and were accordingly thought to have M.S., four had results between 45.4 and 47.7% and were thought to have other neurological or psychiatric (O.N.D.) diseases. No last patient gave a 50.8% result—that is, in the normal range—and her transient disability was thought to be a toxic manifestation of oral contraceptives.

Since the nephropathy of Devic’s disease (neuropatheliasis) has long been the subject of debate we studied two clear cases of this condition and both gave results in the O.N.D. range.

Your article (like that which appeared in the (letter)welcomes the association between measles and M.S. but passes over recent work in relation to other viruses, in particular the finding of high vaccinia antibody levels in the spinal fluid in M.S. Nor does it make reference to the extensive research of Daniels,1 who was able to demonstrate a striking association of antibodies against several viruses in M.S. but found no grounds for associating it specifically with measles.2—We are, etc.,

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Cerebral Oedema in Diabetic Ketoacidosis

SIR,—Dr. Jennifer S. Moore (30 August, p. 540) rightly emphasizes the dangers of rapid administration of hyperosmolar sodium bicarbonate solution to patients with diabetic ketoacidosis. The effect of lowering serum potassium with the induction of hyperosmolar states is well described, as is the paradoxical lowering of intracerebral pH. Dr. Moore does not, however, suggest how rapid intravenous bicarbonate infusion may induce cerebral oedema in this situation. In three of the four cases which she cites death appears to have occurred very soon after hyperosmolar (84%) intravenous bicarbonate was given, and no comment is made regarding the attempted resuscitative treatment administered during the ensuing cardiac arrest. Though the bicarbonate infusion may well have precipitated the fatal arrhythmia, it is not possible to conclude that this therapy produced the cerebral oedema found in necropsy, as cerebral oedema is not inordinately found after cardiac arrest per se.3 This is said to result from the excessive anoxia at the time of cardiac arrest, though the literature on the pathophysiology of this phenomenon is extensive and no succinct explanation is available.

In the case described by Dr. Moore and myself (26 July, p. 20) we witnessed the (O.N.D.) levels of bicarbonate (24%) over three hours, at which time the blood pH was 6.7 and the actual bicarbonate level was unrecordable. The severe metabolic acidosis was exacerbated by pre-existing renal failure, and in this extreme situation we felt that careful administration of intravenous sodium bicarbonate was justified. It is not clear therefore whether the hypokalaemia in this situation could produce cerebral oedema, though paradoxical lowering of the pH of the cerebrospinal fluid (C.S.F.) and brain may have further depressed cerebral oedema, although a post mortem examination of the brain tissue would tend to reverse a shift of fluid from blood to C.S.F. and brain rather than promote it.

Dr. Moore is correct, however, in advocating the use of an isotonic solution (142%) of sodium bicarbonate for patients who have severe plasma hyperosmolality, where this is indicated by the degree of acidosis.—I am, etc.,

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Certification of Death

SIR,—Your leading article on the Government’s proposed implementation of the Brodrick report (30 August, p. 506) opposes such legislation on the ground that accurate mortality statistics are necessary for the identification of environmental hazards. As a district community physician and a crematorium referee, I would be the last to disagree with such a contention except that I cannot see that, for all the wad of forms to be completed, the cause of death is one iota more accurate under this system than under the one to be adopted.

The “ordinary medical attendant” or some acceptable substitute completes form B. He accordingly suggests a post mortem is carried out, nobody can gain anything. The second doctor, in the absence of necropsy, simply rubber-stamps the opinion of his colleague—what other option has he in most cases? The referee can only look through the papers to see that the law has been complied with (in spirit only on occasion)—the stipulation of “ordinary medical attendant” becomes somewhat meaningless in these days of large partnerships and that the cause of death is reasonably consonant with the time scale over which it occurred and adequate in indicating true causes rather than effects. It is not possible for a general practitioner to date the cause of death in detail and, assuming there is no suspicion about the death, many an inadequate cause must pass unqualified. What a chore it would be to correct every epidemiological hollow. Could any mortuary stand the consequent opprobrium?

Thus I confess that, however much it may brand me a blackleg, I must support the proposed legislation and suffer the modest loss of emoluments with fortitude, seeing in your own leading article a regrettable lack of realism.—I am, etc.,

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Estimation of Glomerular Filtration Rate

SIR,—A single-shot isotope method for the determination of the glomerular filtration rate (G.F.R.) has obvious attractions to the clinician seeking information on overall renal function as an initial screening or follow-up procedure. Hard-pressed nursing staff share this enthusiasm as urine collections are avoided. The 51Cr-EDTA clearance correlates well with 24-hour endogenous creatinine clearance, and the single-shot method of analysis described by the authors, using three four blood samples, is now widely
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 with the component analysis of the $^{51}$Cr-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, and four hours 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 for low levels. 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 $^{51}$Cr-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 gives adequate for this purpose.

—We are, etc.,

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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) expressed the general view of experts. However, there is one point I tried to make at the King’s College Hospital meeting that I believe will make this regime 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. This indicates that the patients have an excess of heparinase more suitable for low values. There is evidence that this H.N.A. in the plasma may represent platelet factor 4 liberated from “activated” platelets. However, irrespective of the origin or the theoretical significance of this factor, the findings are clinically significant; particularly high activity occurs in acute deep vein thrombosis and in acute myocardial infarction 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 Benson and Brench) 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 obviously 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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3 Green, P. J., Lancet, 1975, 1, 799.

Urine NAG Activity in Renal Disease

Sir,—The paper by Mr. J. M. Wellwood and others (16 August, p. 408) on urinary N-acetyl-ß-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, 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 no 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 ß-glutamyl transferase by using a random sample where the time interval from the previous voiding is known. An excretion rate can thus be calculated and this has produced no problems due to ex cessive changes in urine volume or to variation in excretion rate throughout the day. —I am, etc.,

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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, using a gamma camera 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 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 diagnosis 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. Twenty-six of these had been 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 small area acclimatization, which could have provided an opportunity for advising on antimalarials. The two West Africans in the series had both discontinued long-term ptyramidine treatment leaving Africa and subsequently developed falciparum infection. With increasing use of