

Proceedings of the Thoracic Society

A Joint Meeting of the Thoracic Society and the Société Française de Pathologie Respiratoire was held on 12–13 March 1971 at the Royal College of Physicians, London. There were nine short papers and three symposia. Summaries follow.

EXCHANGE TRANSFUSION IN POLYCYTHAEMIC COR PULMONALE

R. J. GREGORY, G. SCOTT and T. CLARKE Evidence is given to show that the raised haematocrit and large circulating blood volume frequently associated with respiratory failure are harmful. It is argued that both these factors increase cardiac work and that the raised haematocrit produces a decreased vascular perfusion at both a pulmonary and systemic level. It is shown that by exchanging a plasma substitute for blood large volumes of blood may be venesected rapidly and a lowered haematocrit and circulating blood volume produced. Rheomacrodex is usually transfused and reasons for the choice are given.

An account of the procedure is given in which it is seen that the venesection and transfusion are usually kept at a similar rate. The technique is illustrated with a short film.

Experience gained in at least 30 cases of 'cor pulmonale' is given. Breathlessness and orthopnoea are often strikingly improved and this is frequently mirrored by improvement in blood gases and a reduction in heart size and pulmonary congestion. The results of long-term follow-up appear encouraging and possible reasons for this are given.

The advantages of this procedure are compared with other forms of treatment and the indications for exchange transfusion are discussed.

LUNG DATA TREATED BY COMPUTER

A. J. CHRETIEN, A. HIRSCH and C. ROUSSEL A computer has been used to analyse data obtained from 3,000 patients with chest disease. These data include the answers recorded on a questionnaire, a description of radiographic changes, and the results of spirometric tests of lung function. This paper gives a critical analysis of the methods used and of the results so far obtained.

THE LUNG IN LIVER DISEASE

Introduction: Causes of Hypoxaemia

J. E. COTES Patients with portal cirrhosis may develop hypoxaemia on account of (1) right-to-left shunts including porta-pulmonary and pulmonary arterio-venous anastomoses, (2) pulmonary ventilation-perfusion inequality, (3) defective gas transfer, and (4) displacement of the oxygen dissociation curve. The associated physiological and morbid anatomical features are reviewed briefly.

The Hypoxaemia-Hypocapnia Syndrome in Liver Cirrhosis

F. VERDIER, B. RUEFF and P. DRUTEL The occurrence of hypoxaemia and hypocapnia in cirrhosis of the liver is classically attributed to the presence of veno-arterial shunts secondary to portal hypertension. To investigate this hypothesis we measured the arterial blood gases and related indices in 21 patients before and after surgical relief of portal hypertension by portacaval anastomosis. Following this procedure, the arterial blood pH increased and the PaCO₂ decreased, but the tension and content of oxygen in arterial blood did not change significantly.

We conclude that (1) hypoxaemia is not secondary to portal hypertension but may be due to veno-arterial shunts within the lungs; (2) hypocapnia is independent of hypoxaemia; and (3) in liver insufficiency the occurrence of hypocapnia is of prognostic significance.

Distribution of Pulmonary Blood Flow and Ventilation in Patients with Liver Cirrhosis

F. RUFF, J. M. B. HUGHES, L. D. ILIFF, D. MCCARTHY and J. MILIC-EMILI The regional distribution of ventilation and perfusion was measured with radioactive xenon in 15 patients (10 in Montreal, 5 in London) with liver cirrhosis and arterial hypoxaemia (PaO₂ between 50 and 75 mmHg). All measurements were made in the seated position. Ventilation of the lower lung zones was markedly reduced during tidal breathing compared with normal subjects. During an expiration from total lung capacity, dependent zone gas flow diminished or ceased at higher volumes than in normals. These results suggest gas trapping and probably airway closure in these regions at end expiration and during tidal breathing.

Blood flow was reduced over the lower third of the lung but mostly these changes were less than for ventilation. We calculated that the ventilation-perfusion ratio in the lower third of the lungs was in general less than 0.5. These low VA/Q areas probably contributed substantially to arterial hypoxaemia.

The probable mechanism for the reduced ventilation is narrowing and closure of small airways in the dependent zones. This may be due to lung oedema fluid accumulating in the peribronchial and perivascular tissue spaces.

Effect of Ascites on Pulmonary Function in Hepatic Cirrhosis

J. VINCENT, P. HADCHOUEL, T. TASSIOPOULOS, V. G. LEVY, C. HATZFELD, D. BRILLE and J. CAROLI Lung function

has been assessed on seven patients with hepatic cirrhosis and abundant ascites before and 72 hours after paracentesis with venous reinfusion of autologous concentrated ascitic fluid.

