

Thailand were also attenuated in the guinea-pig, but probably to a lesser degree than the Indian cultures. In contrast, cultures from East African patients were usually of high virulence in the guinea-pig and had patterns of sensitivity to PAS and thiocetazone similar to those of British cultures. The progress of Indian patients treated with isoniazid alone was influenced by the virulence of their pre-treatment cultures, suggesting that virulence, as determined in the guinea-pig, plays a minor part in the course of human disease. Reasons for the existence of attenuated tubercle bacilli in India were considered.

DIFFUSE PULMONARY INVOLVEMENT IN VON RECKLINGHAUSEN'S DISEASE: A NEW SYNDROME

P. D. B. DAVIES said that 27 patients with multiple neurofibromatosis have been studied. Nine of them have diffuse pulmonary abnormalities (two women and seven men, the youngest 35, the oldest 65). Radiologically the lung fields of all nine show fine mottled opacities and small ring shadows, most prominent in the lower zones. Clinically eight of these patients complain only of slight or moderate breathlessness and they have no abnormal physical signs. The ninth patient, the youngest, has the symptoms and signs of recurrent bronchial infections with severe dyspnoea; in her case there is finger clubbing, and crepitations are audible over the whole chest. Physiologically, the lungs of these patients have impaired diffusing capacity and reduced compliance; the patient with bronchial infection also has evidence of gross airway obstruction.

R. ISRAEL-ASSELAIN, J. CHEBAT, CH. SORS, F. BASSET, and A. LE ROLLAND said that up to the present time only specific mediastinal or more rarely sub-pleural or bronchopulmonary neurofibromatous lesions have been recognized as thoracic manifestations of von Recklinghausen's disease. In contrast, the two cases reported concern non-specific diffuse interstitial pulmonary fibrosis.

In the mother the radiological appearances were of dense nodular reticulation with pleural shadowing; these increased over the years and progressive respiratory insufficiency led to death. The necropsy revealed a diffuse interstitial fibrosis.

In the son the abnormalities are of the same type, though less advanced; a lung biopsy was performed which showed a similar but more discrete fibrosis.

Histological examination in the two cases showed an interstitial fibrosis throughout, regularly arranged with zones of leiomyomatosis together with a considerable hyperplastic dystrophy of elastic fibres, very unusual vascular changes, and proliferation of nerve fibres.

Von Recklinghausen's disease affected the mother and three of her brothers together with her son and his child who has no visible pulmonary abnormality.

Diffuse interstitial pulmonary fibrosis has been described in tuberous sclerosis (Bourneville's disease) and in encephalo-trigeminal angiomas (Sturge-

Weber disease) which, with von Recklinghausen's disease, are heredo-familial neuro-ectodermatoses. The finding of interstitial pulmonary fibrosis in von Recklinghausen's disease as well confirms van der Hoeve's grouping together of the three diseases as 'The Phacomatoses' (*Phakos*=spot).

THE ALBUMIN FACTOR IN PLEURAL EFFUSIONS OF DIFFERING AETIOLOGY

W. J. H. LECKIE outlined the possible factors giving rise to fluid accumulation within the pleural cavity, emphasizing the importance of albumin as the major osmotic factor in pleural effusions.

A method was described for estimating the rate of albumin entry into, and discharge from the pleural cavity in patients with pleural effusions due to tuberculosis, primary and secondary tumour, pulmonary infarction, collagen disease, and in hydrothoraces secondary to congestive cardiac failure.

The results expressed as g./24 hr. albumin entering and leaving the pleural cavity were presented individually and collectively, and their significance with regard to the mechanism of pleural effusions was discussed.

CORONARY ARTERIO-VENOUS FISTULA

C. P. NEWCOMBE said that a continuous murmur heard over the praecordium may be due to a congenital fistula between either coronary artery and a cardiac chamber or the pulmonary artery.

The affected artery is tortuous and dilated, frequently with aneurysm formation proximal to the fistula, but beyond it is of normal calibre and distribution.

Diagnosis is established by retrograde aortography. Theoretical complications, cardiac ischaemia due to diversion of blood through the fistula, rupture of the vessel, bacterial endocarditis and pulmonary hypertension seldom, if ever, occur.

Surgery, to obliterate the distal end of the abnormal vessel, is to be considered solely in terms of the size of shunt.

EXPECTORANTS ?

This symposium was convened and introduced by A. JOHN ROBERTSON, who said there was no such thing as an effective expectorant mixture.

S. ALSTEAD referred to conventional views on expectorants as an example of the historic concern for catharsis in therapy. It was still taught that reflex emesis by means of gastric irritants provided a rational basis for the use of expectorants, but the claim lacked acceptable supporting evidence. The evaluation of expectorants must remain a problem for the clinician making observations on patients. In this field experiments on healthy rabbits and rats provided little that was of value to the medical practitioner.

