Emphysema in Coalworkers

SIR,—On returning from abroad I have been most interested to read the paper by Dr. R. Ryder and others on emphysema in coal workers' pneumoconiosis (29 August, p. 481). This study is a most valuable contribution to our understanding of pulmonary disease in coal workers, but I doubt whether the conclusion that emphysema is more prevalent in coalminers than in non-miners has been established. This conclusion depends on the authors' confidence that the miners examined were as representative of all miners as the control subjects were of the general population.

The chief reason for suspecting bias in selection of the miners is the lack of any age gradient of emphysema (and consequently of F.E.V. levels, since F.E.V. and emphysema were closely related). An age gradient of F.E.V. has been reported in all adequate samples of miners that have been investigated. The authors had two explanations for this. First, that advancing fibrosis obscured the emphysema in older subjects: this seems unlikely since there was no gradient of emphysema with age, even in those with pneumoconiosis category O—A. Secondly, a tendency of younger men with emphysema to have "a lower incidence of survival": this should apply equally to the control cases. Indeed if reduction of F.E.V. was so fatal there would be no age gradient of F.E.V. in the general population. It seems just as likely that miners with emphysema were selectively more likely to come to the panel and to die and thus to appear in the series than were men with similar degress of emphysema in the general population. Although it appears that most miners with pneumoconiosis in South Wales come to the panel and so should appear in the series, not all miners die and not all of them stay in the coal mining industry—these are powerful selective factors.

There is another question raised by this conclusion on which the authors do not comment. Since pneumoconiosis category is well related to dust exposure but emphysema is not, emphysema in miners, if it is more prevalent in them than in the general population, must be due to some other factor in the miners' environment than dust exposure. Have the authors any hypothesis as to what this factor could be? The question, of course, does not arise if the high incidence of emphysema in the miners is due to a selective artefact rather than to occupation.—I am, etc.,

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Response to Stress

SIR,—I would like to confirm the view of Professor S. Shuster (August 29, p. 515) that patients with Cushing's disease (pituitary dependant adrenal hyperplasia) usually show a decreased pituitary-adrenal response to stress. In our series of 19 cases only one has shown a normal rise in plasma fluorogenic corticosteroids during insulin-induced hypoglycaemia, and others have made similar observations.[1-4] Two patients have also been found to fail to increase their plasma corticosteroid concentrations during the stress of laparotomy.

It is, however, not yet entirely clear whether such stress unresponsiveness is fundamental to the disease or is the result of high circulating corticosteroid levels. It is unlikely that Cushing's disease is caused by an upward resetting of the feedback control mechanism resulting from the impaired stress response, as suggested by Professor Shuster. Such a mechanism could not account for either the absence of the nyctohemeral rhythm of ACTH secretion found in Cushing's disease, or the very high basal levels of plasma ACTH after adrenalectomy.[5] On the other hand, loss of nyctohemeral rhythmicity and dexamethasone suppressibility of ACTH secretion with high basal plasma corticosteroid levels may also be a feature of untreated severe depression, producing a biochemical picture indistinguishable from that found in Cushing's disease,[6] yet we find that stress responsiveness in these patients is unimpaired.

It is an oversimplification to consider control of ACTH secretion to be located within a single hypothalamic-pituitary pathway. Among many lines of evidence favouring multiple pathways are the observations that amphetamine-induced ACTH release, believed to be produced by an action on centres associated with mediation of the nyctohemeral rhythm, is blocked by the α-adrenergic antagonist thymoxamine, whereas the response to the stress of insulin-induced hypoglycaemia is not.[7 8]

While the fundamental cause of Cushing's disease is uncertain it is most likely that it is due to a defect in the hypothalamic mechanisms controlling secretion of corticotrophin-releasing factor and hence corticotrophin and corticosteroids, rather than to a primary lesion within the pituitary.—I am, etc.,

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Cardiac Arrest and Bone Cement

SIR,—Dr. J. N. Powell and others (8 August, p. 326) suggested that absorption of monomer from methyl methacrylate bone cement might be a cause of acute hypotension with consequent cardiac arrest. The subsequent correspondence which this provoked demonstrated widespread interest and concern over this possibility.

