

# Proceedings of The Thoracic Society

A Joint Meeting of The Thoracic Society and the British Society for Allergy and Clinical Immunology was held on 28-29 January 1977 at the Royal College of Physicians, London. Summaries of the papers follow:

## **Circulating antibody levels to pigeon protein during recovery from acute pigeon breeder's disease**

G. BOYD, D. PARRATT, and F. MORAN Circulating antibody to pigeon protein was measured sequentially during the recovery phase from acute pigeon breeder's disease in a group of seven patients using a radio-immunoassay technique (Nielsen *et al.*, 1974). All were shown to have high levels initially which fell in an exponential manner when no further contact with pigeon protein occurred. This decay to a reduced level of response over a 2-4 month period differed from the responses noted in farmer's lung where the antibody levels to *Micropolyspora faeni* remained elevated for much longer periods. This reflected the soluble nature of the pigeon protein antigen compared with the particulate antigen of the organism responsible for farmer's lung.

If, after resolution of an acute symptomatic episode, patients returned to their previous activities and exposure to pigeon protein persisted, the levels of circulating antibody remained elevated. The continued inhalation of antigen promoted the continued production of antibody which tended to be maintained at a fairly constant level in each individual. Once exposure ceased for a significant length of time, antibody production decreased sharply and fell to a new lower level which persisted for a much longer period and which reflected a new stable state of antibody production.

Following challenge with antigen in one sensitised individual, circulating antibody fell by 30% within 30 minutes of the start of exposure, thus providing objective evidence for the utilisation of antibody during the acute phase of the condition and, therefore, the presence of an Arthus type reaction in the tissues. Thereafter, antibody levels increased slowly to a peak some three weeks later, indicating a secondary response following stimulation of antibody production similar to that seen after challenge with any other antigen.

Nielsen, K. H., Parratt, D., Boyd, G., and White, R. G. (1974). Use of radiolabelled antiglobulin for quantitation of antibody to soluble antigens rendered particulate: Application to human sera from 'Pigeon Fancier's Lung Syndrome'. *International Archives of Allergy and Applied Immunology*, 47, 339-350.

## **Circulating immune complexes in bronchiectasis and other chronic lung diseases**

A. M. HILTON, J. M. T. HOWAT, L. DOYLE, and M. MOORE

Immunological abnormalities, including a high incidence of autoantibodies and changes in immunoglobulin levels, have been reported in many chronic lung diseases. In studies on patients with bronchiectasis of unknown aetiology we have found immunological changes suggestive of autoimmune phenomena, and, in addition to raised immunoglobulins, a high incidence of rheumatoid factor has been observed. As a result of these findings, and in view of the suggestion that rheumatoid factor is produced in response to the formation of antigen-antibody complexes (Lurhuma *et al.*, 1976), sera from 107 patients with chronic lung disorders and 43 healthy controls were examined for immune complexes. For this purpose an anticomplementary technique was used, based on the binding of added complement by complexed immunoglobulins, after heat inactivation of the endogenous C1 (Mowbray *et al.*, 1973). The diseases studied included bronchiectasis, chronic bronchitis and emphysema, asthma, cystic fibrosis, sarcoidosis, and fibrosing alveolitis. The results, expressed in CH<sub>50</sub> units of complement remaining, have significantly lower values in patients' sera compared with controls. These differences cannot be entirely attributed to the artificial anti-complementary activity induced by aggregation of IgG which occurs on heating sera as there is only a weak correlation between CH<sub>50</sub> units left and IgG levels.

These findings suggest that circulating immune complexes are present more frequently in patients with chronic lung disease than in normal controls; their nature and role remain uncertain.

Lurhuma, A. Z., Cambiaso, C. L., Masson, P. L., and Heremans, J. F. (1976). Detection of circulating antigen-antibody complexes by their inhibitory effect on the agglutination of IgG-coated particles by rheumatoid factor or Clq. *Clinical and Experimental Immunology*, 25, 212-226.

Mowbray, J. F., Hoffbrand, A. V., Holborrow, E. J., Seah, P. P., and Fry, L. (1973). Circulating immune complexes in dermatitis herpetiformis. *Lancet*, 1, 400-403.