J. FORBES said that claims for the efficacy of various expectorants are valueless unless supported by objec-

tive evidence based on careful sputum viscometry. Recent efforts to reduce sputum viscosity have mainly concentrated on the use of agents which break down mucoprotein and mucopolysaccharide. Results with various proteolytic enzymes have been disappointing, and side-effects have been troublesome. Aerosol Ascoxal in water is said to be more effective than water alone and does at least seem to be harmless; but to be really useful it must be given more or less continuously.

B. J. BICKFORD said that pain and chest-wall instability inhibit expectoration and analgesics do not overcome this adequately.

Dehydration increases viscosity of sputum and infection may also do so. Patients with an asthmatic tendency have bronchospasm and unusually viscous sputum. Traditional expectorants do little to help.

Physiotherapy, attention to hydration, humidification of the air breathed (steam or 'cold steam'), bronchodilators (ephedrine, aminophylline, or atomized isoprenaline), and antibiotics when indicated are the main lines of treatment.

Profuse watery sputum may occur in diffuse pulmonary disease or after lung resection (pneumectomy). Mercurial diuretics may then be very helpful.

Bronchoscopy and tracheostomy are the last resorts.

INFLUENCE OF HYPOTHERMIA ON PULMONARY VASCULAR RESPONSE TO VENTILATION HYPOXIA

I. DE BURGH DALEY said that in isolated lungs of the dog under controlled ventilation and perfusion with heparinized autologous blood the pulmonary vascular response to ventilation hypoxia is determined by two conditions: (1) the temperature of the blood, and (2) the time taken to change over from the natural pulmonary circulation to the artificial perfusion system (the ischaemic period). Ventilation hypoxia increased the pulmonary vascular resistance (PVR) at all blood temperatures tested (28.5 to 41.5° C.) when the ischaemic period had been 4 to 12 minutes. At lower blood temperatures and longer ischaemic periods ventilation hypoxia caused a decrease or no change in PVR.

THE LUNGS IN RENAL DISEASE

M. MACLEOD said that pulmonary congestion (fluid lung) is common in overhydrated patients with oliguria. Clinical and radiological features vary in severity, are rapidly reversible but may progress to acute pulmonary oedema. Histological changes are non-specific. They consist of alveolar congestion with intra-alveolar oedema and haemorrhage of varying degree.

Pulmonary haemorrhage may be prominent in patients with glomerular nephritis (lung purpura) and may precede signs of renal involvement.

In the absence of overhydration patients with renal failure have scanty physical signs in the lungs but

often show surprisingly extensive radiological shadows. Histological sections of this fibrinous pneumonia (solid oedema) show intra-alveolar exudate, hyalinized to form membranes lining the sacs and dense plugs in the alveolar ducts with fibroblastic organization in all degrees. No convincing mechanism for this organization has yet been suggested.

Defects in the fibrinolytic and thromboplastic activity of lung and other tissues in patients with renal disease have been found. The possible significance of these findings was discussed.

THE THORACIC DUCT AND CHYLOTHORAX

J. K. ROSS said that the volume of chyle transmitted by the thoracic duct is very variable but can amount to three or more litres in 24 hours. The important part played by the thoracic duct system in fat transfer is well known, but it also has a major role in protein metabolism and in the life of the lymphocyte.

The effects in an individual of a thoracic duct fistula, when allowed to persist, can be disastrous.

The single most important decision in the management of chylothorax is how long to persist with measures short of thoracotomy and direct control of the chylous leak.

A course of action, based on the physiological facts of thoracic duct function and on an appreciation of the natural behaviour of thoracic duct fistulae, was put forward.

THE LUNGS AND LIVER DISEASE

This symposium was convened and introduced by D. GERAINT JAMES, who said that the hepatic veins, right side of the heart, and pulmonary arteries provide a ready route for tumour emboli, cysts, and parasites to pass from the liver to the lungs. Circulatory effects of portal hypertension may lead to intrathoracic changes, such as mediastinal portal-systemic collaterals draining into the azygos vein or rarely into the pulmonary veins. Multiple pulmonary arteriovenous shunts may be responsible for the cyanosis of cirrhotic patients.

Needle liver biopsy provides for the chest physician histological confirmation of sarcoidosis, amyloidosis, and carcinoma. Finally, the liver and the lungs may be simultaneously involved in multi-system diseases. The symposium which followed drew attention to these three topics, namely, the hepatopulmonary circulation; needle liver biopsy; and the pulmonary manifestations of a multi-system disease, active juvenile cirrhosis.

