urinary excretion of calcium even when differences in glomerular filtration rates were disregarded. As possible explanations for their observation of maximum excretion during the period May-September, with a zenith in July or August, they mentioned changes in dietary calcium intake and the seasonal variations which the serum level of 25-hydroxycholecalciferol (25-OHCC) is known to undergo, or possibly a combination of both, since the zenith of serum 25-OHCC occurs later than that of the urinary calcium excretion.

We have studied the same problem by performing simultaneous determinations of the 24-hour urinary calcium excretion and the 24-hour clearance of creatinine in 26 healthy volunteers taking a standard diet. The estimated contents of this diet were 800 mg of calcium, 900-1100 mg of phosphorus, and 60-140 mmol (mEq) of sodium per day and 1 g of protein per kg body weight per day. There were 17 male subjects aged 21-29 (average 24) years and nine females aged 20-54 (average 34) years. Twelve, including five females, were studied from May to September inclusive and 14 (four females) from October to April inclusive. Assessment was undertaken as well of the 24-hour urinary calcium excretion, both uncorrected (UCaV (mg/24 h)), and corrected for variations in the clearance of creatinine (Ccr (ml/min)) according to the formula $(UCaV \times 100)/Ccr$. The importance of relating UCaV to Ccr in one way or another has been stressed repeatedly.¹⁻⁴ As evaluated by Student's *t* test the clearance-corrected excretion was found to be significantly higher during summer, the mean ($\pm$ S.D.) being 225 ± 61 mg/24 h as against 165 ± 37 mg/24 h during the winter ($t = 3.115$, $P < 0.01$). The figures for uncorrected excretion were 230 ± 66 mg/24 h and 199 ± 47 mg/24 h respectively ($t = 1.404$, $P > 0.10$). Despite the small number of observations the monthly averages displayed a pattern (see fig.) very similar to that so nicely presented by Dr. Robertson and his colleagues.

This pattern was recognizable even when males and females were considered separately.

Our observations indicate that seasonal variations in the daily urinary excretion of

calcium may take place independently of dietary changes.—We are, etc.,

I. TRANSBØL
F. SCHØNAU JØRGENSEN

Medical Department F,
Gentofte Hospital,
Hellerup,

B. LUND
O. H. SØRENSEN

Medical Department E,
Frederiksberg Hospital,
Copenhagen,
Denmark

- 1 Nordin, B. E. C., Hodgkinson, A., and Peacock, M., *Clinical Orthopedics*, 1967, 52, 293.
- 2 Transbøl, I., et al., in *La Sarcoidose*, *Rapp iv Conf. Internat.*, p. 618, eds. J. Turiaf, and J. Chabot. Paris: Masson, 1967.
- 3 Transbøl, I., Hahnemann, S., and Hornum, I., *Acta Medica Scandinavica*, 1968, 184, 33.
- 4 Peacock, M., Robertson, G. W., and Nordin, B. E. C., *Lancet*, 1969, 1, 384.

Liver Flukes: a Warning

SIR,—I would like to correct a point in Dr. A. T. Hunt's letter (1 March, p. 510) dealing with liver flukes. The Tidenham epidemic¹ in fact occurred in the winter of 1968-9 and not in June 1972 as he states.—I am, etc.,

A. H. DAVIES

Chepstow, Gwent

- 1 Hardman, E. W., Jones, R. L. H. and Davies, A. H., *British Medical Journal*, 1970, 3, 502.

** The mistake was ours, not Dr. Hunt's, and was inadvertently introduced in transferring a reference from the text to the foot of his letter. The relevant passage should have read: "In my description of the Tidenham epidemic, published in June 1972. . . ." We apologize for any misunderstanding that this may have caused.—ED., B.M.J.

