pulmonary infection. This left unanswered the reason for the increased proneness of these children to infection but encouraged the clinician in intensive treatment.

### RADIOLOGICAL APPEARANCES

C. J. HODSON said that the radiological appearances of 'cystic fibrosis' build up slowly over the years to a characteristic gross picture which is pathognomonic. A series of changes are concerned, one of which is specific at an early age and all of which allow for a

close correlation with acute incidents and chronic morbid processes. In carefully supervised cases many children survive with only minimal lung pathology.

#### TREATMENT IN A SPECIAL UNIT

WINIFRED F. YOUNG said that the prognosis in cystic fibrosis usually depends on the severity of pulmonary disease. Although not present at birth, infection followed by progressive damage to the lungs often dates from the first few months of life. Early diagnosis before or at the time of the first episode of bronchitis should give the best chance of effective treatment.

Experience in the management of children, including many from early infancy, gave very disappointing results while their bronchitis was treated only for short periods along the same lines as in patients without the underlying disorder. Subsequently, children with cystic fibrosis had been given more intensive treatment during their initial episodes, and their long-term care had been centred at the hospital. The incidence and severity of pulmonary disease were much lower in the group available for treatment early and systematically than in cases given inadequate or late treatment, or remote from regular follow-up care.

The advantages of the centre include availability of the medical team for in-patients and out-patients at both a city and a country hospital; treatment supported by experienced staff in the laboratories and the radiology and physiotherapy departments; and a variety of accommodation to suit the individual needs of both infants and older children, according to the severity of their illness.

#### IMMUNOLOGY OF SARCOIDOSIS

G. JAMES said that whereas immediate-type hypersensitivity is normal, delayed-type hypersensitivity is depressed, possibly due to defective, hyporeactive cellular antibodies. This phenomenon is neither restricted to sarcoidosis nor to tuberculin, for it is also evident when cutaneous tests are made with other antigens, including pertussis, mumps, trichophytin, oidiomycin, and even pine-pollen. Although lack of response to the intradermal injection of bacterial, viral, and fungal antigens is a cardinal feature of sarcoidosis, this is not evident with a potent chemical sensitizer, dinitrochlorobenzene.

Whereas cellular antibodies are defective, circulating (serological) antibodies are unimpaired. Normal levels of tuberculin and of typhoid antibodies are found. The response to typhoid-paratyphoid vaccine is normal, with production of 19 S globulins following primary immunization and 7 S globulins following secondary inoculations.

Abnormal globulins occur in one-third of patients comprising  $\gamma$  or  $\alpha_2$  globulins, or both. There is no correlation between these abnormalities and other clinical or immunological upsets, nor are they helpful

in the diagnosis or assessment of the activity of sarcoidosis. He reported results of serum immunoglobulin levels which were also abnormal in sarcoidosis.

Sarcoid granulomas are produced by Kveim antigen, a phenomenon which is simulated by beryllium and zirconium patch tests, and by the lepromin reaction, all being individually specific to the disease in question.

#### PULMONARY HYPERSENSITIVITY TO THE GRAIN WEEVIL

DAVID HUGHES had performed studies on a number of subjects working in flour mills or/and with positive skin reactions to weevil extract. Inhalation of weevil extract had produced an immediate response in several subjects associated with falls in F.E.V.<sub>1.0</sub> of 20 to 25% and lesser falls in vital capacity. The F.E.V.<sub>1.0</sub> could be restored to its original value by a bronchodilator aerosol. In one instance a marked Arthus-type reaction occurred three hours after the inhalation and was associated with a rise in pulse rate and temperature, crepitations at the lung bases, and a fall in transfer factor of 25%. The time sequence and significance of these immediate and delayed responses were discussed.

JOHN LUNN said that inhalant allergic responses to the grain weevil had occurred in two laboratory workers. Evidence that this insect produces similar responses in millworkers had been confirmed by (1) detecting weevil protein in airborne mill dust and in many grain consignments; (2) finding approximately twice the rate of positive skin reactions in millworkers compared with a control group; and (3) finding reductions in F.E.V.<sub>1.0</sub> after weevil protein inhalations of up to 22% associated with subjective symptoms.

Two studies confirmed these findings: (1) a pilot study of 75 workers from two grain mills; and (2) a survey of 118 workers, the entire population of one mill. Standardization of respiratory symptoms and histories in the latter study was ensured by using the M.R.C. questionnaire.