STANLEY SHALDON, discussing cyanosis in liver disease, said that in 12 patients with portal cirrhosis and varying degrees of arterial oxygen saturation (87 to 97%) there was no correlation between clubbing, arterial oxygen saturation, or the presence of porta-pulmonary shunting. The presence of porta-pulmonary shunting was demonstrated by consecutive

injections of Kr^{85} (radio-active Krypton) into a peripheral vein and the spleen. In only one patient was such a shunt demonstrated, and this patient never had significant arterial oxygen in saturation.

In two patients with portal cirrhosis, gross cyanosis, clubbing, and arterial oxygen saturations of 70 to 75 %, no porta-pulmonary shunts were demonstrated. However, using simultaneous injections of Coomassie Blue and Kr^{85} , intra-pulmonary shunting of 30 to 40 % was demonstrated in both cases. It is concluded that the cause of cyanosis in liver disease is most likely to be due to intra-pulmonary shunting and never due to porta-pulmonary shunting.

SHEILA SHERLOCK discussed needle biopsy of the liver and said that this method has now passed into general use. It should only be performed in hospital with adequate resuscitation available. Special care should be taken in jaundiced patients. Prothrombin time should be normal and platelets exceed 100,000/c.mm. The blood group must be known and compatible blood must be available.

The techniques used are Menghini or Vim-Silverman. The puncture may be intercostal or, if the liver is enlarged, sub-costal.

Complications include haemorrhage, pleurisy, pneumothorax, biliary peritonitis, and puncture of other viscera.

The procedure is useful in diagnosing jaundice and cirrhosis. Hepatic granulomas can be seen, but the changes are usually non-specific. Amyloid disease involving the liver can be diagnosed. Hepatic changes due to drugs either by promazine (cholestatic), hydrazine (hepatocellular), or para-amino salicylate (mixed) type, may be noted.

LEILA LESSOF discussed lung changes in active juvenile cirrhosis and said that the chest radiographs of 60 patients suffering from juvenile ('lupoid') cirrhosis were examined. In this retrospective study 24 radiographs showed abnormality including pulmonary collapse, effusion, cardiac enlargement, and mottled shadowing in the lung fields. After reviewing the films case notes were analysed, and it was found that there was a high incidence of disease of other organs, particularly the large bowel, thyroid, and kidneys.

THE INFLUENCE OF MITRAL VALVOTOMY ON THE INCIDENCE OF SYSTEMIC EMBOLI

L. J. TEMPLE said that a retrospective survey of nearly 500 patients who had undergone closed mitral valvotomy had been carried out: (1) The incidence of embolism pre-operatively was noted and its relationship to age, severity of lesion and cardiac rhythm. (2) The incidence of embolism at operation and its

relationship to pre-operative embolism was noted. (3) The post-operative embolism and its relationship in time to the operation was studied. The difficulties of any follow-up of less than 20 years and the dangers of extrapolation were stressed. (4) A group of medically treated patients were separately analysed for embolism. (5) Any changes in surgical technique were related where possible to post-operative embolism incidence. (6) The policy in relation to mitral valvotomy and the prophylaxis of emboli was reviewed.

CARDIOPULMONARY ASPECTS OF MANNED SPACE FLIGHT

C. H. KRATOCHVIL said that the internal gaseous environment of the Project Mercury spacecraft consists of essentially pure oxygen under a pressure of 5.5 psi (284 mm. Hg). With this pressure and no dilution of the oxygen by other gases the astronaut should be protected against both hypoxia and dysbarism. In addition, a full pressure suit is worn for protection in the event of loss of cabin pressure. The cardiovascular effects of acceleration are minimized by optimal positioning of the astronaut in his restraining couch so that the G-forces will be in the transverse axis. The physiological data obtained in the past five successful Mercury flights were discussed. The most remarkable finding has been the normality of the astronauts in this new and stressful environment.

J. ERNSTING said that whereas a sealed cabin atmosphere consisting of air at one atmosphere pressure is attractive, engineering considerations dictate that in many circumstances the pressure must be less than one atmosphere. The minimum partial pressure of oxygen is dictated by the importance of preventing hypoxia both in the steady state and following a sudden failure of the pressurization of the cabin. The maximum oxygen tension is limited by the toxic effects of this gas upon the alveolar-capillary membrane. The permissible concentration of inert gas (nitrogen) in relation to the total environmental pressure is determined by the incidence of decompression sickness. The concentration of inert gas also determines the rate at which oxygen is absorbed from a closed gas-containing space within the body. Thus longitudinal and transverse accelerations cause marked lung collapse in the absence of an adequate concentration of inert gas. The acceptable concentrations of various toxic gases and volatile substances produced by human metabolism and by equipment within the cabin must be defined. The interaction of these various requirements was considered in relation to the atmosphere of a space vehicle.