Schistosome Antigen in Transplanted Kidney

SIR,—I was enlightened to read of the demonstration of circulating soluble antigens and antibody in schistosomiasis by Drs. M. A. Madwar and A. Voller (22 February, p. 435). I have recently treated a patient with a long history of schistosomiasis (*Schistosoma mansoni*), nephrotic syndrome, and ultimate renal failure. Renal biopsy and nephrectomy studies revealed the glomerular hallmarks of immune-complex nephropathy. The patient received a renal transplant and subsequently underwent antischistosome therapy with niridazole. He developed a transient "one-shot" immune complex nephritis. With the use of specific anti-schistosomal adult worm antiserum the antigen was revealed in the glomerular mesangium of the transplant biopsy. Thus that "prerequisite for immune-complex disease" has been found in the kidney. These studies will soon be reported in full elsewhere.—I am, etc.,

DANIEL B. GOULD

Huntingdon Valley,
Pennsylvania, U.S.A.

Abuse of Fenfluramine

SIR,—Fenfluramine has been considered to be not a drug of abuse, because of initial unpleasant side effects.¹ Hawks² found no evidence of its abuse among addicts asso-

ciated with the addiction research unit. Götestam and Gunne³ showed that amphetamine-dependent subjects had no preference for fenfluramine against placebo. However, Levin⁴ described 60 drug-dependent young males who claimed to have used fenfluramine as a drug of abuse. Euphoria, derealization, and perceptual changes were reported effects. I wish to report a case of fenfluramine abuse.

The patient, a 28-year-old woman, was referred because she had been forging prescriptions for fenfluramine for the past six months. She had begun taking fenfluramine four years previously when her weight was about 170 lb (77 kg) and her height 5 ft 5 in (1.62 m). Initially she noticed nausea, vomiting, dizziness, and drowsiness on dosages of 80 mg a day. Weight loss was quite rapid, and for the past year she had remained at about 115 lb (52 kg). Her longest period of abstinence was six months. In the past seven months while taking on average 240 mg of fenfluramine daily she had noticed feelings of euphoria, excess energy, and little need for sleep. There was increased appetite and libido. There were no obsessional-compulsive symptoms. She found alcohol potentiated the effect of fenfluramine-induced euphoria. During this seven-month period she noticed increasing tolerance to the dosage. She had forged prescriptions on three or four occasions. She did not appear to have been abusing any other drug.

The patient's desire to lose weight was sufficient to overcome the initial unpleasant side effects. This pattern has been observed with more classical drugs of abuse—for example, morphine. There is little reference in the literature to the very obvious stimulant effect of fenfluramine found in this case.—I am, etc.,

H. P. ROSENVINGE

Knowle Hospital,
Fareham, Hants

- 1 Oswald, I., et al., *British Medical Journal*, 1971, 3, 70.
- 2 Hawks, D. V., *British Medical Journal*, 1970, 1, 238.
- 3 Götestam, K. G., and Gunne, L. M., *British Journal of Addiction*, 1972, 67, 39.
- 4 Levin, A., *British Medical Journal*, 1973, 2, 49.

Serum Muramidase Activity in Untreated Cancer

SIR,—We read with interest the paper by Professor E. H. Cooper and others (14 September, p. 662) on raised serum muramidase levels in colorectal cancer. They consider that the raised muramidase activity results from stimulation of the reticuloendothelial system. It is accepted, however, that muramidase is mostly derived from disintegrating granulocytes and that serum muramidase levels are an index of granulocyte destruction.^{1,2} When granulocyte production equals destruction muramidase levels are also an index of granulocyte bone marrow production,¹ and they have been used for monitoring recovery of granulopoiesis in patients with neutropenia.^{2,4} The results, however, were unreliable in patients with fever and bacterial infection,² since in cases of bacterial infection serum muramidase levels are raised owing to increased destruction.^{2,5}

We measured by the turbidometric method of Litwack⁶ the serum muramidase levels in 120 patients with various untreated malignant tumours, including 20 cases of colorectal cancer, and compared them with the levels in 50 controls. All were within the normal range and there was no significant difference between the patients and the controls. This agrees with the findings of Jollès et al.⁷ Our patients with colorectal

cancer were fewer than those of Professor Cooper and his colleagues but we included only selected cases. Patients with bacterial infection, confirmed by the nitroblue tetrazolium test,⁸ were excluded. That raised serum muramidase levels may in some cases of untreated cancer be due to local bacterial infection cannot be ruled out, particularly in colorectal cancer, which often infiltrates the superficial layer of the mucous membrane. This may explain why only some patients have raised serum muramidase levels.