Abnormalities at the first study included reductions in total and vital capacity, alveolar hyperventilation, hypoxaemia, a low CO transfer factor and a moderately increased right-to-left shunt.

After rapid evacuation of the ascites the residual volume was increased and the degree of shunting was reduced. The blood gas tensions did not change to a significant extent.

These preliminary results suggest that paracentesis has only a slight effect on pulmonary function. The results of further studies will be reported.

The Mechanism of Arterial Hypoxaemia in Hepatic Cirrhosis

N. N. STANLEY Factors causing arterial hypoxaemia were studied by gasometric methods in 32 patients with hepatic cirrhosis. Right-to-left shunting was higher than in 14 control subjects, but it accounted for less than half of the observed reduction in arterial O₂ saturation. In most of the cases with arterial hypoxaemia the arterial-alveolar N₂ difference (a—ADn₂) was increased indicating pulmonary ventilation-perfusion inequality. In four cases the extent to which this was due to regional inequality was assessed by the radioactive xenon technique. In the seated position all cases showed preferential distribution of ventilation to the upper lung zones, while blood flow was directed mainly to the lower zones. Uneven pulmonary blood flow was also found in the supine position.

Carbon monoxide transfer factor was often strikingly low and was apparently caused by reduction of both membrane diffusing capacity and pulmonary capillary volume. However, analysis of the cardiac output and blood gas data suggested that in some cases with high cardiac outputs the pulmonary capillary transit time was too brief for complete oxygen equilibration between end-pulmonary capillary blood and alveolar air. Thus right-to-left shunting, regional inhomogeneity, and a reduced transit time all contribute to hypoxaemia.

Experimental Production of Hepatic Necrosis and Pulmonary Hypertension by Fulvine

J. M. KAY, D. HEATH, P. SMITH, G. BRAS and JOAN SUMMERELL Until recently, the major cause of hepatic cirrhosis in Jamaica was veno-occlusive disease of the liver. This condition commonly results from the ingestion of the pyrrolizidine alkaloid fulvine in 'bush tea' prepared from the leguminous plant *Crotalaria fulva*. Fulvine is chemically similar to monocrotaline which produces pulmonary hypertension in rats.

Thirty young female rats were given a single dose of fulvine either by intraperitoneal injection or by stomach tube. Eleven animals died of massive liver

necrosis and two of pneumonia within 23 days of receiving fulvine. They showed no signs of hypertensive pulmonary vascular disease. The remaining 17 rats which survived from 24 to 37 days developed hypertensive pulmonary vascular disease with right ventricular hypertrophy together with thickening of the pulmonary trunk and muscular pulmonary arteries. In four animals an acute necrotizing pulmonary arteritis also occurred. Seven of these animals showed a mild centrilobular hepatic necrosis which was considered to be a manifestation of right ventricular failure.

We suggest that in patients developing 'primary pulmonary hypertension' a careful history should be taken to elicit the possibility of recent ingestion of drugs or plant extracts that may have caused elevation of the pulmonary arterial pressure.

Comparison of Lung Physiology and Pathology

C. GOLD, J. E. COTES and A. E. A. READ Two cases with portacaval shunts are described in which breathlessness was associated with the features of a transfer defect, including hypoxaemia, exercise hyperventilation, and a low transfer factor. The hypoxaemia was due to ventilation-perfusion inequality. At necropsy the lung of case 1 was congested and showed profuse dilatation of all vessels throughout its structure, with additional vascular plexuses containing transverse vessels around the bronchi and in the subpleural zone. In case 2 grossly dilated vessels were present alongside the large and small bronchi and there were prominent peribronchiolar capillary plexuses, but no clear-cut transverse vessels were seen. The interpretation of these findings is discussed.

A COMPARISON OF THE SAME FACTORS IN (a) PATIENTS SURVIVING 10 YEARS, AND (b) PATIENTS DEVELOPING A SECOND PRIMARY TUMOUR AFTER SUCCESSFUL RESECTION FOR BRONCHIAL CARCINOMA

R. ABBEY SMITH Fifty-one patients surviving more than 10 years after operation and 35 patients developing second lung primary carcinoma after operation were studied.

The possible effects of occupation, pleural infection at the time of operation, the smoking habits before and after operation, and the family history in relation to carcinoma in close relatives were studied in the two groups. Differences between these factors in the two groups were sought which might seem to affect survival to 10 years or the development of a second lung carcinoma. The difficulties in obtaining accurate causes of death from close relatives is re-emphasized.

