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Proceedings of the Thoracic Society

The Summer Meeting of the Thoracic Society was held on 2–3 July, 1971, at the University of Norwich. There were 11 short papers, three symposia, and one lecture. Summaries follow.

ALPHA-1 ANTITRYPSIN DEFICIENCY AND EMPHYSEMA

Genetic Aspects of Alpha-1 Antitrypsin

P. J. L. COOK At present nine different alleles are known in the Pi system producing 45 theoretically possible electrophoretic patterns on starch gel electrophoresis. So far 18 of these patterns have been seen and the subject has been reviewed by Fagerhol and Laurell (1970).

The frequency with which different Pi genotypes occur in the population of Great Britain has been investigated and it is estimated that about 3% of this population are of Pi type MZ, that is 'carriers' of the gene producing alpha-1 antitrypsin deficiency. Pi type MS also occurs in about 5% of this population. Individuals with two S alleles produce less antitrypsin than those with two M alleles but more than those with two Z alleles.

The concentration of alpha-1 antitrypsin present in the plasma depends not only upon the individual's genotype but also upon his state of health. Such environmental variation coupled with certain theoretical considerations makes the biochemical diagnosis of 'carriers' difficult.

Studies on the normal population show that approximately one baby in 5,000 is born in England with a deficiency of alpha-1 antitrypsin (Pi type ZZ). But family and population studies suggest that it is by no means inevitable that he will suffer from chest or liver disease during his lifetime.

REFERENCE

Fagerhol, M. K., and Laurell, C.-B. (1970). In *Progress in Medical Genetics*, Vol. 7, pp. 96–111.

Alpha-1 Antitrypsin Deficiency and Emphysema

D. C. S. HUTCHISON, P. J. L. COOK, N. A. MARTELLI, and P. HUGH-JONES We have studied 61 patients with radiological evidence of pulmonary emphysema, in whom the condition occurred either alone or in association with bronchitis. Eight patients were found to have alpha-1 antitrypsin deficiency; the main features were progressive exertional dyspnoea of early onset (usually between the age of 30 and 45), gross reduction of FEV_1 and TLco and emphysema predominantly affecting the lower zones.

These eight patients have been compared with a further group of 20 who had emphysema of equal severity but normal serum alpha-1 antitrypsin levels. Among the latter, the onset of exertional dyspnoea and of chronic bronchitis (if present) occurred later in life, and the brunt of the disease fell more commonly upon the upper zones. Bullae occurred in 20 of the 28 patients and were found with equal frequency in the two groups.

The prevalence of alpha-1 antitrypsin deficiency among these patients with severe emphysema was 29%. This unexpectedly high figure may have been due partly to selection, as many had been referred by other chest physicians for assessment of their suitability for surgery. There do not appear, however, to be fundamental differences between our patients with severe emphysema and those in other similar reports in the literature.

We have not found definite evidence that heterozygotes are more prone to develop emphysema.

Alpha-1 Antitrypsin Deficiency and Pulmonary Emphysema

G. O. THOMAS and M. C. JONES During the period 1967–70, estimations of serum alpha-1 antitrypsin, using Ericksen's method for measuring trypsin inhibitory capacity (T.I.C.), were performed on selected patients attending Brompton Hospital with chronic airways obstruction and on 87 subjects, mainly blood donors or patients with non-respiratory disease, who acted as controls. Among 87 patients in whom a diagnosis of emphysema was established on the basis of clinical, radiological, and physiological criteria, 16 were found to be deficient in alpha-1 antitrypsin (T.I.C. $< 0{\cdot}4$ mg/ml), 5 had 'intermediate' levels (0·4–0·8 mg/ml), and 66 were 'non-deficient' (T.I.C. $> 0{\cdot}8$ mg/ml). Blood samples and brief histories were obtained from 68 relatives of the 16 deficient patients.

It was found that patients with emphysema and alpha-1 antitrypsin deficiency developed dyspnoea at a much earlier age (mean 35·6, range 29–49 years) than 'intermediate' or non-deficient patients (mean 50·4, range 23–64 years). An important exception was the only non-smoker in the deficient group whose age at the onset of dyspnoea was 49 years. Of all patients with emphysema presenting with breathlessness under 40 years of age 60% were alpha-1 antitrypsin deficient.

The clinical findings were otherwise much the same in the three groups of patients among whom cigarette smoking and chronic bronchitis were equally common. Although the radiological changes of emphysema in the deficient group of patients were invariably symmetrical and basal in distribution, a similar picture was observed in some of the non-deficient patients.