## **Local and systemic antibody responses to *Haemophilus influenzae* in chronic respiratory disease**

F. G. BULL and ROBERTA SMITH Infectious agents such as *Haemophilus influenzae* are believed to contribute to the episodic worsening in condition of the chronic bronchitic. We investigated this problem by quantitating the humoral antibody response to *H. influenzae* in paired samples of serum and sputum with a solid-

phase immunoradiometric assay. The  $H_1$  antigen was isolated by a combination of gel filtration, ion exchange chromatography, isoelectric focusing, and affinity chromatography. It is a relatively stable monomeric protein, molecular weight 28 000 daltons. It was not detected in a number of other bacteria and fungi and seems to be a distinctive marker of *H. influenzae*.

About 50% of chronic bronchitics have high and persistent levels of serum IgG to  $H_1$ . In contrast, the corresponding specific sputum antibody, predominantly 11S-IgA and IgG, can fluctuate over a wide range in the same time period. This illustrates the difficulty in assessing the immune response in the lower respiratory tract by reference to serum precipitins.

Using a similar assay, we find evidence of serum antibody to a lipopolysaccharide component of *H. influenzae* which may have a protective role. However, antibodies to  $H_1$  are unlikely to be protective as  $H_1$  is an internal component of the bacterium. Rather, they may contribute to the pathology of the disease through type 1 and type 3 reactions. Indeed, there are indications of IgE to bacterial components which may be associated with a local transient eosinophilia seen in some of these patients. This may be related to the asthmatic symptoms occurring in some chronic bronchitics.

#### Mediators of immediate-type hypersensitivity in sputum from chronic bronchitics

L. S. TURNBULL, L. W. TURNBULL, J. W. CROFTON, and A. B. KAY The sputa from bronchitics contained histamine (26/26), slow-reacting substance (25/26), IgE (26/26), and eosinophils (13/20). The levels of prostaglandins  $PGE_2$  and  $PGF_{2\alpha}$  were negligible. Similar results were obtained from 14 'episodic' asthmatics. In contrast to the 'episodic' asthmatics most of the bronchitics (24/26) showed no evidence of generalised tissue sensitivity in terms of negative tests to a variety of common allergens. Histamine and IgE sputum levels from 'chronic' asthmatics were virtually undetectable although SRS-A was present. However all of these patients were receiving corticosteroids. Sputum from patients with bronchial carcinoma (11), bronchiectasis (7), and pneumonia (5) contained minimal amounts of histamine and other anaphylaxis-associated agents.

These results suggest that in chronic bronchitis there is some element of local (type-1) hypersensitivity but its significance in the pathogenesis of the disease is yet to be determined.

#### Genetics of extrinsic and intrinsic asthma

J. BROSTOFF *Extrinsic asthma* HLA antigen frequencies were studied in allergic subjects who presented with either eczema or hay-fever. A1:B8 was significantly increased in patients with eczema compared with those with hay-fever and the general population. A3:B7 was increased in patients with

hay-fever and asthma but decreased in those with eczema alone.

*Intrinsic asthma* Eighty per cent of patients with intrinsic asthma, where extrinsic factors have been excluded, are homozygous for HLA W6. This is the first indication of a strong genetic component in intrinsic asthma and suggests that it may be a recessive disease.

#### Complement abnormalities in extrinsic and intrinsic asthma.

J. MOWBRAY In the course of studying families with isolated complement component defects, the association between asthma and such abnormalities became apparent. Definitive studies of atopic children with extrinsic asthma and a group of adults with intrinsic asthma have confirmed these associations. The incidence of C2 levels at about the half level was 8% in extrinsic asthma and 40% in intrinsic asthma. The gene for C2 lies in the HLA region and thus genetically determined C2 deficiency would be expected to and does show association with particular HLA antigens. This association has been found with the low C2 levels present in extrinsic, but not in intrinsic asthma.

Study of other complement components suggests that the low levels of C2 are not due to consumption of complement by the disease process, and their significance will be discussed as possible indicators to a genetically determined trait for asthma. The results add to the evidence obtained from tissue typing that there are two distinct diseases inherited separately. The mode of selection of the patients with intrinsic asthma has excluded from the study any patients who might have been extrinsic before their current intrinsic status.

