used. The recent modification of this method by obtaining a single blood sample three to five hours after injection (Mr. M. Fisher and Dr. N. Veall, 7 June, p. 542) simplifies the technique further. We would like to comment on the clinical value of this modification, using data from approximately 300 patients in which the G.F.R. was measured by a two-component analysis³ of the ⁵¹Cr-EDTA clearance curve, using seven blood samples taken within five hours of injection.

We have found a similar trend to that obtained by Mr. Fisher and Dr. Veall when two, three, four, and five hour regressions are used, confirming the value of the method when the G.F.R. is normal or moderately reduced (> 30 ml/min). There is reduction in accuracy when the G.F.R. falls below this level, but a further blood sample taken after another two or three hours enables the single-slope method of analysis to be used, with considerable improvement in accuracy.

The optimum timing of a single blood sample for greatest accuracy appears to depend on the level of the G.F.R., with a two- or three-hour sample appropriate for estimation of high values and a four- or five-hour sample more suitable for low values. The suggestion that correction for body surface area may improve accuracy is not borne out by our data, and body weight correction is also of little value, implying that individual differences in ⁵¹Cr-EDTA distribution are not significantly influenced by these parameters.

The simplicity of a single blood sample outweighs the modest improvement in accuracy obtained with multiple samples and we welcome this modification. For serial follow-up of individual renal problems reproducibility is more important than absolute accuracy, and we find that the single-sample technique proves adequate for this purpose.—We are, etc.,

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- ¹ Garnett, E. S., Parsons, V., and Veall, N., *Lancet*, 1967, 1, 818.
- ² Chantler, C., *Clinical Science*, 1969, 37, 169.
- ³ Sapirstein, L. A., et al., *American Journal of Physiology*, 1955, 181, 330.

Adjustment to Low-dose Heparin to Prevent Thrombosis

SIR,—Your leading article on "Low-dose Heparin and the Prevention of Venous Thromboembolic Disease" (23 August, p. 47) is, I think, a very fair summary of current opinion. However, there is one point I tried to make at the King's College Hospital meeting that I believe will make this regimen even more effective.

It has been known for a long time that the results of various clotting tests involving the addition of heparin are short relative to controls in many of these patients.¹ This indicates that the patients have an excess of heparin neutralizing activity (H.N.A.). There is evidence that this H.N.A. in the plasma may represent platelet factor 4 liberated from "activated" platelets.² However, irrespective of the origin or the theoretical significance of this H.N.A., wide differences are found clinically; particularly high activity occurs in

acute deep vein thrombosis³ and in acute myocardial infarction⁴ and this must influence the effect of the heparin therapy.

In general I am sympathetic to the concept of giving a single standard dose per ampoule twice or thrice daily. Nevertheless, it seems only rational to make some allowance for the amount of heparin which will be immediately neutralized. Monitoring the heparin level (for example, by the method of Denson and Brennar⁵) is not easy in a busy routine laboratory and is probably not justified except in special cases, but a single pre-treatment assay of H.N.A. is easy and quick. It has not yet been shown whether adjusting the dose to the patient's weight and the current level of H.N.A. is in fact beneficial, but logically such adjustment should give better protection and decrease the risk of haemorrhage. I am, and I hope others are, working on this problem.—I am, etc.,

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- ¹ O'Brien, J. R., *Thrombosis et Diathesis Haemorrhagica*, 1974, 32, 116.
- ² O'Brien, J. R., et al., *Lancet*, 1974, 2, 656.
- ³ Green, P. J., *Lancet*, 1975, 1, 799.
- ⁴ O'Brien, J. R., et al., *Journal of Clinical Pathology*, In press.
- ⁵ Denson, K. W. E., and Brennar, J., *Thrombosis et Diathesis Haemorrhagica*, 1973, 30, 471.

Urinary NAG Activity in Renal Disease

SIR,—The paper by Mr. J. M. Wellwood and others (16 August, p. 408) on urinary N-acetyl- β -D-glucosaminidase (NAG) raises several points which are worthy of comment.

In expressing enzyme activity, "nmol h⁻¹" would surely be better converted to U or mU as defined in the Enzyme Commission recommendations,¹ which would avoid the possible confusion between hours of incubation time and hours of urine output.

The authors state that there is no age dependence of urinary NAG excretion, but more details would have helped, since in fig. 1 there is an increase in mean value with age which seems to be quite marked for males when the first decade is excluded. The apparent fall in mean excretion for females between the fourth and fifth decades is also interesting since this would coincide with the time of the menopause; is this of any significance?

The authors express urinary enzyme excretion in relation to urinary creatinine output in order to avoid variations in daily urine volume and to avoid timed collections of urine. They then continue by noting increased NAG excretion in patients with renal disease and in particular those with increased serum creatinine. But is it not possible that the apparent increase in NAG excretion results from a reduced creatinine output in the urine, which may be present in renal disease with elevated serum creatinine, and not from a true increase in NAG excretion rate? Unfortunately details of the urinary creatinine output are not given in the paper. The NAG values given in the paper can be accepted as being due to a true increase in NAG excretion rate only if it has been shown that there is normally a significant direct correlation between NAG excretion rate and urinary creatinine output, so that a fall in urinary creatinine is associated with a fall in NAG excretion. Then in renal disease an increase in NAG expressed per mg creatinine

will truly be due to an increased excretion rate of the enzyme.

The problem of timed collections has been overcome for urinary γ -glutamyl transferase by using a random sample where the time interval from the previous voiding is known.² An excretion rate can thus be calculated and this has produced no problems due to excessive changes in urine volume or to variation in excretion rate throughout the day.—I am, etc.,

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- ¹ International Union of Biochemistry, *Enzyme Nomenclature*, Amsterdam, Elsevier, 1965.
- ² Beck, P. R., M.Sc. Thesis, University of Birmingham, 1974.

Myocardial Scanning

SIR,—We were interested in the paper by Dr. J. T. Innes and others (30 August, p. 517) on myocardial scanning using ^{99m}Tc-stannous pyrophosphate, having ourselves used a similar technique in 52 patients with suspected myocardial infarction. A rectilinear scanner rather than a gamma camera was used, thus making it within the resources of most district general hospitals. This was mounted on a simple mobile frame so that scanning could be performed at the bedside with minimal disturbance to the patient. A dose of 8 mCi of the isotope was found sufficient.

Positive scans were found from 17 hours to 18 days after the onset of symptoms. We found the anterior scan to be the most useful view, an abnormal result being indicated by asymmetry about the sternum. When infarction was "definite" from the story, electrocardiogram, and enzyme changes the scan was positive in all of 15 patients, when "likely" in 12 of 16, and when "doubtful" in nine of 21.

Heart scanning using ^{99m}Tc-stannous pyrophosphate seems useful in the assessment of suspected myocardial infarctions. These preliminary studies suggest that it is reliable, safe, sensitive, and of particular value when previous damage makes electrocardiographic interpretation difficult and when raised enzyme levels cannot be attributed with confidence to the heart.—We are, etc.,

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Malaria in Scotland

SIR,—During 1970-4 104 cases of malaria were reported from laboratories in Scotland.¹ Twenty-six of these admitted to this department fell into three categories.

All 13 Asians had been visiting Asia after living in the United Kingdom for several years. None had taken malaria prophylaxis, though before starting their trip most had acquired smallpox vaccination, which could have provided an opportunity for advising on antimalarials.

The two West Africans in the series had both discontinued long-term pyrimethamine on leaving Africa and subsequently developed falciparum infection. With increasing use of