Correspondence

SIR—I write as a graduate scientist who has been working for nearly 16 years in a hospital pathology laboratory. In the light of this experience I would like to comment on the Zuckerman Report,1 an important article concerning it (7 December, p. 593), and on some of the correspondence from medically qualified pathologists which has followed.

The Zuckerman Report and the letters from Professor S. C. Frazer (21 December, p. 768) and Dr. A. L. Woolf (11 January, p. 114) are only too correct when they point out the lack of status, career prospects, and financial reward for most graduate scientists in the N.H.S. compared with that available from other employers. Changes along the lines of the Zuckerman Report will have to be made if the N.H.S. is to attract enough good scientists, for few people would agree with the inference of your leading article that more are not needed.

Steroid “Pseudohormatism” in Asthma

SIR—The introduction of dioscodronoglucate (Intal, FPL 670) into the therapeutic regimen for asthma has allowed reduction, or even withdrawal, of cortico- steroid drugs in many patients in whom this had not previously been possible, and so-called steroid “pseudohormatism” has supervened in 9 out of 26 patients. None of the patients had a past history of arthritis. Control of the asthma remained satisfactory.

Features of the asthma in the nine affected patients (Table I) were similar to those in the 17 unsatisfactory patients. Details of prednisone corticosteroid treatment in the affected group are shown in Table II.

1 Zuckerman Report, 1969, p. 593.

SIR,—Although much information has been gathered on the structure and ultrastructure of the endometrium during the menstrual cycle, little is known about the enzymatic changes which ultimately lead to the onset of menstruation. Cohen and his co-workers suggested from histochemical observations that tissue disintegration during the menstrual phase may be caused by the breakdown of lysosomes and the release of autolytic enzymes which they contain, but quantitative biochemical studies of the lysosomes of the human endometrium appear to be lacking.

Lysosomes and Menstruation

In 1963 Woessner and Brewer drew attention to an increase in the activity of the lysosomal enzyme acid cathepsin D in the human uterus during postpartum involution. They postulated that the enzyme was involved in the degradation of uterine collagen, and other studies on the endometrium of the rat during early pseudopregnancy also suggest that this is true. Since the breakdown of endometrial tissue during menstruation presumably involves a loss of collagen from the connective tissue matrix, it was decided to investigate the activity of acid cathepsin D in samples of human endometrium taken at hysterectomy or by curettage, and dated according to well-established histological criteria.

The activity of the enzyme was measured using a haemoglobin substrate in tissue homogenates derived from 28 samples of endometrium, 12 from the proliferative and 16 from the secretory phases of the cycle. The mean values for the specific activities (expressed as _µ_moles of tyrosine liberated per gramme fresh weight per hour), together with their standard errors, were 42.7 ± 3.5 and 88.6 ± 11.3 respectively. Statistical analysis of the data showed that despite considerable variation within the samples the difference in the mean is highly significant (P < 0.01).

In addition, the increase in cathepsin activity appears to be progressive, being lowest in the early proliferative and highest in the late secretory phase.

We believe that this increase in enzyme activity is associated with the dissolution of the connective tissue framework of the endometrium, and that the onset of menstruation is therefore due, at least in part, to the involvement of lysosomal enzymes. It is hoped that investigations currently in progress will establish whether other hydrolytic enzymes are also involved, and whether lysosomal enzymes play a similar role in the implantation of the human egg as they do in the rat.—We are, etc.,

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SIR—...
The clinical features of the steroid "pseudo- rheumatism" were similar to those described.1,2 Generalized aching, stiffness, and loss of strength and energy occurred in all. Aching in the upper part of the body and across the shoulders prevented sleep in three patients. Stiffness was especially noticeable in the morning on rising, and during the day following periods of inactivity. The joints were affected specifically: shoulders in six; elbows, knees, and ankles in five; small joints of the hands in four; neck in three and wrists and feet in two patients. The bones ached in one patient and in another the insertion of the Achilles tendon was particularly tender. Other symptoms included periods of restlessness in five patients. Loss for recent events in two patients, paraesthesia of the fingertips in five patients, and anorexia in one patient. In one patient, who had an intraarticular, painful and tender indurated nodule appeared on the dorsum of one foot, in front of both knees, and behind both thighs. This patient had a past history of meralgia paraesthetica. The symptoms were out of step with the signs and no radiographic changes were seen.

Haemoglobin, white cell count, erythrocyte sedimentation rate, serum sodium, potassium, and chloride, serum sodium, potassium, and chloride, serum albumin, globulin, and alkaline phosphatase, blood sugar, serum uric acid, and total serum proteins and electrophoresis were normal in all but three patients.

Late, Rose Waaler, and antinuclear factor tests were negative, and L.E. cells were not demonstrated.

The plasma cortisol and response to tetracosactrin 0.25 mg. was estimated in only three patients (Nos. 4, 6, and 8) and the results were normal in all three. In patient No. 4, the resting level was low and the response to tetracosactrin was subnormal, and in patient No. 6, although the resting level was normal limits. The response to tetracosactrin was probably reduced. These results suggest that adrenal suppression was present.

