nisms isolated from the pregnant patients when compared with women with acute "cystitis," both groups coming from the same geographical area.[6] It cannot, therefore, be valid to make the comparison in your editorial as support for geographical variation in sulphonamide resistance.—We are, etc.,

R. N. GRÜNEBERG

Department of Bacteriology,
University College Hospital,
London W.C.1

D. S. REEVES

Department of Bacteriology,
St. Mary's Hospital Medical School,
London W.2

1 The Bacteriology Committee of the Association of Clinical Pathologists, *Journal of Clinical Pathology*, 1965, **18**, 1.
2 Grüneberg, R. N., and Brumfitt, W., *British Medical Journal*, 1967, **3**, 649.
3 Williams, J. D., and Smith, E. K., *British Medical Journal*, 1970, **4**, 651.
4 Mond, N. C., Percival, A., Williams, J. D., and Brumfitt, W., *Lancet*, 1965, **1**, 514.
5 Williams, J. D., Brumfitt, W., Leigh, D. A., and Percival, A., *Lancet*, 1965, **1**, 831.
6 Williams, J. D., and Leigh, D. A., *British Journal of Clinical Practice*, 1966, **20**, 177.

SIR,—I read your leading article on treatment of bacteriuria in pregnancy (12 December, p. 631) with interest but feel some points need clarification. The studies on treatment which we did in north London[1] did show that a high cure rate of bacteriuria was obtained with a short course of chemotherapy but there are certain features of the population in central areas of industrial cities which make the introduction of a single-dose regimen a necessity for many patients. Many are at work, have large families, and generally lead harassed lives. The addition of a further supply of tablets to their iron and folic acid, antiemetics, and aperients results in some variation in rate at which the tablets disappear. It is sometimes necessary to test the urines of patients for antimicrobials to confirm they are continuing treatment.

The reason why streptomycin was added to sulphonamide given to our patients was because of the relatively common occurrence of sulphonamide resistance in Birmingham. The effect of the streptomycin on these strains was shown in Table III of our paper (12 December, p. 652) and the figures (11 cleared out of 15 compared to 2 out of 11 with sulphonamide alone) are significant (p=less than 0·05).

Finally there are the problems of toxicity and teratogenicity. These cannot be dealt with adequately in a letter but important information on the skin reactions to long-acting sulphonamides was obtained during the epidemic of meningitis in Morocco in 1967, when 110,000 people were treated with sulphadoxine.[2] Marked differences were found between people treated with single doses and multiple doses. After multiple therapy, cutaneous reactions occurred in 1·4% of 61,318 patients, with 10 deaths. After single-dose therapy only 5 minor skin reactions were found in 36,673 patients—an incidence of 0·013%.—I am, etc.,

J. D. WILLIAMS

Department of Pathology,
Dudley Road Hospital,
Birmingham 18

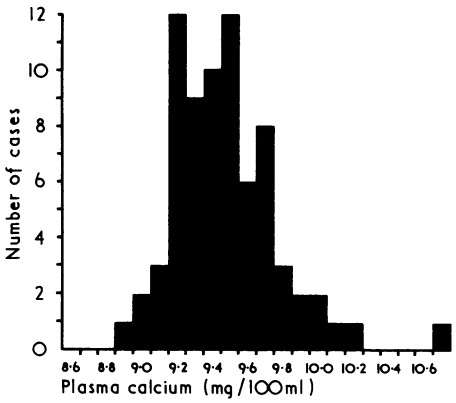
1 Williams, J. D., Brumfitt, W., Leigh, D. A., and Percival, A., *Lancet*, 1965, 1, 831.
2 Bergoend, H., Löffler, A., Amar, R., and Maleville, J., *Annales de Dermatologie*, 1968, **95**, 481.

Idiopathic Hypercalciuria and Hyperparathyroidism

SIR,—We welcome the attempts of Dr. P. Adams and others (5 December, p. 582) to develop provocative tests for the diagnosis of hyperparathyroidism but we are concerned at the implication in their paper that a large proportion of patients now diagnosed as suffering from idiopathic hypercalciuria will prove to have parathyroid adenomata. This is not our view nor is it our intepretation of the results they describe. In particular we question the validity of their normal range for serum calcium.