The observation that bacterial infection is associated with raised serum muramidase levels prompted us to measure these in 40 patients, of whom 28 had a local and 12 a systemic infection. Some of the patients had cancer and others did not. The serum muramidase level was raised in all of the patients with systemic infections but in only five of the 28 with local infections. All of these five had cancer and their local infection was in tissue surrounding the neoplasm. The nitroblue tetrazolium test was positive in four out of the five.

Our findings lead us to believe that a raised serum muramidase level in some cancer patients is only a secondary phenomenon and is of no diagnostic or prognostic value.—We are, etc.,

W. W. JEDRZEJCZAK
M. SIEKIERZYŃSKI

Clinical Department of Radioisotopes,
Institute of Postgraduate Medical Education,
Warsaw, Poland

- 1 Hansen, N. E., *British Journal of Haematology*, 1973, 25, 771.
- 2 Hansen, N. E., Andersen, V., and Karle, H., *British Journal of Haematology*, 1973, 25, 485.
- 3 Hansen, N. E., et al., *Journal of Clinical Investigation*, 1972, 51, 1146.
- 4 Guerry, D., et al., *Journal of Clinical Investigation*, 1973, 52, 3220.
- 5 Szmitowski, S., et al., *Folia Haematologica*, 1974, 101, 935.
- 6 Litwack, G., *Proceedings of the Society for Experimental Biology and Medicine*, 1955, 89, 401.
- 7 Jollès, P., Sternberg, M., and Mathé, G., *Israel Journal of Medical Sciences*, 1965, 1, 445.
- 8 Park, B. H., Fikrig, S. M., and Smithwick, E. M., *Lancet*, 1968, 2, 532.

Hepatitis in Selective IgA Deficiency?

SIR,—The unique observation of Benbassat *et al.*¹ that hepatitis occurred in five out of 12 patients with selective deficiency of serum IgA led them to suggest that increased susceptibility to hepatitis may be due to the defect in their local and humoral immune mechanisms. Tests for hepatitis B surface antigen and antibodies (HBsAg and anti-HBs respectively) were not carried out on those five patients for establishing the differential diagnosis of hepatitis. Since Ogra² has demonstrated specific IgA antibodies to HBsAg in exocrine secretions, Benbassat *et al.* suggested that a defect in the normal protective action of IgA in the alimentary tract combined with the defect in humoral immunity could result in a tendency to infections by viruses, particularly when the portal of entry of the viruses is the gut.

Selective absence or deficiency of IgA has been a subject of particular interest to us since the first demonstration of serious anaphylactic transfusion reactions caused by class-specific anti-IgA.³ In further pursuit of this investigation Vyas *et al.*⁴ have formed a registry of healthy blood donors selectively lacking IgA (aIgA). A total of 83 aIgA donors and 30 donors with IgA deficiency were tested for HBsAg using solid-phase

radioimmunoassay (AUSTRIA™, Abbott) and for anti-HBs using hemagglutination assay.⁵ A control group of healthy age- and sex-matched donors with normal levels of IgA were concurrently investigated. None of the sera were positive for HBsAg; the incidence (3.8%) of anti-HBs was similar in the aIgA and IgA-deficient persons in comparison with the control group. These data lead us to believe that persons lacking IgA or deficient in IgA have no overt susceptibility to hepatitis B virus infection.—We are, etc.,

G. N. VYAS
G. K. BASANTANI
H. A. PERKINS

Department of Clinical Pathology
and Laboratory Medicine,
University of California Medical Center, and
Irwin Memorial Blood Bank,
San Francisco, California

- 1 Benbassat, J., Keren, L., and Zlotnic, A., *British Medical Journal*, 1973, 4, 762.
- 2 Ogra, P. L., *Journal of Immunology*, 1973, 110, 1197.
- 3 Vyas, G. N., Perkins, H. A., and Fudenberg, H. H., *Lancet*, 1968, 2, 312.
- 4 Vyas, G. N., et al., *Journal of Laboratory and Clinical Medicine*, 1975. In press.
- 5 Vyas, G. N., and Shulman, N. R., *Science*, 1970, 170, 332.