THE ROLE OF HYALURONIC ACID IN THE DIAGNOSIS OF PLEURAL MESOTHELIOMA

P. DEGAND, A. BOERSMA, J. P. MUH, R. HAVAZ and A. TACQUET High levels of hyaluronic acid were found in the pleural fluid of 16 out of 62 patients with recurrent pleural effusions. Of these 16 cases, 13 had

histologically proven mesothelioma and there was clinical evidence to suggest this diagnosis in the remaining three. Pleural effusions from four patients with secondary pleural tumours were also investigated and in none of these was hyaluronic acid found. The methods used for the detection of hyaluronic acid by electrophoresis and by ion-exchange chromatography are described.

IMMUNE REACTIONS IN THE LUNG

Extrinsic Allergic Alveolitis

C. MOLINA Extrinsic allergic alveolitis may present as recent, chronic and fibrosing, or associated with bronchiolar lesions. In recent cases cough, dyspnoea and loss of weight are present, together with micronodular infiltrations, diffuse giant and epithelioid cell granulomata in the alveolar walls, and a restrictive ventilatory defect. There is usually resolution, spontaneously or with corticosteroids, but early fibrosis and capillary lesions may presage important sequelae. In the chronic group, diagnosis is more difficult as precipitins may disappear and the biopsy may show fibrosis of a non-specific nature. The prognosis is bad, with disturbances of haemodynamics and capillary perfusion. Alveolitis with bronchiolar lesions, emphysema, and obstructive ventilatory defect may occur and immediate and intermediate allergic reactions may be present together. Skin, inhalation, and serological tests are important for diagnosis, using actinomycete and avian antigens. Cases due to other organic dusts are discussed, as well as the effects of infection and foreign body reactions which may make diagnosis more difficult.

Immunological Aspects of Respiratory Allergy in Budgerigar Fanciers

J. PEPYS, J. FAUX, L. WIDE, F. E. HARGREAVE, and J. L. LONGBOTTOM Precipitins against pigeon serum proteins and extracts of droppings have been reported in up to 40% of apparently healthy pigeon fanciers. In our investigation of budgerigar fanciers, all the subjects with precipitins had respiratory disease, mainly allergic alveolitis.

Specific reaginic (IgE) antibody was found in all the atopic budgerigar fanciers with asthma, and in only 2 out of 17 of the non-atopic subjects with alveolitis. The use of haemagglutination tests and the presence of unrelated antigens in extracts of droppings are discussed.

Infrastructural Study of Pulmonary Reactions after Inhalation of Organic Antigens in Sensitized Rabbits

S. KOCHMAN, J. C. MARTIN and J. M. DUBOIS DE MONTREYNAUD It is well known that inflammatory granulomas may result in pulmonary fibrosis as in 'farmer's lung'.

It appeared to us to be of interest to study the early structural changes occurring immediately after

the inhalation of the antigen concerned in a previously sensitized animal.

'Fauve de Bourgogne' rabbits were given biweekly injections of an antigenic extract of *Micropolyspora faeni*. Precipitation arcs appearing after six weeks showed that sensitization had occurred.

The animals were then given an aerosol of the same antigen with Cerchar type apparatus in which there is no risk of atmospheric dissemination.

Control animals show no ill effects due to this inhalation whereas sensitized animals die in 5 to 35 minutes.

The respiratory organs are immediately removed and fixed in osmic acid. After inclusion in epon, the sections are stained with lead and with uranyl acetate and studied under a Philips E M 300 microscope.

Marked parietal and intra-alveolar oedema is observed, but the state of the microvessels deserves special mention.

The endothelium of the capillaries is swollen and the lumen is filled by a fine fibrinoplastic precipitate.

The various cells associated with immediate type hypersensitivity (lymphoblasts and mastocytes) are found in the precipitate and, more particularly, large numbers of platelets undergoing a viscous change. These aspects are characteristic of active and diffuse intravascular clotting. Certain blood vessels are completely obliterated by this active thrombosis.

The granulomatous lesions which have been described could be secondary to these microthrombi.

The prevention of these lesions by anticoagulants and by anti-platelet serum is described and discussed.

Immunology of Cryptogenic Fibrosing Alveolitis

M. TURNER-WARWICK The clinical syndrome recognized as cryptogenic fibrosing alveolitis is unlikely to have a single cause. Nevertheless this disorder has distinctive immunological features when compared with extrinsic allergic alveolitis both with regard to circulating antibodies and to immunological tissue reactions seen in lung biopsies.

The possible immunopathogenesis of cryptogenic fibrosing alveolitis are discussed, based on these findings. While evidence of intravascular complexes is only rarely found, in other cases there is evidence that autoantibodies may react with dead inflammatory cells, especially macrophages. Although the initiation of tissue damage in the lung is likely to be due to some other cause, antigen/antibody complexes formed on these cells may aggravate the inflammatory response and accelerate fibrosis.