Accepting an autosomal recessive mode of inheritance, no difficulty arose over the recognition of patients

homozygous for the alpha-1 antitrypsin deficient gene. However, the family studies emphasized the lack of precise correlation between the heterozygous state and blood levels of alpha-1 antitrypsin, making identification of the former unreliable on the basis of intermediate blood levels alone.

WEGENER'S GRANULOMATOSIS OF THE LUNG

H. L. ISRAEL and A. S. PATCHEFSKY Twelve patients with pulmonary Wegener's granulomatosis are reported. In seven instances the disease appeared to be limited to the lungs. Four patients had upper respiratory tract involvement and one had cutaneous and subcutaneous lesions. A link between pulmonary and disseminated forms of this syndrome was provided by one patient who had a solitary pulmonary lesion for four years, following which involvement of the upper respiratory tract and the other lung developed. The course of the disease was extremely variable, being acutely malignant in three instances, while one patient has had the disease for 12 years with little deterioration of health. Nine patients received cytotoxic therapy. One death occurred as the result of drug toxicity; at necropsy no evidence of granulomatous angiitis remained. Prolonged remission was observed in two patients treated with chlorambucil and in one treated surgically.

TRACHEO-OESOPHAGEAL FISTULA

H. R. S. HARLEY Six cases of tracheo-oesophageal fistula occurring during treatment by tracheostomy and assisted ventilation have been collected through the courtesy of my colleagues in Cardiff and in the London Society of Thoracic Surgeons. These, together with cases collected from the literature, are reviewed.

Such fistulae may be caused by accidental injury, operative injury, or pressure-infective necrosis inflicted by the inflated cuff or, occasionally, by other parts of the tracheostomy tube. These may suitably be called traumatic, surgical, and ulcerative fistulae.

The differential diagnosis of the three types, and the course, treatment, and prognosis of those due to pressure-infective necrosis are discussed.

BRONCHIAL BRUSHINGS

J. J. FENNESSY The majority of pulmonary neoplasms are readily diagnosed by routine methods. There is, however, a number of patients in whom the diagnosis of the lesions seen in the lung periphery on the chest radiograph will remain obscure. In these cases we employ a technique, transbronchial brushing and forceps biopsy, and have found that this method has a valid place in the diagnosis of pulmonary lesions. The series reported is based on the experience with over 400 examinations of this type performed at The University of Chicago hospitals since 1964.

An arterial catheter is preshaped so that its shape corresponds to the anticipated contour of the segmental bronchus in which the lesion lies. Following topical anaesthesia of the upper airway the catheter is inserted into the bronchial tree with the aid of an arterial guidewire under fluoroscopic control. By manipulations of the catheter and guidewire the instrument is advanced into the appropriate segmental bronchus and is passed peripherally in position as close as possible to the lesion to be biopsied. After optimal position has been achieved, the guidewire is removed and the brushes are passed through the lumen of the catheter and are plunged into the lesion. Microscopic slide preparations are made from the brushes and are fixed at once in alcohol. A small forceps may also be passed through the catheter to obtain forceps biopsy. Following biopsy the area is irrigated with Ringer's solution or saline and the washings are retained for cytological and bacteriological examination.

By this method a possible cytological diagnosis of carcinoma was established and approximately 70% of those patients were subsequently proved to have a primary bronchogenic carcinoma. The method was less reliable in patients subsequently proved to have metastatic carcinoma or lymphoma. The complication rate is low and the procedure is well tolerated by patients. We feel that this method has a valid place in the diagnosis of pulmonary lesions beyond the reach of the bronchoscope.

THE CAROTID BODY

Introduction

DONALD HEATH In the past pathologists have virtually confined their interest in the pathology of the carotid body to the study of its neoplasm, the chemodectoma. However, it has been shown recently that the carotid bodies change in structure in response to chronic hypoxia. There appears to be a case for examining them routinely at necropsies on cases of cardiopulmonary disease.

The Carotid Bodies of Animals at High Altitude

C. EDWARDS The volumes of the carotid bodies of a group of guinea-pigs, rabbits, and dogs from high altitude were measured by an application of Simpson's rule to serial histological sections and compared with those of a similar group of animals from sea level. The histological features of the carotid bodies and the percentages of various cell types in them were also compared in the two groups.

Enlargement of carotid bodies in the high altitude animals was due to a relative hyperplasia of the light variety of type I cells. It is suggested that the enlargement of the carotid body is a response to the chronic hypoxia of low barometric pressure. It is also suggested that the light type I cell is specifically stimulated by chronic hypoxia.

