thyroxine 0.1 µg/100 ml, total fats 1,820 mg/100 ml, cholesterol 523 mg/100 ml, urea 516 mg/100 ml, creatinine 6.6 mg/100 ml, and uric acid 17 mg/100 ml. The glomerular filtration rate measured by creatinine clearance was 7 ml/min. The bladder was drained by an indwelling catheter and the patient was given triiodothyronine. After 10 days she recovered bladder control, the urea was 80 mg/100 ml, and the creatinine clearance 25 ml/min. The electroencephalogram became normal. After four months the urea was 42 mg/100 ml and the creatinine clearance 82 ml/min, and the patient was well in herself.

Though myxoedema has been shown clinically and experimentally to cause weakness of the bladder muscle⁴ we have not found any reports in the literature of renal failure occurring, as in our case. Retention of urine must now be included among the various clinical forms in which myxoedema presents itself.—We are, etc.,

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Toxic Amblyopia from Ibuprofen

SIR,—Your correspondent Mr. C. A. L. Palmer (23 September, p. 765) has reported an apparent further example of toxic amblyopia resulting from ibuprofen therapy. The treatment of patients suffering from rheumatic disorders may include several drugs capable of causing ocular side effects, and the situation may be further complicated by lesions due to the disease process itself, the effects of previous therapy, or coincident ocular disease in middle-aged and elderly patients. In this respect prospective studies involving "baseline" ophthalmic examinations may be helpful, and in a study of 34 patients suffering from rheumatic disorders who had not yet received ibuprofen abnormalities were found in six cases, including one example of macula degeneration and one of retinal pigmentation. An additional study involving 38 patients already receiving ibuprofen revealed three patients with evidence of visual field defects and pigmentary changes in the region of the macula, presumed to be degenerative, not associated with impairment of vision and remaining unchanged when therapy with ibuprofen was stopped for four months.

Nevertheless, the evidence that ibuprofen has caused toxic amblyopia is convincing in Mr. Palmer's patient and in two cases published by Collum and Bowen.¹ As these are the only examples so far reported in respect of ibuprofen—a drug that has achieved universal use in the treatment of rheumatic disorders—it would appear that this complication is rare. It was not encountered in a personal series of 293 patients treated during a five-year period² although visual symptoms were among the list of possible side effects considered during review of these patients. It is unlikely

that toxic amblyopia of such rapid onset and severity would have been missed.

Although it may be premature to draw conclusions from three cases, they seem to have had certain features in common. The symptoms of toxic amblyopia appeared early in the course of treatment and after a comparatively small dosage of the drug; the symptoms were sufficiently rapid in progression and sufficiently severe, especially the deteriorating visual acuity, to compel the patient either to stop the drug or to seek ophthalmic advice; and the signs and symptoms of toxic amblyopia disappeared within a few days or weeks of stopping ibuprofen. There is no evidence to date to suggest that ibuprofen has any toxic effect on the retina comparable to the changes seen with chloroquine preparations used in the treatment of rheumatoid arthritis.

Further examples of toxic amblyopia associated with ibuprofen therapy will almost certainly occur and should be reported to the Committee on Safety of Medicines and to the manufacturers, so that the frequency and significance of this side effect can be fully evaluated. In the meantime it would appear to be a rare, reversible, and troublesome but not dangerous effect, possibly limited to a few patients who have an especial liability.—I am, etc.,

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Blood Sugar Measurement by Dextrostix Reflectance Meter Method

SIR,—In suspected cases of asymptomatic diabetes we performed intravenous glucose tolerance tests in which blood sugars were determined by the hexokinase micromethod and by the Dextrostix reflectance meter method. Since the results by each method were in good agreement we expected a similar agreement in the glucose assimilation coefficient by either method. When determining the glucose assimilation coefficient from a semilogarithmic graph, however, we noticed that the regression line connecting the single blood sugar values showed a steeper slope in the Dextrostix reflectance meter method than in the hexokinase micromethod. Thus the coefficients were higher by the Dextrostix method.

The steeper slope was obviously due to higher results with Dextrostix blood glucose determinations at the beginning of the intravenous glucose tolerance test. This simulated a faster reduction in blood sugar levels during the test. Plotting all the comparative investigations ($n = 169$), a correlation of $r = 0.892$ for the whole range was obtained. The blood sugar values up to a level of 200 mg/100 ml were about 30 mg/100 ml lower by the Dextrostix method than by the hexokinase method. All values above 200 mg/100 ml were considerably higher by the Dextrostix method than by the hexokinase method.

The Dextrostix reflectance meter method should not replace routine laboratory methods in the supervision of diabetic patients, and it is not, in our opinion, exact

enough for detecting early diabetes.—We are, etc.,

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Mannitol Infusions and Lithium Excretion

SIR,—We investigated the immediate effects of infusions of mannitol 20% on lithium excretion in nine dogs. We infused 400 ml of the mannitol solution through the femoral vein at the same time as an isotonic solution of lithium chloride was perfused through another vein. As a result a significant increase ($P < 0.001$) was found in lithium excretion and the urine volume and the excretion of sodium and potassium also increased significantly. The initial excretion of lithium was 185.9 µEq/min and after mannitol it increased to 284.7 µEq/min in two hours. Plasma mean values of lithium showed no increase at the end of the second hour. They were 11.3 and 11.1 mEq/l. respectively before and after mannitol infusion.

On the other hand, the mean plasma level of lithium in another two control dogs who were infused with isotonic lithium chloride increased from 12.9 to 18.4 mEq/l. in two hours. So we concluded that infusion of mannitol 20% may be valuable in the treatment of lithium intoxication, in addition to haemodialysis,^{1,2} whereas other diuretics have no noticeable effect on lithium excretion.^{3,4}—I am, etc.,

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- 3 Foulks, J., Mudge, G. H., and Gilman, A., *American Journal of Physiology*, 1952, 168, 642.
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Cancer Research

SIR,—The publication as a Green Paper of Lord Zuckerman's report on cancer research¹ appears to me to be a prime example of the after-dinner story concerning the man who looked for his car keys under the nearest street lamp, instead of in the dark where he had lost them, because the light was better. The mammoth red herring that keeps being trailed across the path is that what we need is new ideas and not money in cancer research. The truth, I believe, is the very opposite. Almost without exception, when what is claimed as new is examined more carefully, it has been recorded in the literature previously and often a long time ago.

Though we may not wish to model our efforts with respect to cancer on the way that the Americans have used the money made available by President Nixon, I believe we should take the American space programme as our yardstick and set up a programme outside the present penny-pinching regimes. We need to give our mature and experienced scientists and clinicians, as well as our young and enthusiastic graduates, a worthwhile prospect for the future instead of the present three-and five-year grant system which greatly diminishes the attraction for those who have real talent to offer.

Sir Michael Woodruff, in a review lecture