Ischaemic Heart Disease in Young Women

SIR,—Dr. F. M. Oliver (1 February, p. 267) has offered further information in support of his claim to have found hypertension in 34% of a group of young women suffering from ischaemic heart disease. He now tells us that in some of those whom he describes as hypertensive the clinical recognition was made after blood pressure measurement on more than a single occasion. Indeed, of those "with myocardial infarction" 28 out of 81 had a "diastolic blood pressure of 100 mm Hg or more recorded on three or more separate clinical examinations."

What we still do not know is how many of these patients were found to have been hypertensive before their infarction. Does the phrase "with myocardial infarction" mean that in all of them it was found retrospectively? It would seem so, to judge by Dr. Oliver's reply to my comments on the influence of ischaemic heart disease upon the electrocardiographic diagnosis of left ventricular hypertrophy, his only remaining index of hypertension since in his original paper (2 November 1974, p. 253) he says nothing of retinal or necropsy findings. He agrees that "previous myocardial infarction" virtually excludes the contribution that S-T and T-wave changes can make to the recognition of such hypertrophy while maintaining nonetheless that increases in the relevant S and R waves "showed" the condition in 23% of his infarction patients. No doubt all R waves so robust as to withstand anterior infarction deserve respect, but are not these values also of doubtful significance in the presence of a damaged and perhaps dilated myocardium?

Certainly, if Dr. Oliver found some of these women to have diastolic levels of 100 mm Hg on repeated examinations spread over weeks this would suggest that most of them had been mildly hypertensive before their infarction even though the recordings were made a year later. But an association between hypertension and angina cannot justify his inference that "hypertension is an important pre-infarction risk factor in young women." This is the view long nourished by

the Framingham studies. It derives, however, from a process of reasoning that equates symptoms with ischaemic heart disease regardless of morbid change. My own feeling is that there is better evidence to suggest that hypertension commonly provokes angina (and infarction rarely but rather more readily in women than men) in subjects whose coronary vessels have already been damaged by atheroma and moreover that it plays no more than a slight and occasional part in the genesis of that atheroma.—I am, etc.,

I. MCD. G. STEWART

Victoria Hospital,
Blackpool

Women Doctors in the N.H.S.

SIR,—The letter from Dr. Nancy K. Shrubshall (8 March, p. 573) is ungenerous to women doctors, and for a psychiatrist (and a woman) she shows some lack of perception. Of course her male colleagues treat her with absolute fairness, and it is right that they should do so since she is willing to work (and apparently to think) entirely on their terms. I wonder why she views her profession as a procrustean bed on which you can lie only if your limbs have been stretched or chopped to fit?

It is easy to sneer at women doctors for "gratifying their maternal instincts." Does she feel the same about men who gratify their political, sporting, artistic, or paternal instincts while practising medicine or are all male doctors actively engaged in saving life for 24 hours every day? A great many women doctors do manage to hold the balance between work and family without detriment to either—much more difficult and rewarding than "eating your cake and having it." But penal taxation and unfair discrimination in pensions and allowances are harder burdens to bear than unkind words.

If totalitarian and antifeminist attitudes were ever to return us all to the *Kinder, Küche, Kirche* world of the past, then even Dr. Shrubshall's freedom to practise as she wishes might be lost. It would be wiser surely to exhibit a little more tolerance and allow other women their freedom too.—I am, etc.,

MARY DUGUID

Wallasey

SIR,—Dr. Nancy K. Shrubshall (8 March, p. 573) is apparently under the impression that enabling married women doctors to work is an act of charity, of no benefit to anyone except those fortunate ladies themselves.

After 10 years' hard work I am a reasonably well-informed efficient G.P. Whom does it benefit if I now give up for 16-20 years to bring up the children I regard as welcome members of the family, not optional extras? There is plenty of work to be done and plenty of willing employers with flexible timetables. I do not feel it unreasonable to expect some financial gain after paying basic essentials such as electricity bills, rates, etc. Fillet steaks, Dr. Shrubshall, have long ceased to be part of the family menu.—I am, etc.,

SUSAN M. HAMMOND

Exeter