#### Inhibition of rosette-forming cells from normal subjects by sarcoidosis serum

B. H. DAVIES, C. D. PRICE, and W. JONES-WILLIAMS Marked inhibition of the capacity of normal lymphocytes to form rosettes with sheep red blood cells has been found when incubated in the presence of serum from patients with sarcoidosis. Normal numbers of rosettes were found in the presence of normal human or fetal calf serum. The reduction in rosetting cells ranged from 6 to 40% in a selected group of patients. A correlation was attempted to the clinical stage of the disease, tuberculin reactivity, and the presence of a positive Kveim test. Electrophoretic separation of the serum proteins in sarcoid patients reveals a complex distribution of proteins throughout the  $\beta$  and  $\gamma$  fractions. It is suggested that the sarcoid granuloma may be the source of the inhibitory fraction present in sarcoid serum.

#### Biochemical localisation of an occult intrathoracic neoplasm

L. H. REES, W. J. JEFFCOATE, G. M. REES, and G. M. BESSER A case is described of Cushing's syndrome in

a 36-year-old man. From an early stage of investigation a diagnosis of ectopic ACTH secretion was suspected, although the tumour was occult and eventually localised by whole-body venous catheterisation. Levels of ACTH and MSH were higher in the thymic region than elsewhere, and on this basis a thymic neoplasm was suspected. Two months later anterior mediastinal tomography confirmed a mediastinal mass which proved to be a thymic carcinoid tumour which was successfully resected. The value of venous catheterisation in this situation is described, as is the use of ACTH and MSH measurements as biochemical markers of neoplasia (Rees, 1970).

Rees, L. H. (1970). The biosynthesis of hormones by non-endocrine tumours. *Journal of Endocrinology*, 67, 143-175.

### Surgical management of constrictive pericarditis

D. C. T. WATSON, M. J. DRAKELEY, H. R. MATTHEWS, and J. B. MEADE The safety and adequacy of pericardiectomy for constrictive pericarditis are related not only to the aetiology of the disease but also to the surgical approach and methods.

Since 1959, 27 patients with constrictive pericarditis have been treated surgically. Their ages ranged from 16 to 69 (mean 47.4) years and 21 were male.

Thirteen had calcific pericarditis and four of the 14 patients with no calcification had positive tuberculous histology.

Eleven patients were explored via a left thoracotomy and one via a right thoracotomy. The remaining patients had a median sternotomy, six of them with the use of cardiopulmonary bypass.

The technique of dissection and the merits of the various approaches are considered.

There were two operative deaths, both in the thoracotomy group, due to uncontrollable haemorrhage during dissection.

A short period of cardiopulmonary bypass adds little to the risk of the operation and reduces operative hazards by allowing safer and easier dissection round an empty heart which can be completely freed from the adherent pericardium.

### Traumatic rupture of the diaphragm and its sequelae

M. M. CASSIM and J. T. M. SANDY Traumatic rupture of the diaphragm is an uncommon but dangerous injury. There appears to be an increase of this injury due to several factors. While penetrating injury to the diaphragm is a common condition in major metropolitan cities, the relative rarity of blunt traumatic rupture of the diaphragm is well illustrated by several authors. The objects of the presentation are:

1. to review the experience with diaphragmatic injuries at Vancouver General Hospital, British Columbia, Canada, during the last 20 years;
2. to report on 39 patients sustaining this type of injury with detailed analysis;
3. to analyse the cases presenting as late sequelae in which:

four cases of internal thoracic hernia were observed,

four cases presented with strangulated bowel obstruction with mass in the thoracic cavity,

one case presented with posttraumatic oesophageal hiatal hernia, and

one case of Budd-Chiari syndrome was seen due to herniation of liver with venous outflow obstruction.

A plan of management is outlined to enable physicians effectively to treat this rare but dangerous condition with improved morbidity and mortality.

### Celestin tube insertion in Oxford 1973-74: a review of the complications and a case report of an unusual complication

A. J. GUNNING and R. HIGSON The use of the Celestin tube for the relief of obstructive dysphagia is now well established throughout the world. There are only a limited number of reports dealing with complications, chiefly because the tube is used in a condition (carcinoma of the oesophagus) which has a very poor prognosis and the tube is only in place for a short period.

The extension of the use of the tube to other obstructive lesions in the oesophagus (peptic stricture) has led to the tube being in place for periods of up to two years. The occurrence and incidence of complications have increased.

The common complications associated with Celestin tube insertion are wound infection, tube blockage, tube migration, gastrointestinal bleeding, and lung infection.