The Carotid Body in Emphysema

DONALD HEATH The carotid bodies were weighed in a series of cases coming to necropsy. The lungs were fixed in distension and 'point-counted' so that the presence, severity, and type of emphysema could be determined accurately. There was no relation between, on the one hand, the type and severity of emphysema and, on the other, the degree of right ventricular hypertrophy or the size of the carotid bodies. Rather there

appeared to be a relation between the weight of the carotid bodies and the weight of the right ventricle and it is likely that the link was hypoxia.

Respiratory Control in Chronic Hypoxia

GWENDA BARER and ANGELA JOLLY In states of chronic hypoxia ventilatory responses to either hypoxia or hypercapnia may be reduced. An irreversible blunted response to hypoxia has so far been observed only in men subjected to hypoxia from early life, in cases of cyanotic congenital heart disease, and in high altitude natives. It is not present in patients acquiring lung disease in adult life. The blunting has been attributed to depression of peripheral chemoreceptor mechanisms.

Apparent blunting of the ventilatory response to hypoxia was produced in young rats kept in a hypoxic environment (400 mmHg) for two to three weeks. Their ventilation increased by one-third to one-half that seen in control rats when they breathed low oxygen mixtures. Modified results were obtained in other tests of peripheral chemoreceptor activity; small doses of cyanide failed to stimulate respiration and two breaths of oxygen did not reduce ventilation during hypoxia. The size of the carotid bodies was measured in these rats. Mean carotid body volumes were 9·3 $\mu m^3 \times 10^6$ (range 4·1 to 17·8) in 14 controls and 26·7 μm^3 (range 16·1 to 36) in six test rats. The implications of these findings for human disease are considered.

ATRIAL MYXOMA

J. F. GOODWIN, R. S. CROXSON, D. JEWITT, W. P. CLELAND, H. H. BENTALL, and A. KRISTINSSON Over a period of 10 years 12 patients with atrial myxoma have been studied. The tumour was in the left atrium in 11, and in the right atrium in one patient. Eight left atrial myxomata and the one right atrial myxoma were successfully removed surgically. Three patients died before operation, the diagnosis having been made in life in two of them. Seven patients with left atrial myxoma have been followed for up to 10 years after operation, five for between 5 and 10 years. Two patients died four and six years respectively following operation for pulmonary neoplasia without evidence of recurrence. Angiocardiography and cardiac catheterization in four patients postoperatively revealed complete relief of left atrial and pulmonary arterial hypertension. No evidence of a space-occupying lesion in the left atrium was seen.

The importance of early diagnosis and surgical treatment is discussed and the technique of the operation is commented upon. The value of echocardiography in establishing the diagnosis and thus avoiding the necessity of angiography is mentioned. It is concluded that although recurrence, which has been reported in the literature, is very rare, regular follow-up is advisable.

PEPTIC OESOPHAGITIS AND HIATUS HERNIA

B. P. MOORE This paper is based upon observations of 137 adult cases seen over a period of 15 years.

In spite of many writings on hiatus hernia, peptic stricture of the oesophagus, and columnar epithelial lining to the lower oesophagus, the subject is still confused.

It is suggested that two separate conditions are present for which there are no widely accepted names. 'Simple hiatus hernia' and 'columnar epitheliosis of the oesophagus' are suggested.

The two conditions are to be distinguished from one another by mucosal biopsy at oesophagoscopy, by the finding at thoracotomy of perioesophagitis, thickening of the lowest segment of the oesophagus and palpable ulcers at a distance from the cardia, by the study of resected specimens and the response to standard repair operations. Very commonly, they cannot be distinguished by radiology, and this has been an important source of confusion.

On this basis, 82 of the series are grouped as 'simple hiatus hernia' and 55 as 'columnar epitheliosis of the oesophagus'. When surgical treatment is indicated, standard repair should give good results in the former group but vagotomy and pyloroplasty are now added for the latter.

LUNG FUNCTION IN SICKLE CELL ANAEMIA

G. J. MILLER and G. R. SERGEANT In sickle cell anaemia lung volumes were reduced because the thoracic dimensions were small relative to body size. The transfer factor was diminished by anaemia, small lungs and a reduced diffusion capacity of the alveolar-capillary membrane (Dm) which was not simply a consequence of small lungs. The pulmonary capillary blood volume was raised. Non-smokers had significantly larger reductions in Dm and more pulmonary complications than smokers.

Exercise studies showed that maximum oxygen uptake was reduced, and excessive lactic acidaemia contributed towards hyperventilation. Dead space/tidal volume relationships indicated that there was a mild ventilation-perfusion imbalance, the cause of which was probably located in the pulmonary circulation.