If the monomer were to be a cause of fatal collapse with any frequency there should be a difference in the mortality rate between patients who have received a Thompson prosthesis with cement and those who have received an uncemented Austin Moore prosthesis. A review of 139 cases of primary prosthetic replacement of the femoral head following fracture has recently been carried out in this unit (Woodyard and Wrighton—unpublished work), primarily to compare the clinical results of the two techniques of prosthetic replacement.

Fifty prostheses were cemented, and 89 were uncemented. The mortality rate during the first postoperative month was found to be 16% for the cemented Thompson prostheses and 17% for the uncemented Austin Moore prostheses. There were no fatalities on the operating table. In the uncemented group two patients died on the second postoperative day. In the cemented group one patient died on the day of operation, approximately four hours after the operation had been completed. This patient was aged 88, in congestive heart failure with auricular fibrillation, mentally disorientated, had a blood urea of 123 mg./100 ml., and a haemoglobin of 9·3 g./100 ml. Her blood pressure fell after halothane was introduced into the anaesthetic, and never rose again after the operation had been completed. The blood pressure fell before the cement was introduced into the femur. There was no sudden episode of collapse on the operating table.

These figures suggest that the monomer does not have any regularly fatal effect, and we would strongly support the sentiments of Mr. D. W. Parsons (19 September, p. 710) that it would be unwise to alter a technique found satisfactory unless it can be proved that it is the cause of complications.

The review of Woodyard and Wrighton showed conclusively that the clinical results of the cemented Thompson prostheses were superior to those of the uncemented Moore's prostheses.—We are, etc.,

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SIR,—We were aware of the risk of hypotension occuring in operations for prosthetic replacement of the femoral head and total hip arthroplasty before the start of the recent correspondence on this subject (8 August, p. 326; 22 August, p. 465; 29 August, p. 523; and 5 September, p. 588). For this reason, monitoring of pulse, blood pressure, and E.C.G. was undertaken routinely. We wish to report the following incident.

The patient was a woman aged 78 confined to bed and chair for four years on

account of a painful hip owing to ischaemic necrosis complicating an old fracture of the femoral neck. During the operation of McKee-Farrar total hip replacement considerable osteoporosis was encountered, and insertion of the femoral component required twice the usual amount of cement. Immediately following reduction of the hip, profound hypotension and bradycardia occurred. There were no warning signs on the E.C.G. Cardiac arrest ensued, and attempts at resuscitation were unsuccessful.

Necropsy showed air and fat in the pelvic veins on the side of the operation, right heart, and in the coronary vessels. There was marked myocardial degeneration. The cause of death was considered to be air embolism acting on a previously defective myocardium.

It would seem possible that air (or fat) embolism might account for some of the cases of transient hypotension with recovery. We now use a polythene tube while inserting the cement and note the considerable quantities of fat and air which are expelled through it. We also feel that we should use an oesophageal stethoscope and a central venous pressure line (for diagnosis and treatment) as recommended recently by O'Higgins.[1]—We are, etc.,

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REFERENCE

1 O'Higgins, J. W., *British Journal of Anaesthesia*, 1970, **42**, 459.

Breast-milk Jaundice

SIR,—The leading article on "Breast-milk Jaundice" (25 July, p. 178) was, in our opinion, misleading in several clinical and experimental aspects.

In considering the differential diagnosis of jaundice persisting beyond the first ten days of life the leader discusses a mixed group of diseases. It is diagnostically more valuable to differentiate disorders associated with predominantly conjugated (direct-reacting) hyperbilirubinaemia (for example, neonatal hepatitis, biliary atresia, galactosaemia, etc.) from those associated with unconjugated (indirect-reacting) hyperbilirubinaemia (for example, congenital defects in bilirubin conjugation, inhibition of bilirubin conjugation, etc.) During the first week of life, newborn breast-fed infants have a higher incidence of clinical icterus than is observed in bottle fed infants; however, this icterus is of brief duration and must be distinguished from the prolonged jaundice of certain breast-fed infants which is associated with pregnane-3α, 20β-diol in human milk.

The leader suggests that some infants are icteric due to the relatively low intake of milk while breast-feeding. In our experience, infants with breast-milk jaundice and "inhibitor" activity in their mother's milk have good weight gains and thrive. Persistence of inadequate milk intake for the prolonged period suggested should result in marked malnutrition.

