this field, after studying large numbers of subjects of all ages,[1-3] would probably consider them to be unrealistically high as a guide to the lower limit of normality. It is also difficult to know what importance can be attached to the findings of a low total bone value in a narrow trephine (0·3 cm) bone biopsy sample since it is known that there may be wide variations in the individual patient depending upon the site selected.[3]

Regarding the number of patients with osteomalacia, we are told that osteomalacia was diagnosed when the osteoid index was 0·8% or more, since the index was less than 0·7% in all normal subjects. It is well recognized that it is unreliable to diagnose osteomalacia merely on the basis of an excess of osteoid. This is particularly the case in azotaemic renal osteodystrophy where excess osteoid formation may be a feature of osteitis fibrosa associated with increased osteoblastic activity even in the absence of osteomalacia. The diagnosis of osteomalacia can be difficult in these circumstances and it is necessary to take cognizance of the amount of osteoid, the width of osteoid seams, and the nature and distribution of the calcification front.[4]

Regarding osteitis fibrosa, apparently this was diagnosed and graded on the number of identifiable areas of bone "scalloping." The main difficulty here is that resorption of bone in these sick patients may not necessarily be due to osteitis fibrosa, and it is desirable to take into account the number of osteoclasts and amounts of marrow fibrosis and woven bone formation.[4]

One final point concerning the time of onset of osteomalacia in azotaemic renal osteodystrophy. Recent published work[4] based on detailed quantitative histology of bone is in keeping with the view that the first bony abnormality to arise is usually osteitis fibrosa due to secondary hyperparathyroidism, with subsequent development of a mineralization defect and osteomalacia. This concept is also consistent with the results of studies of serum parathyroid hormone levels in patients with chronic renal failure.[5]—I am, etc.,

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Q-fever Endocarditis

SIR,—In Dr. Graham W. Hayward's Croonian Lecture (23 June, p 706 and 30 June, p. 764) on infective endocarditis *Rickettsia burneti* is mentioned as a causative organism in the section on vegetations but ignored in the sections on diagnosis and treatment. Though it is not considered to be a common cause of the disease, four cases have been diagnosed in this laboratory in the past six years. It is therefore our practice to look for antibodies to *R. burneti* in a specimen of blood collected during the time blood cultures are being taken from cases of infective endocarditis. The diagnosis is made by the demonstration, not of a rising titre because this is a chronic infection, but of high titres of antibody to both phase 1 and phase 2 antigens. Dr. Hayward's recommendation that "bacteriologically negative patients should be treated as if they had a resistant organism such as the enterococcus" implies that patients suffering from Q-fever endocarditis should be treated with the ineffective combination of penicillin and streptomycin, although evidence is accumulating that other antibiotics may at least arrest the progress of the disease. Tetracycline has been used successfully either alone[1-4] or combined with lincomycin,[5] co-trimoxazole[6] or chloramphenicol.[7]

In this connexion we are able to quote the outcome of case 6 of Kristinsson and Bentall,[7] the only patient in their series who was considered unsuitable for surgery. He terminated his tetracycline treatment in December 1967, after about 10 months, and had no more antibiotic therapy. He required digoxin and diuretics to control his cardiac failure but continued working intermittently as a car park attendant. His antibody titres to *R. burneti* fell during treatment and then appeared to stabilize, the results for the last two sera being:

Date	Phase 1	Phase 2
10 December 1968	1/160	1/160
5 December 1969	1/160	1/80

He died in August 1971 after a road traffic accident. At necropsy there was mitral stenosis but the other valves were normal. The vegetations on the mitral valve were fibrosed and no rickettsiae were seen in them. Some of this tissue was inoculated into guinea-pigs; they did not develop antibodies to *R. burneti*. We suggest that this patient's Q-fever endocarditis was cured by tetracycline and chloramphenicol.

In view of the successes claimed for both medical and surgical treatment we consider that the early diagnosis of infective endocarditis due to *R. burneti* is important. The delay involved in waiting until other forms of treatment have failed may result in serious valvular damage.

We are grateful to Drs. A. J. B. Edwards, M. George, and R. B. H. Tierney for information about this patient.

—We are, etc.,

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Epidemiology of Simple Hypospadias

SIR,—Professor H. Campbell and his colleagues (7 July, p. 52), using data relating to malformations notified to local health authorities in England and Wales in 1967-71, show that the incidence of hypospadias did not vary according to the month of birth. They point out that this finding differs from that reported by Dr. C. J. Roberts and Mrs. S. Lloyd (31 March, p. 768) from South Wales, where there were fewer cases than expected in pregnancies commencing in the period April-September (corresponding broadly to January-June births). Two earlier studies also gave conflicting results. One carried out by the College of General Practitioners in 1954-60[1] showed no seasonal variation, but in the United States Wehrung and Hay[2] reported an appreciable excess of cases among infants born in the first half of the year.

These inconsistencies prompted us to look at our records relating to hypospadias in Birmingham births. We examined two 10-year periods, 1950-9 and 1963-72, but since the two distributions were similar we have combined them into a single table. Like Dr. Roberts and Mrs. Lloyd we have excluded cases associated with other malformations. Expected numbers, based on the monthly distribution of all Birmingham births, represent the number of cases that would have occurred if the monthly incidence had remained constant.

Month of Birth	No. of Cases	
	Observed	Expected
January	26	26·9
February	21	24·8
March	20	28·1
April	31	26·9
May	31	27·7
June	26	26·5
July	24	27·0
August	30	25·8
September	25	25·9
October	27	25·5
November	29	23·8
December	24	25·1

The close agreement between observed and expected numbers leads us to conclude that in Birmingham, as in the country as a whole, there is no appreciable seasonal variation in the incidence of hypospadias.—We are, etc.,

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Lithium Toxicity in the Newborn

SIR,—Although reports to the Registrar of Lithium Babies (Dr. M. Schou and others, 21 April, p. 135) include two infants "floppy" at birth and one case of perinatal asphyxia out of a total of 113 liveborn infants, there have been no detailed reports published of problems encountered in the neonatal period in infants delivered to lithium-treated mothers whose serum lithium was below the toxic level of 2 mEq/l.[1] Toxic symptoms have been noted in one infant whose serum lithium level was 2·4 mEq/l. on the second day of life but whose mother's level, post-delivery, was 4·4 mEq/l.[2] Silverman *et al.*[3] noted no long-term effects in an infant whose serum lithium level was 1·1 mEq/l. at birth, but a degree of hypotonia was present for 48 hours.

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