LUNG STUDIES IN NEW GUINEA

J. E. COTES Collaboration with the New Guinea Institute of Human Biology as part of the U.K. Contribution to the International Biological Programme led to a team of five clinicians, physiologists, and technicians spending an average time of six months in New Guinea during 1970, first on KarKar Island near Madang and then in the environs of Goroka in the Highlands. We investigated the lung function and exercise performance of the local people, laid the foundations for a prospective study of lung disease, and learnt a lot about the territory. This talk describes some of the experiences of the team including a visit to the Goroka show.

CHANGES IN PULMONARY FUNCTION IN CHRONIC BRONCHITIS

Can Severe Chronic Airways Obstruction be Identified before Onset of Disability?

R. S. MITCHELL, GLADYS A. DART, and G. F. FILLEY Eighty subjects, 69 of them male, aged from 21 to 71 at initial

examination, all with non-disabling chronic bronchitis and/or mild dyspnoea on exertion, were followed at regular intervals for from 2 to 14 years. The changes in exercise tolerance, ventilatory capacity and gas transport, and the onset of physical disability and mortality are presented.

Early Functional Changes: Introduction

N. B. PRIDE Recent experimental work, notably by Macklem and Mead, has shown that the small airways of less than 2 mm diameter contribute only about 20% of the normal total airways resistance. As a result considerable disease of the small airways may be present before definite abnormalities develop in tests of overall airway function, such as airways resistance or the FEV_1. The best techniques for detecting the earliest stages of disease of the small airways may well be those which depend on demonstrating unequal ventilation of different areas in the lung.

Distribution of Inspired Gas in Early Bronchitis

J. M. B. HUGHES, R. E. GREENE, L. D. ILIFF, and J. MILIC-EMILI Radioactive gas studies have shown that in the upright position in normal subjects the lower zones receive a greater fraction of the inspired tidal volume than the upper zones. For inspirations at slow or moderate rates, the distribution of inspired gas is determined by the compliance of lung regions; at resting lung volumes the lower zones are less expanded and more compliant than the upper zones, and consequently ventilate better. At fast flow rates gas distribution is influenced more by differences in airway resistances, and since the less expanded lower zones have a higher flow resistance the apical regions now ventilate better than the basal areas.

In patients with simple bronchitis (excess cough and production of mucoid sputum) but normal FEV_1, lower zone ventilation was much reduced on a slow inspiration compared with normal subjects while the distribution of gas on a fast inspiration was normal.

These results suggest that abnormalities of gas distribution may be found before tests of overall function such as FEV_1 change significantly. Early bronchitis seems to be characterized by changes in regional compliance rather than in regional airway resistance, implying that functionally the disease is affecting principally peripheral lung units, small bronchi, and bronchioles.

Closing Volume

D. J. MABERLEY, S. FREEDMAN, and A. E. TATTERSFIELD Towards the end of a full slow expiration from total lung capacity there is an abrupt change in the relative concentrations of gas from upper and lower parts of the lung which appear at the mouth. This is easily detected using a 'foreign' gas as a marker and has been attributed to closure of airways in the dependent parts of the lung. The lung volume at which this change occurs, 'closing volume', is closely related to age and it has been shown to be abnormally high in some subjects with simple bronchitis in whom spirometric and other tests are normal. The test is very easy to perform and is reproducible.

Frequency Dependence of Compliance

D. C. FLENLEY, A. R. GUYATT, J. SIDDORN, and H. BRASH A fall in the dynamic lung compliance as the rate of breathing increases will arise if the time constants for ventilation of parallel air spaces within the lung are significantly different. If the static elastic properties of the lungs are normal, such a change in dynamic compliance may indicate an increase in resistance of some of the small airways. We have repeatedly measured the dynamic compliance at various frequencies of breathing in 14 normal subjects with apparatus of adequate frequency response. We have also determined the static pressure volume curves of their lungs, and their flow volume curves during a forced expiration. We propose criteria describing the normal response of frequency dependence of compliance, based on these observations, and discuss the value of this measurement in detecting asymptomatic obstruction of small airways.

EFFECT ON EARLY BRONCHITIS OF DIFFERENT TYPES OF CIGARETTE

S. FREEDMAN and C. M. FLETCHER Since many people are likely to continue smoking cigarettes it is important to produce and test types of cigarettes which may be less harmful. To this end regular measurements of cough, expectoration, and ventilatory capacity have been made on 225 men smoking three different types of cigarette for 18 months. The men (aged 25 to 54 years) were all regular smokers with chronic productive cough who were unable or unwilling to give up. They were divided into three closely matched groups and each smoked exclusively one of three different cigarettes: A, B, and C, each with the same nicotine delivery but with different filters affecting the tar and vapour phase components. The cigarettes were provided free and were equally acceptable to the smokers: only 32 men had dropped out after 18 months. The average cough frequency and sputum volume became consistently lower in those smoking C than in the other groups, although spirometric measurements differed very little. The need for further studies of this kind and the problem of carrying them out are discussed.