The demonstration of significant hypercalcaemia requires the careful determination of normal ranges in individual laboratories.[1 2]

We base our normal range (8·9-10·2 mg/100 ml) on data obtained by our colleague Mrs. M. Forbes, and shown in the Figure. Plasma calcium levels were determined in duplicate using emission flame photometry in 73 normal volunteers after a full overnight fast. Reproducibility in determinations on the same specimen was ± 1%. The values for calcium were corrected for changes in plasma specific gravity.[1 3] The subject with the value of 10·7 mg/100 ml has been kept under observation. His calcium level has risen slightly and his plasma phosphorus has fallen. We think he has hyperparathyroidism but since he remains well and free of symptoms parathyroid surgery has not been undertaken. He clearly belongs to a different population from the other 72 subjects; hence our normal range of 8·9-10·2 mg/100 ml.



Distribution of plasma calcium in 73 normal volunteers. The values are corrected for changes in plasma specific gravity.[1 3]

We consider that conclusions based on ranges of normal as wide as those described by Dr. Adams and his colleagues (9·0-10·7 mg/100 ml) are open to suspicion. Nor are we surprised that they found parathyroid tumours in some of the 19 patients they reported since most of these had fasting plasma calcium levels above 10·0 mg/100 ml. We suspect hyperparathyroidism in any patient with renal stones when the fasting plasma calcium is above 10·0 mg/100 ml in our laboratories. Among the first 300 patients with parathyroid tumours successfully diagnosed and treated at University College Hospital almost 100 had uncorrected fasting plasma calcium levels below 11·0 mg/100 ml. As a further diagnostic measure in these cases with marginal hypercalcaemia we determine the important plasma ionized calcium level using the method of Rose[4] with modifications. While we entirely agree with the final conclusion of Dr. Adams and his colleagues that their 19 patients may represent two different populations, we think these might have been distinguished in large part by more adequate definition of their upper limit of normal for serum calcium and by direct determination of the ionized calcium component. This would greatly lessen the number of indications for provocative tests.

During the last 20 years at University College Hospital and in consultation elsewhere we have seen only six proved cases of hyperparathyroidism with unequivocally normal total plasma calcium levels. In each of these definite, though always minimal, hypercalcaemia was demonstrated later, before surgical exploration was undertaken. During the same time among the many patients referred with renal stones we have seen about 50 patients with idiopathic hypercalciuria who had unnecessary and unrewarding surgical explorations of the neck performed elsewhere. Fortunately the number of these cases has been diminishing in recent years. We regret the implication (unsupported as we see it by adequate evidence) that perhaps half the patients diagnosed as idiopathic hypercalciuria may be suffering from hyperparathyroidism. We fear that this might lead to a new crop of unnecessary operations for hypercalciuria, a mistake we have not yet made ourselves.—We are, etc.,

D. R. DAVIES
C. E. DENT
LYAL WATSON

University College Hospital,
London W.C.1

1 Dent, C. E., *British Medical Journal*, 1962, **2**, 1419, 1495.
2 Watson, L., in *Modern Trends in Endocrinology*, ed. H. Gardiner-Hill and F. T. G. Prunty. London, Butterworths, in press.
3 Dent, C. E., and Watson, L., *Lancet*, 1968, **2**, 662.
4 Rose, G. A., *Clinica Chimica Acta* 1957, **2**, 227.

SIR,—In the interesting paper from Cambridge (5 December, p. 582) hypercalcaemia was provoked in 5 of 19 patients with renal stone by phosphate deprivation. The mechanism by which alteration in dietary inorganic phosphate produces a change in urinary excretion of calcium has caused speculation, and we have recently added to this.[1]

We gave a diet with a very low content of calcium and magnesium to normal adults, patients with hyperparathyroidism, and patients also with renal stones but without hyperparathyroidism, to see if we could distinguish so-called "idiopathic" hypercalciuria from "borderline" hyperparathyroidism. Similar marked renal conservation of both minerals occurred in all the subjects, and the test was a failure. It is also implied that the definition of hypercalciuria is not easy.

We recorded a significant drop in plasma calcium over 10 days on the diet, and as our patients with hyperparathyroidism showed normal renal conservation we agree with MacFadyen and colleagues[2] that lowered urinary calcium on reducing calcium intake can be explained by reduction in glomerular filtered load without change in tubular reabsorption. Variation in phosphate intake altered urinary calcium and magnesium in the normals and in hyperparathyroidism, and we think that this also can be attributed to change in filtered load on change in plasma calcium. Eisenberg[3] has pointed out that decrease in urinary calcium on phosphate loading occurs in normocalcaemic hypoparathyroidism, so that the effect was unlikely to be due to change in tubular reabsorption from alteration in secretion of parathyroid hormone. The Cambridge group have shown lowered phosphate intake may raise the plasma calcium, and earlier Eisenberg[4] reported low phosphate intake exaggerates hypercalcaemia in hyperparathyroidism. Changes in urinary calcium on phosphate loading or deprivation can now be well explained.