#### EFFECT OF CORTICOSTEROIDS AND CORTICOTROPHIN ON GROWTH IN ASTHMATIC CHILDREN

M. FRIEDMAN (introduced by P. DAVIES) said that corticosteroids often inhibit growth in children with asthma when administered for prolonged periods of time. Evidence was presented that growth inhibition does not occur when corticotrophin is given instead of corticosteroid therapy in doses sufficient to control the signs and symptoms of the disease being treated. The possible mechanisms of steroid-induced growth retardation were considered. Data concerning growth hormone secretion in response to insulin-induced hypoglycaemia in children treated with exogenous steroids and corticotrophin were presented.

### HETEROLOGOUS AORTIC VALVE TRANSPLANTATION

A. J. GUNNING and C. M. G. DURAN (introduced by A. J. GUNNING) said that the behaviour of pig aortic valves transplanted into the descending aorta of dogs had been studied in 48 dogs. Although a large number of dogs died early in the series because of technical difficulties and rupture of the donor aortic wall, a successful technique was eventually worked out. This consisted of suturing the heterograft inside a tube of Dacron and suturing the graft between the divided ends of the descending aorta of the dog. The host's aortic valve was made incompetent.

Fifteen dogs survived three to six months, at which times they were sacrificed. The valves were competent and of normal appearance in all specimens. Histologically the valves showed the same changes as were seen in the homograft series previously reported.

This experimental work had now been applied clinically in this country and in France.

### HETEROGRAFT REPLACEMENT OF THE AORTIC VALVE

J. P. BINET, A. CARPENTIER, and J. LANGLOIS said that following experimental work by C. Duran (Oxford) they had chosen heterografts for aortic replacement for two principal reasons: aseptic conditions are better than for homografts; and valves of all sizes are easily available.

Valves are conditioned in a mercurial solution and preserved in saline solution, a method which appears to give better results than lyophilization. Their first 19 valves were inserted with a single mattress suture. In this series they had had eight deaths, not attributable to the valve itself, and they had had to replace four heterografts with ball valves. In the second series of eight cases the valves were implanted with a different technique, designed to secure the bottoms of the cusps to the aortic wall.

Altogether 15 patients had a perfect heart and general condition, without any symptoms of aortic insufficiency. They required no immunological or anticoagulant treatment. There were no cases of systemic embolism, and no immunological reactions had been observed. The first patient operated on in September 1965 is in perfect condition.

Technical problems and immunology (on both the systemic and cellular levels) were discussed.

### THE CAUSATION OF LUNG CANCER OCCUPATION AND LUNG CANCER

RICHARD DOLL said that the study of the occupational hazards of lung cancer is of wide interest, not only because it indicates ways in which the disease can be prevented in particular industries but also because the results throw light on the causes of lung cancer in the general population and on the mechanism of carcinogenesis in man.

Most occupational hazards were originally suspected as a result of clinical impressions and were established on a firm statistical basis only some years later. These include hazards due to ionizing radiations, chromates, nickel ore, asbestos, coal tar, arsenic, and mustard gas. Other hazards certainly exist in relation to some types of mining and they may well appear in other industries in the future.

Exposure to asbestos and coal-tar derivatives is widespread outside specific industrial occupations, and quantitative observations in and outside industry allow one to make crude estimates of the extent to which they contribute to cancer incidence in the general public.

### SOME EXPERIMENTAL BIOLOGICAL EFFECTS OF CIGAR AND CIGARETTE SMOKE

R. D. PASSEY and MICHAEL BLACKMORE said that the death rate from lung cancer and the mortality rate for other causes of death are notably higher for the cigarette smoker than for the smoker of cigars.

Experiments were described in which groups of rats had been exposed to cigarette smoke and to the smokes of cigar and Burley tobacco, the results of which lent support to this observation. Important practical implications involved were discussed.

### HISTOLOGICAL CHANGES IN THE TRACHEOBRONCHIAL EPITHELIUM OF RATS EXPOSED TO TOBACCO SMOKE

DAVID LAMB said that marked differences are found between the epithelial damage produced by smoke from cigarette tobacco and the changes produced by smoke from cigar or Burley tobacco. Despite these differences the goblet cell increase produced by each type of tobacco smoke is similar.

These results were compared with the changes produced by a simple chemical irritant, sulphur dioxide.