In this communication, an as yet unreported fatal complication is described of 3 cm of the distal end of the Celestin tube fragmenting off and acting as a bolus. This end migrated down to the terminal ileum, dragging the nylon thread with it. The taut nylon thread eroded throughout the bowel wall, causing a fatal peritonitis.

### Correction of haemolytic anaemia in non-leaking prosthetic aortic valves

M. J. DRAKELEY, H. R. MATTHEWS, and J. B. MEADE Haemolytic anaemia after replacement of the aortic valve with a prosthetic ball valve is usually due to a paravalvular leak or to metal-to-metal contact. In the absence of these two features, small valve orifice is a most important factor. This paper describes four patients who developed haemolytic anaemia after aortic valve replacement and who were successfully treated by replacement of the Starr Edwards (SE) ball valve with a Björk-Shiley (BS) tilting disc valve.

Paravalvular leak as a cause of the haemolysis was excluded by phonocardiography, cine angiography, and by inspection at operation.

Disc valves with comparable annular diameters have significantly larger orifice areas than ball valves. The 7A SE valve (orifice area 1.21 cm<sup>2</sup>) was replaced

with a 19 BS valve (1.50 cm<sup>2</sup>) and SE valves 8A (1.43 cm<sup>2</sup>), 9A (1.70 cm<sup>2</sup>), and 10A (1.89 cm<sup>2</sup>) were all replaced with a 23 BS valve (2.50 cm<sup>2</sup>).

Mean haemoglobin levels rose from 9.8 to 12.2 g/dl within two weeks of the valve exchange, and mean lactic dehydrogenase levels fell from 1850 to 385 units per litre in the same period.

This experience indicates that patients with haemolysis due to prosthetic valve obstruction can effectively be treated if the prosthesis is changed to one with a larger orifice area for a comparable annular diameter.

**A 10-year follow-up of 337 consecutive cases of bronchial carcinoma seen at a chest clinic**

R. SHINER, J. M. TURNER, J. MIKHAIL, and M. W. MCNICOL Between 1957 and 1962 detailed information was recorded on all cases of bronchial carcinoma seen at the Willesden Chest Clinic. The total number was 337. Ten-year follow-up information is available on all of them. Histological confirmation of the diagnosis was available in 261 (77%), the distribution of cell types being as follows: squamous 150, adeno 33, oat cell 63.

One-hundred-and-twenty-seven patients (38%) were submitted to thoracotomy and, of those, 88 (26%) had a successful surgical resection. In 39 (12%) the lesion was found to be inoperable at thoracotomy and, of these patients, 23 were treated with 'radical radiotherapy' postoperatively and 16 received no treatment. Radical radiotherapy (super voltage) treatment with a 'curative' tumour dose was given to another 66 patients (20%). This selection was made on clinical grounds and this treatment was given although it was known that 14 of the patients already had extra-thoracic metastases. The largest group, 144 (43%), received no specific therapy. Of these, 48 already had extrathoracic metastases at the time of diagnosis. The remainder were judged unfit for radical therapy by nature of poor respiratory function, age, and other intercurrent illness. The mean age in this no treatment group was 65.1 years, significantly higher than the mean of 57.8 years in the other groups. The distribution of histological types between the groups showed a predominance of squamous lesions in the surgical and radical radiotherapy groups.

Results of treatment were:

	No.	1 year		2 years		5 years		10 years	
		Alive/ working		Alive/ working		Alive/ working		Alive/ working	
Successful surgery	88	64	46	47	38	33	24	26	20
Inoperable at thoracotomy									
→DXT	23	7	1	0	0	0	0	0	0
Inoperable at thoracotomy—no further treatment	16	4	0	0	0	0	0	0	0
Radical DXT	66	15	0	2	0	1	0	1	0
No treatment	144	29	1	5	0	2	0	0	0

Our findings (using an unselected group of patients seen in a district chest clinic) are generally comparable to those of the larger series reported from specialised centres. They confirm the relatively good results of surgical therapy but show no significant benefit for treatment in the other groups either in prolongation of life or improvement in quality of life as judged by the ability to return to work.

We believe that the value of treatment other than surgery must be seriously questioned.