TANTALUM BRONCHOGRAPHY

S. W. CLARKE, P. D. GRAF, and J. A. NADEL By using finely powdered tantalum as the bronchographic contrast medium airway dynamics can be studied uninfluenced by the problems associated with instilling liquid media into the bronchial tree. In addition primary magnification can be utilized to examine very small airways, provided the focal spot of the X-ray tube is sufficiently small.

In the present study we applied these techniques to examine the response of airways to injected microemboli in cats and dogs. After injection of barium sulphate into the pulmonary circulation transpulmonary pressure swing increased in both species by a mean of 59%. Radiographs taken before and after embolization showed

that airways less than 1 mm in initial diameter constricted markedly (mean reduction 27%). Airways up to 3 mm in diameter also constricted but to a lesser degree and at a slower rate, while airways over 3 mm in diameter were either unaffected or dilated slightly. There was a significant correlation between the degree of constriction of the smallest airways (< 1 mm in diameter) and the increase in transpulmonary pressure swing, suggesting that constriction at this level is the principal determinant of mechanical changes (chiefly compliance) in the lungs after microembolism.

We were able to visualize airways as small as 250 μ in diameter with this bronchographic technique which is also applicable to man.

PULMONARY EMBOLISM PRESENTING AS ASTHMA

W. J. WINDEBANK, G. BOYD, and F. MORAN It is well recognized that bronchial constriction may occur as a result of pulmonary arterial occlusion (Sasahara and Stein, 1965) and occasional reports have drawn attention to the occurrence of asthma-like symptoms as a presenting feature of pulmonary embolus (Webster *et al.*, 1968; Salem *et al.*, 1968). This does not appear to be widely recognized, and there may be considerable difficulties in confirming the diagnosis even with standard techniques considered to be adequate. We have observed four patients who illustrate these points. The first had severe unilateral bronchospasm following sudden squeezing of the calf, known to be the site of deep venous thrombosis demonstrated by labelled fibrinogen studies. In three others, pulmonary angiography demonstrated delayed flow and/or occlusion of pulmonary vessels following incidents of severe wheezing. Each had recurring attacks, and some haemoptysis was produced on at least one occasion by two of the patients. One had ulcerative colitis and another suffered the first episode during a pregnancy—both known precipitating causes of pulmonary embolism. Two patients, however, produced eosinophils in the sputum. Abnormalities of pulmonary blood flow may occur in asthma and produce angiographic appearances very difficult to distinguish from those caused by embolism.

The possible interrelationships of the two diseases will be discussed with particular reference to the pulmonary angiographic findings.

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PRIMARY HAEMANGIOPERICYTOMA OF THE LUNG

J. B. MEADE Tumours arising from the vascular pericytes were given the name haemangiopericytoma by Stout and Murray in 1942. The tumour occurs most commonly in the third and fourth decades but its presence has been noticed at birth. It has no particular features which permit definitive clinical diagnosis. The tumour is rare and is exasperating in the variability of its biological behaviour.

Haemangiopericytomas occur in all regions of the body but reports of primary pulmonary lesions are exceedingly rare. We present details of two such primary pulmonary haemangiopericytomas, which we have recently treated by surgical excision, together with a full review of the world literature. The pathology of the tumour—including the morphology of its parent cell, the pericyte of Zimmermann—is discussed. It is suggested that the propensity of this tumour to change suddenly from a benign to an aggressively malignant growth makes early surgical intervention the treatment of choice.

WEIGHT LOSS AND THE PROGNOSIS OF BRONCHIAL CARCINOMA

J. E. C. WRIGHT Loss of weight is common in patients with carcinoma of the bronchus. Little is known of the relationship of this weight loss to operative findings and prognosis, or the relationship of weight change after operation to prognosis.

This paper is a prospective study of 100 consecutive cases of carcinoma of the bronchus treated at the London Chest Hospital under the care of Mr. J. R. Belcher.

The definition of weight loss is discussed, and this was found in 40% of our cases. The relationship of weight loss to tumour histology, sedimentation rate, and operative findings and procedure is detailed. The effect of preoperative weight loss on eventual survival is shown.

All patients were seen personally at six weeks and one year following operation. Weight was recorded on each occasion. The relationship of postoperative weight change to prognosis is shown. Particularly at one year, patients who lose or fail to gain weight following operation are shown to have a significantly poorer outlook.