The leader states that "the inhibitory substance was at first thought to be 3α,20β-pregnanediol" and seems to conclude that this unusual steroid plays no role in the syndrome. We disagree with this conclusion based upon the following considerations. 3α,20β-pregnanediol has been isolated from inhibitory human milk by ourselves,[1,2] and from urine obtained from women with "inhibitory" milk and infants with breast-milk jaundice.[3] Ramos *et al.*[4] refer to a single attempt to isolate the steroid by Professor Wotis; however, the source of the milk studied and the methods utilized are not provided. Their failure to reproduce the syndrome in vivo by feeding 3α,20β-pregnanediol may result from differences in the vehicle used to solubilize the steroid.

The role of pregnane 3α,20β-diol in the syndrome of breast-milk jaundice is not completely clear. Yet this unusual isomer has only been found in this syndrome where it is present in milk and urine. There must be a relationship between this observation and the clinical syndrome. Lathe and Adlard's[5] findings are interesting but not conclusive regarding the pathogenesis. One wishes that they had provided details regarding the solubilization of steroids and how they were added to the in vitro system.

We agree that there are numerous unanswered questions regarding the pathogenesis of breast-milk jaundice and that further studies are required. The syndrome is probably of multiple aetiology, and all jaundiced breast-fed infants do not have 3α,20β-pregnanediol in their urine and milk.—We are, etc.,

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Benign Sixth-nerve Palsy

SIR,—A leading article (27 April 1968, p. 190) brought to notice the condition of benign sixth-nerve palsy in children. Ten children with this condition seen over a period of 13 years have been described by Knox and colleagues.[1] I would like to draw further notice to this condition by describing the features in a child who was recently under my care.

A 16-month-old boy was admitted to Seacroft Hospital with a history that six weeks previously he had suddenly developed bilateral external rectus palsies. The right eye recovered within four days, but the left rectus palsy had continued until the time of his admission. The day prior to the onset of the palsies he developed an upper respiratory infection with a clear nasal discharge.

There were no other neurological findings on admission. Skull *x*-ray, E.E.G., and cerebrospinal fluid were normal. Haemoglobin was 85%, W.B.C. 15,100/cu.mm. with a differential count showing 56% of lymphocytes, E.S.R. 8 mm./hour. Blood culture and urine chromatography for amino-acids and sugars was normal. Viral studies were performed by complement fixation tests on paired sera. Negative tests occurred against mumps, herpesvirus, influenza A and B, adenovirus, psittacosis, Q fever, myxovirus, and respiratory syncitial virus.

Three weeks from the time of his admission, complete recovery of the left eye had occurred.

The relative lymphocytosis in the peripheral blood of our patient is similar to the findings in five of the patients described by Knox *et al.* They postulated the aetiology was a viral neuritis. Though I have found no serological evidence in my patient to support this theory the preceding upper respiratory infection would be in keeping with such a suggestion.—I am, etc.,

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REFERENCE

1 Knox, D. L., Clark, D. B., and Schuster, F. F., *Pediatrics*, 1967, **40**, 560.

Bloodstained Tears

SIR,—I would like to report an unusual clinical finding—namely, that of bloodstained tears.

A boy aged 8 years with abdominal pain was recently admitted to this hospital. His appendix was removed and histology showed submucosal hyperaemia. The next day the classical skin lesions of Henoch-Schönlein purpura appeared. They spread profusely to involve his legs, buttocks, elbows, and hands. He developed profuse bloody diarrhoea and conjunctivitis and became very ill. For three days at the height of the illness copious bloodstained tears were being secreted by haemorrhagic conjunctivae.

He was treated successfully with systemic steroids and local antibiotic drops to the eyes, and is now well.—I am, etc.,

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Consultancy in Radiology

SIR,—Your correspondence on consultancy in radiology (20 June, p. 736; 11 and 25 July, pp. 110 and 227; 1 August, p. 286; 5 September, p. 590) has underlined the serious position radiology and radiologists are facing. There are said to be about 60 unfilled consultant posts; in fact the true figure is probably very much larger as the Department of Health often refuses requests for additional consultant staff.

One must ask the question why are so few interested in radiology in Britain? A recent survey showed that in 1968 30 radiologists emigrated from the United Kingdom and there is no reason to suppose that this figure will diminish.

There are, I suggest, three outstanding reasons: firstly, a strong and reasonable dislike of physics; secondly, a loss of contact with patients; and thirdly, the very poor financial reward for a long and arduous course.