**Pulmonary function in acromegaly**

C. C. EVANS, L. J. HIPKIN, and G. M. MURRAY It has been suggested that there is an increase in the lung volumes in both male (Brody *et al.*, 1970; Toppell *et al.*, 1973) and female (Toppell *et al.*, 1973) acromegals. Respiratory mortality is increased threefold above normal in acromegaly but the reason for this is unknown (Wright *et al.*, 1970).

The lung volumes of 12 female and eight male patients with acromegaly, chosen because of the absence of associated cardiorespiratory disease, were determined physiologically by helium dilution and radiographically. Enlarged lung volumes were found in half the males but in none of the females, due allowance being made for the presence of a significant thoracic kyphosis. Upper airway narrowing was suggested by an increase in the expiratory/inspiratory flow ratio in six patients, four of whom were male, and acromegaly of the larynx was observed in the three subjects consenting to laryngoscopy. Upper airway obstruction is more likely to account for respiratory death in acromegaly than disordered pulmonary function in enlarged acromegalic lungs. The fasting level of growth hormone could not be related to these respiratory findings but they were more likely to occur when the duration of the disease was long.

Brody, J. S., Fisher, A. B., Gocmen, A., and DuBois, A. B. (1970) Acromegalic pneumomegaly: lung growth in the adult. *Journal of Clinical Investigation*, **49**, 1051–1060.

Toppell, K. L., Atkinson, R., and Whitcomb, M. E. (1973). Lung growth in acromegaly. *American Review of Respiratory Diseases*, **108**, 1254–1258.

Wright, A. D., Hill, D. M., Lowy, C., and Russell Fraser, T. (1970) Mortality in acromegaly. *Quarterly Journal of Medicine*, **34**, 1–15.

**Significance of an increased carbon monoxide transfer factor**

D. J. LIPSCOMB, PAMELA W. EWAN, I. T. GARDINER, and J. M. B. HUGHES The rate of uptake of carbon monoxide (TLco/VA or Kco) appears to be a sensitive index of the volume of the pulmonary capillary bed in ventilated areas of the lung. Previously, attention has focused on diseases where Kco has been low, such as emphysema or fibrosis. In contrast, in our clinical pulmonary function laboratory during the last 15 months, we have seen many patients in whom the single-breath Kco was high. A raised Kco was associated with lung haemorrhage, as in Goodpasture's syndrome and some collagen diseases, asthma, muscle

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weakness, and a variety of other conditions. In patients with intrapulmonary haemorrhage, sequential measurements showed  $K_{co}$  to be a highly sensitive indicator of bleeding in the absence of haemoptysis or radiological change (Ewan *et al.*, 1976).

The volume of the pulmonary capillary bed is influenced by the degree of inflation of the lung; at high lung volumes the capillaries are stretched and narrow (Glazier *et al.*, 1969) and take up less carbon monoxide than at lower volumes when they are relaxed and full of blood. By measuring  $K_{co}$  at TLC and FRC we have demonstrated in normal subjects and a variety of patients that, as lung volume falls,  $K_{co}$  rises exponentially. This probably accounts for the high  $K_{co}$  seen in patients with muscle weakness.

Ewan, P. W., Jones, H. A., Rhodes, C. G., and Hughes, J. M. B. (1976). Detection of intrapulmonary haemorrhage with carbon monoxide uptake; application in Goodpasture's syndrome. *New England Journal of Medicine*. In press.

Glazier, J. B., Hughes, J. M. B., Maloney, J. E., and West, J. B. (1969). Measurements of capillary dimensions and blood volume in rapidly frozen lungs. *Journal of Applied Physiology*, 26, 65-76.

#### Effect of blood transfusion on carbon monoxide transfer factor

ELIZABETH H. CLARK, R. L. WOODS, and J. M. B. HUGHES Serial measurement of pulmonary diffusing capacity is used to detect pulmonary haemorrhage in patients with Goodpasture's syndrome. Day-to-day changes in haematocrit are common in these patients and blood transfusion is often required. The transfer factor for carbon monoxide is influenced by fluctuations in the haemoglobin level. Cotes *et al.* (1972) studied patients before and after gradual correction of chronic iron deficiency anaemia. They found that the relationship of transfer factor to the haemoglobin concentration fitted the Roughton and Forster (1961) equation.

