principal differences are that *Coxiella burnetii* is not dependent on an arthropod vector, does not share the Proteus XK antigens, and produces a different disease complex in man. The creation of a new genus *Coxiella* within the family Rickettsiaceae is therefore justified in the eyes of the distinguished authors of Bergey.¹ I cannot help but agree with them and suggest that if the "criteria" of Dr. Smith were adopted taxonomy would frankly be impossible.—I am, etc.,

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REFERENCE

- ¹ Bergey's *Manual of Determinative Bacteriology*, edited by R. S. Breed, E. G. D. Murray, and N. R. Smith, 1957, 7th ed., p. 947. Baltimore.

some play a similar role in the implantation of the human egg as they do in the rat.—We are, etc.,

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REFERENCES

- ¹ Cohen, S., Bitensky, L., Chayen, J., Cunningham, G. J., and Russell, J. K., *Lancet*, 1964, 2, 56.
² Woessner, J. F., jun., and Brewer, T. H., *Biochem. J.*, 1963, 89, 75.
³ Wood, J. C., and Psychoyos, A., *C.R. Acad. Sci. (Paris)*, Ser. D., 1967, 265, 141.

Lysosomes and Menstruation

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. Cohen¹ 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.

In 1963 Woessner and Brewer² 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 studies³ 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 substrate² 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 means 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 lyso-

Scientists in Medicine

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 on your leading 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.

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REFERENCE

- ¹ Report of the Committee on Hospital Scientific and Technical Services, 1967-8. H.M.S.O., London.

Steroid "Pseudorheumatism" in Asthma

SIR,—The introduction of disodium cromoglycate (Intal, FPL 670) into the therapeutic regimen for asthma has allowed reduction, or even withdrawal, of corticosteroid drugs in many patients in whom this had not previously been possible, and so-called steroid "pseudorheumatism"¹⁻³ 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 unaffected patients. Details of previous corticosteroid treatment in the affected group are shown in Table II.

TABLE I.—Features of Asthma

Patient	1	2	3	4	5	6	7	8	9
Sex	F	F	F	M	F	F	M	M	F
Age (years)	31	26	42	50	60	51	34	49	52
Age of onset of asthma (years)	1	2	9	11	54	47	32	35	31
History of sensitivity	+	+	+	+	+	+	0	0	0
Prick skin test reactions	+	+	+	+	+	+	+	+	0
Broncho-pulmonary aspergillosis	0	+	0	+	0	+	0	0	0

TABLE II.—Details of Prednisone Therapy

Patient	1	2	3	4	5	6	7	8	9
Duration (years)	12	1.7	0.6	10	5	2.5	2.25	10	12
Average daily maintenance dose (mg.)	10	10	12.5	10	2.5	10	7.5	7.5	10
Daily dose at onset of symptoms (mg.)	0	0	2.5	1	0	1	0	2.5	2
Period of reduction (months)	3	5	1	3	2	6	5	2	0
Period to symptoms (months)	3	5	3	3	3	6	6	3	2

The clinical features of the steroid "pseudorheumatism" were similar to those previously described.¹⁻³ Generalized aching, stiffness, and loss of strength and energy occurred in all. Aching in the upper arms 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 asymmetrically: 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 painful and tender. Other symptoms included periods of restlessness in five patients, memory loss for recent events in two patients, paraesthesia of the fingertips in five patients, and anorexia in one patient. In one patient, who had intrinsic asthma, painful and tender indurated nodules 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 proportion to the signs and no radiographic changes were seen.

Haemoglobin, white cell count, erythrocyte sedimentation rate, serum sodium, potassium, and chloride, blood urea, serum calcium, phosphorus, and alkaline phosphatase, blood sugar, serum uric acid, and total serum proteins and electrophoresis, were all within normal limits. Latex, Rose Waaler, and antinuclear factor tests were negative, and L.E. cells were not demonstrable.

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 only one of these (No. 8). 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, 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 prednisone 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 "pseudorheumatism" 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) on increasing the prednisone from 2.5 to 6 mg. per day. There was some doubt about whether it is wise to increase the dose of corticosteroid to control symptoms in all cases, because some patients in whom this had been done subsequently redeveloped symptoms at the higher dose.¹ In two patients (Nos. 3 and 5) the symptoms were controlled by indomethacin 25 mg. thrice daily. Aspirin and paracetamol were of no value. As the "pseudorheumatic" symptoms persisted over a number of weeks, treatment became necessary in seven of the nine patients affected.

The pathogenesis of the steroid "pseudorheumatism" 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 tetracosactrin.

Similar symptoms have been reported in healthy volunteers, following a single dose of prednisolone 40 mg. when plasma 17-hydroxycorticosteroid levels were falling but were still within normal range.⁴ With the advent of new drugs, such as disodium cromoglycate, in the symptomatic treatment of asthma, steroid "pseudorheumatism" and other steroid withdrawal symptoms are likely to become a pressing clinical problem.

Careful medical supervision during slow withdrawal of corticosteroids cannot be over-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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- 2 Slocumb, C. H., *Bull. rheum. Dis.*, 1952, **3**, 21.
- 3 Slocumb, C. H., *Proc. Mayo Clin.*, 1953, **28**, 655.
- 4 Good, T. A., Benton, J. W., and Kelly, V. C., *Arthr. and Rheum.*, 1959, **2**, 299.

Pneumomediastinum and Diabetic Hyperpnoea

SIR,—The letters reporting pneumomediastinum in association with diabetic hyperpnoea by Dr. H. S. Brodribb (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 pneumomediastinum twice at an interval of five years in Dr. Brodribb'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 pneumomediastinum complicating bronchopneumonia and measles bronchopneumonia respectively in siblings.¹

Another hypothesis would be that certain diseases—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 pneumomediastinum has been a not uncommon complication of measles, and of Block,² who described a group of patients with measles similarly affected, certainly suggests some specific alveolar damage in measles.

The woman described by Dr. Grieve and others differed from our patient and that of Dr. Brodribb in that respiratory symptoms probably antedated the diabetic coma, and that inflammatory changes in the lung were found on radiography, so that it is possible that the respiratory infection precipitated both the pneumomediastinum and the coma.—I am, etc.,

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REFERENCES

- 1 McNicholl, B., *Arch. Dis. Childh.*, 1960, **35**, 389.
- 2 Block, T., personal communication, 1964.

Avulsion of the Upper Limb

SIR,—Concerning Dr. I. Barziano's three cases of upper arm avulsion (11 January, p. 118) I report 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 of a drilling rig at the top of which is a platform with the uppermost part of the drill rotating in the centre.

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 ground 100 ft. (30.5 metres) or so below. He was then driven 45 miles (72 km.) to Drumheller 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 denied any pain—"not until I reached hospital, doc, and you came on the scene"), with grants from the Workmen's Compensation 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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Amputations for Ischaemia

SIR,—We would like to comment on the leading article on amputations for ischaemia (11 January, p. 69), with full agreement that 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 and to save the 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 above-knee type of prosthesis complete with an ischial tuberosity