PLASMA CORTISOL LEVELS IN ASTHMA

J. COLLINS, P. W. R. HARRIS, T. J. H. CLARK and J. TOWNSEND Plasma cortisol levels were measured at rest and following an intravenous injection of hydrocortisone hemisuccinate in doses of 2, 4, and 8 mg/kg bodyweight in normal subjects and in patients with acute bronchial asthma or severe irreversible chronic airways obstruction. No statistic-

ally significant differences were found between the groups of patients and normal subjects in the maximum plasma cortisol levels achieved or in their rate of decay at each dose level. Previous treatment with corticosteroids did not influence the responses achieved. In patients with status asthmaticus the response to injection was monitored by serial measurements of PEFR and although some patients reported subjective improvement 2 to 4 hours after injection no measurable improvement was detected.

As a result of these studies and previous reports by other workers which have suggested that plasma cortisol levels in excess of 100 $\mu\text{g}/100\text{ ml}$ must be achieved for effective treatment of status asthmaticus, we suggest that the optimal dose of intravenous hydrocortisone hemisuccinate in this condition is 4 mg/kg bodyweight with supplementary injections of similar size at intervals of 3 hours.

DISODIUM CHROMOGLYCATATE IN THE TREATMENT OF BRONCHIAL ASTHMA

A. MEYER, N. DONAT and A. CLAUZEL One hundred asthmatic patients have been treated with disodium chromoglycate, with good results in 72%. Of those patients with pure allergic asthma, 87% improved but the response rate in corticosteroid-dependent patients was 60%. Twenty-two patients took part in a double-blind cross-over trial: 82% responded favourably to disodium chromoglycate and 14% to the placebo. Spirometric measurements were carried out in 60 of the 100 patients during disodium chromoglycate treatment: 63% showed both clinical and spirometric improvement, 27% clinical improvement only, and 10% spirometric improvement only.

THE HAZARDS OF AORTIC CANNULATION FOR OPEN-HEART SURGERY

J. B. MAGNER The ascending aorta is becoming more popular as the site for replacement of the blood from the pump oxygenator.

Although much has been written about the dangers of femoral or iliac aortic cannulation there is not yet much evidence on the dangers of the use of the aorta.

Four types of complication of the use of the aorta for cannulation are described, and also the methods of recognition and prevention.

SCOLIOSIS

General Considerations

P. A. ZORAB Spinal curvature has two effects on cardiopulmonary function which deserve special attention.

One occurs during childhood and adolescence when increasing scoliosis may lead to worsening lung function. The other may occur much later in life—often in the fourth or fifth decade—when cor

pulmonale may develop over a matter of a few months. Why this should happen is not known.

These problems may be better understood if the different types of scoliosis are kept clearly in mind. A brief description is therefore given as an introduction.

Two important considerations are the regional lung function (described by Dr. W. A. Littler and Dr. I. K. Brown) and the changes which occur in cor pulmonale later in life (described by Professor P. Sadoul and Dr. M. Goulon).

Regional Lung Function

W. A. LITTLER and I. K. BROWN Regional lung function has been studied in 35 scoliotic patients using ^{133}Xe . The mean age of the patients was 18 years and none had been in cardiac or respiratory failure.

Measurement of the angle of the curve was made according to the method of Cobb (1948) from radiographs taken in the standing position. The curves were classified as high if the vertebra at the apex of the curve was located between Th 1–Th 6, as mid between Th 4–Th 10, and as low between Th 9–L4. Only the primary curve was considered. In 70% of patients the angle of this curve measured more than 60°.

The mean pattern of perfusion in the low and mid groups was not significantly different from that of 10 normal subjects nor was there any real difference between the pattern in the convex and concave lungs. However, in the high group three distinct patterns emerged: (a) perfusion greater at the base than at the apex in both lungs (5 patients); (b) perfusion even, or greater at the apex in both lungs (5 patients); (c) perfusion greater at the apex in the concave lung only (2 patients).

Possible factors relating to these differences are discussed.

The mean pattern of ventilation in the three groups was not significantly different from that in the normals although there was a wide individual variation. When these patterns were related to the angle and site of a particular curve it was concluded that a high curve of greater than 60 degrees was the most likely to result in an altered ventilation-perfusion pattern.

Cor Pulmonale

P. SADOUL It is very uncommon for cor pulmonale to occur in patients under 20 years of age suffering from scoliosis, however severe. Cor pulmonale among scoliotic patients is, however, not uncommon in later life and the physiological changes then to be found may be striking. This may not be reversible and, in general, the problem of treatment may be difficult, though by no means hopeless. This group of scoliotic patients are among those commonly encountered by physicians and our own experience in this field is discussed.