Rankin *et al.* (1961) studied five patients with acute blood loss, before and after transfusion. Their results did not confirm the Roughton and Forster relationship but this discrepancy may be explained by the poor and rapidly changing clinical state of the patients. The aim of the present study was to assess the accuracy of the commonly used correction factor in rapidly changing haemoglobin concentrations. The subjects studied were anaemic as the result of blood dyscrasias and required transfusion on an elective basis. Spirometry, single breath carbon monoxide uptake, and alveolar volume were measured before and at varying intervals after transfusion.

A fall in alveolar volume was observed immediately after transfusion, and the overall diffusing capacity did not rise to the level predicted by the change in haematocrit. However, when TLCO was corrected for the fall in alveolar volume, the change in TLCO per unit alveolar volume ( $K_{co}$ ) in relation to the change in haematocrit corresponded closely to the haemoglobin correction factor commonly in use.

Cotes, J. E., Dabbs, J. M., Elwood, P. C., Hall, A. M., McDonald, A., and Saunders, M. J. (1972). Iron-deficiency anaemia: its effect on

transfer factor for the lung (diffusing capacity) and ventilation and cardiac frequency during sub-maximal exercise. *Clinical Science*, 42, 325-335.

Rankin, J., McNeill, R. S., and Forster, R. E. (1961). The effect of anaemia on the alveolar-capillary exchange of carbon monoxide in man. *Journal of Clinical Investigation*, 40, 1323-1330.

Roughton, F. J. W. and Forster, R. E. (1961). Relative importance of diffusion and chemical reaction rates in determining rate of exchange of gases in the human lung, with special references to true diffusing capacity of pulmonary membrane and volume of blood in the lung capillaries. *Journal of Applied Physiology*, 11, 290-302.

#### Hypertrophy of rat right and left ventricular wall in prolonged hypoxia or hypercapnia

N. T. BATEMAN and I. R. CAMERON Chronic hypoxia induces pulmonary hypertension and right ventricular hypertrophy (Hunter *et al.*, 1974). The left ventricle remains normal until right ventricular diastolic pressure rises and peripheral oedema develops (Rao *et al.*, 1968). The effects of prolonged hypercapnia, in the absence of hypoxia, on right and left ventricular mass are not known, though acute hypercapnia increases cardiac output and blood pressure after a transient depression (Noble *et al.*, 1967; Richardson *et al.*, 1961). We have measured the weight of the left ventricular and right ventricular free wall in rats exposed to prolonged hypoxia, hypercapnia or the two combined, and have compared these findings with those in control groups. The changes in extracellular space under these conditions have been studied.

Adult male rats were maintained in an environmental chamber for up to 28 days. Groups were maintained hypoxic (inspired  $O_2$  12%, balance  $N_2$ ), hypercapnic ( $O_2$  20%,  $CO_2$  6%, balance  $N_2$ ), or hypoxic and hypercapnic ( $O_2$  11%,  $CO_2$  5%, balance  $N_2$ ). After exposure varying from 1 to 28 days the left ventricular free wall, septum, and right ventricular free wall were removed and weighed, and the extracellular space was calculated from the distribution volume of  $^{51}Cr$  EDTA.

The left ventricular weight was taken as the sum of left ventricular free wall and septal weight. All weights are expressed as a proportion of body weight to allow direct comparison of the groups ( $n$ =at least 10 in each group). Progressive increase in right ventricular weight (control:  $41.0 \pm 1.2$  mg/100 g; hypoxia  $63 \pm 1.6$  mg/100 g; mean  $\pm$  SEM,  $P < 0.001$ ) without change in left ventricular weight ( $171 \pm 2.1$  mg/100 g;  $168 \pm 2.7$  mg/100 g; NS) was observed in hypoxia. Hypercapnia induced an increase in both right ( $47.6 \pm 2.1$  mg/100 g;  $P < 0.05$ ) and left ( $193 \pm 4.3$  mg/100 g;  $P < 0.005$ ) ventricular weights after seven days but this fell to  $44.0 \pm 1.0$  mg/100 g (NS) and  $187 \pm 3.1$  mg/100 g ( $P < 0.001$ ) respectively after four weeks. Combined hypoxia and hypercapnia produced intermediate results (RV 1 week  $52.5 \pm 1.4$  mg/100 g; four weeks  $56.2 \pm 2.3$  mg/100 g ( $P < 0.001$ ). LV one week  $180 \pm 3.0$  mg/100 g ( $P < 0.02$ ); four weeks  $174 \pm 3.0$  mg/100 g (NS)). There was no change in extracellular space in any group despite muscle hypertrophy. Our results confirm that selective right ventricular hypertrophy occurs in hypoxia. Both ventricles hyper-

trophy in hypercapnia. These effects are not additive in combined exposure, nor does hypertrophy of this degree alter extracellular space.