The joint symptoms did not occur until the daily dose of prednisolone reached 2.5 mg. or less, and appeared after four to eight weeks in four patients. Two other patients noticed excessive fatigue. The symptoms of "pseudo-rheumatism" were relieved in three patients (Nos. 2, 8, and 9) by increase in the corticosteroid dose, while in one patient (No. 5) corticotrophin had a similar effect. Partial relief occurred in one patient (No. 6) by increasing the prednisone from 2.5 to 6 mg. per day. There was some doubt whether it is wise to increase the dose of cortico- steroid to control symptoms in all cases, because some patients who had been treated with corticosteroids had subsequently redeveloped symptoms at the higher dose.2 In two patients (Nos. 3 and 5) the symp- toms of pseudo-rheumatism resolved within 24 to 36 hours. Aspirin and paracetamol were of no value. As the "pseudo-rheumatic" symptoms persisted over a number of weeks, treatment became necessary in seven of the nine patients affected.

The pathogenesis of the steroid "pseudo- rheumatism" is not clear. The possibility of relative or real corticosteroid deficiency cannot be excluded, the latter possibility being supported by the reduced response in two of the three patients tested with tetraco- actrin.

Similar symptoms have been reported in healthy volunteers, following a single dose of prednisolone 40 mg. when plasma 17-hydroxycorticoid levels were falling but were still within normal range. With the advent of new drugs such as dexamethasone and prednisolone, in the symptomatic treatment of asthma, steroid "pseudo-rheumatism" and other steroid withdrawal symptoms are likely to become a pressing clinical problem.

Careful medical supervision during slow withdrawal of corticosteroids cannot be emphasized, and patients should also be advised to increase the dose or reintroduce the drug during periods of stress unrelated to the asthma.-We are, etc.,

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Pneumomediatin and Diabetic Hyperpnoea

SIR,—The letters reporting pneumomediatin in association with diabetic hyperpnoea by Dr. H. S. Brodbrib (21 December, p. 773) and by Dr. N. W. T. Grieve and others (18 January, p. 186) following our report (23 November, p. 493) suggest that this association is probably not as rare as the scarcity of previous reports suggests. The occurrence of pneumomediatin twice at an interval of five years in Dr. Brodbrib's patient may indicate, as he suggests, a congenital weakness of the alveolar wall. I suggested the same possibility to account for the occurrence of pneumomediatin complicating bronchopneumonia and measles bronchopneumonia respectively in siblings.1

Another hypothesis would be that certain patients— for instance, some pulmonary infections, measles, and diabetic ketoacidosis—may have a specific weakening effect on the alveolar wall. The experience of this hospital, where pneumomediatin has been a not uncommon complication of measles, and of Block,2 who described a group of patients with measles similarly affected, certainly sug- gests some specific alveolar damage in measles.

The woman described by Dr. Grieve and others differed from our patient and that of Dr. Brodbrib in that respiratory symptoms probably antedated the diabetic coma, and that in hospital changes in the lung were found on radiography, so that it is possible that the respiratory infection precipitated both the pneumomediatin and the coma.

I am, etc.,

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REFERENCES

Amputations for Ischaemia

SIR,—We would like to comment on the leading article on amputations for ischaemia (11 January, p. 69), where a case of amputation for arteriosclerotic vessel occlusion is a frequent operation which merits careful attention, as it is a reconstructive procedure to produce a new organ of locomotion in conjunction with a prosthesis.

Taking into consideration the success of the patellar tendon-bearing prosthesis we feel that every effort should be made to achieve a below-knee stump with a knee joint. The Gritti-Stokes operation gives better healing in comparison with the through-knee amputation, but the stump is very rarely weight-bearing, and these patients are usually fitted with an ankle-knee type of prosthesis complete with an ischial tuberosity

Putting his arm across to pull himself up, his sleeve caught in the gears. Fortunately the drill was engaged in hard rock and the rotation slow, so that while his arm was being drawn in the unfortunate victim was able to wave and shout for help. The noise of the machinery prevented his cries from being heard, and had it not been for the camp cook coming out of the cookhouse and casually glancing up the outcome would probably have been fatal. The drill being stopped, this 19-year-old managed to extricate himself from his clothing, leaving his arm behind, and single-handed and unaided he climbed down the metal ladder to the 100 ft. (30.5 m) level below. He was then driven 45 miles (72 km.) to Drum- heller Hospital, where I saw him.

There was no shock and the blood pressure was normal. A sleeve of skin hung loosely against the chest wall. The whole arm had been avulsed, including the scapula and the outer one-third of the clavicle. In theatre the skin was separated to show the stump of the subclavian artery beating regularly at 70 per minute in the centre of a bloodless field. I doubt if more than a cupful of blood had been lost from the torn vascular ends, which certainly corresponds with Dr. Barziano's findings. All that was required was the application of a few "safety" ligatures, refashioning the flap, and drainage. Convalescence was uneventful.

This very remarkable young man (he died any pain—not until I reached hospi- tal, doc, and you came on the scene"), with grants from the Workmen's Compen- sation Board of the Province of Alberta, went on to qualify at university, and he is now, I believe, a schoolteacher.—I am, etc.,

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Avulsion of the Upper Limb

SIR,—Concerning Dr. I. Barziano's three cases of upper arm avulsion (11 January, p. 118) I have here a more extensive avulsion which I dealt with in Canada some 12 years ago.

The young man, a worker in the oil fields, had in the course of his duties to climb up the long ladder at the top of which is a platform with the uppermost part of the drill rotating in the centre.

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