Hunter, C., Barer, G. R., Shaw, J. W., and Clegg, E. J. (1974). *Clin. Sci. Mol. Med.*, **46**, 375–391.

Noble, M. I. M., Trenchard, D., and Guz, A. (1967). *J. appl. Physiol.*, **22**, 147–152.

Rao, S., Cohn, K., Eldridge, F., and Hancock, E. (1968). *Amer. J. Med.*, **45**, 229–241.

Richardson, D. W., Wasserman, A. J., and Pattersen, J. L. (1961). *J. Clin. Invest.*, **40**, 31–43.

### Resolution of pulmonary hypertension in a rat model of human hypoxic disease

E. LEACH, J. HERGET, A. SUGGETT, and G. R. BARER  
Rats kept in 10% O<sub>2</sub> for two to three weeks developed right ventricular hypertrophy (RVH) and muscularisation of pulmonary arterioles. These changes, especially in the vessels, resolved more slowly on return to air. Rats subjected to an intermittent normoxic recovery régime designed to simulate that of patients with chronic obstructive lung disease on long-term O<sub>2</sub> therapy showed some resolution of RVH but no vascular resolution (Leach *et al.*, 1976). These changes have now been correlated with measurements of pulmonary artery pressure (P<sub>Pa</sub>) measured with a catheter under anaesthesia while rats *breathed air* (Herget and Paleček, 1972).

Mean P<sub>Pa</sub> was 15.8±0.6 (SEM) torr in 17 control rats and 35.8±2.0 torr in 15 rats after three weeks in 10% O<sub>2</sub> (hypoxic group, P<0.001). After longer hypoxia (5, 9, or 11 weeks) P<sub>Pa</sub> was not raised further. In seven rats after six weeks' recovery in air, P<sub>Pa</sub> was 26.9±1.6 torr (P<0.02 cf hypoxic group; P<0.001 cf control group) but in six rats after 20 weeks' recovery in air P<sub>Pa</sub> was 15.0±2.5 torr (P>0.5 cf control group). In nine rats allowed six weeks of intermittent normoxic recovery (8 or 16 hours daily in air, the rest in 10% O<sub>2</sub> after the initial three weeks' hypoxia) P<sub>Pa</sub> was 32.4±3.8 torr (P>0.3 cf hypoxic group).

Thus pulmonary hypertension develops rapidly in hypoxic rats and resolves much more slowly in air.

Since the hypertension was present during air breathing it is probably attributable to structural changes in vessels which were also shown to persist for many weeks in a normal environment. There was a significant correlation in all rats between P<sub>Pa</sub> and both RVH and thickening of pulmonary arterioles (P<0.001).

There was no reduction in pulmonary hypertension or arteriolar thickening after six weeks on the intermittent normoxic recovery régime. This model illustrates possible limitations to the effects of O<sub>2</sub> therapy.

Herget, J. and Paleček, F. (1972). Pulmonary arterial blood pressure in closed chest rats. Changes after catecholamines, histamine and serotonin. *Archives Internationales de Pharmacodynamie et de Thérapie*, **198**, 107–117.

Leach, E., Howard, P., and Barer, G. R. (1976). Resolution of changes in the heart and pulmonary vessels during intermittent normoxia—a rat model for human long-term oxygen therapy. *Clinical Science and Molecular Medicine*, in press.

### Host defence defects in chronic respiratory infections

P. COLE

#### Serological tests in chest infections

A. C. NICHOLLS

#### Clinical immunology of *Candida albicans*:

(a) Laboratory aspects; (b) Clinical aspects

J. PEPYS, J. L. LONGBOTTOM, and G. EDGE

#### Fungal spores in the human lung

A. SEATON and J. MULLINS

#### Allergic disease in various ethnic groups

J. MORRISON SMITH

#### Neonatal sensitisation and allergy

J. F. SOOTHILL

#### Neonatal antigen avoidance and the prevention of allergy

D. J. MATTHEW