ence with four other patients was less dramatic. One patient had acute typhoid fever and did not respond to two tablets (6 mg trimethoprim-30 mg sulphamethoxazole per kg body weight) but responded to three tablets. Another patient had paratyphoid A fever and continued to have positive blood cultures up to the 17th day while on the drug; blood was sterilized only when we doubled the dose. Two other salmonella paratyphi A urinary carriers with pretreatment positive blood cultures continued to have positive blood cultures up to the 8th and 21st day while on the drug again at the same low dosage (6 mg trimethoprim, 30 mg sulphamethoxazole per kg body weight). We have increased their dosage.

Based on this experience we recommend that other workers increase the dose according to body weight.—We are, etc.,

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Prolonged Corticosteroid Therapy

SIR,—My pleasure in reading that Dr. L. Westerhof and others (28 November, p. 534) have confirmed our conclusion that "... the therapeutic efficacy of small doses of corticosteroids is due to summation of exogenous and endogenous steroid, since small doses do not suppress secretion of cortisol by the adrenal"¹ was diluted by their dismissal of our work as not having been done on patients who had *prolonged* corticosteroid therapy. It is difficult to understand this misreading of our paper since we went out of our way to point out that the findings had been obtained in patients "... who had been taking corticosteroids for an average of 26 months. This dose was therapeutically adequate in all and had not been altered for an average of 15 months." One of the patients had in fact been taking corticosteroids continuously for 54 months. Our findings are therefore very relevant to the practical problem of prolonged corticosteroid therapy.

The therapeutic efficacy of doses of corticosteroids within the physiological range is still questioned by some, apparently because they believe these small doses will suppress pituitary-adrenal function. The paper by Dr. Westerhof and colleagues is therefore timely in drawing our attention once again to an aspect of applied physiology which has a good deal of therapeutic importance.—I am, etc.,

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¹ Shuster, S., and Williams, I. A., *Lancet*, 1961, 2, 674.

An Unusual Cause of Oesophageal Stricture

SIR,—A lady of 78, who was a mild diabetic, was admitted to hospital in June of this

year having swallowed a Clinitest tablet by mistake. Immediately after she felt a very hot burning sensation in her throat, and she started to sweat profusely and then to vomit. Her doctor correctly gave her the advice to drink large quantities of water, followed if possible by citrus fruit juice and olive oil, as the tablets are clearly marked "caustic" on the bottle. She was unable to drink very much as she was continuously vomiting. The next day the pain was a little better but she had dysphagia which rapidly progressed until she had to be admitted to hospital.

I oesophagoscoped her on three consecutive occasions, but the improvement did not last longer than two weeks before she again needed dilation. I did not think that she was suitable for a major resection which would be required to deal radically with the stricture at this level, so I inserted a Celestin tube. Since then she has remained well, but on one occasion recently, had to be re-admitted as her tube had become obstructed by food debris.

Clinitest tablets contain 38.5% of sodium hydroxide, and when one of these tablets is placed in a test tube of water a very considerable amount of heat is produced. One can well imagine the acute inflammation which occurred when this tablet was temporarily held up at the level of the aortic arch (fig.).—I am, etc.,

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Phenytoin Tolerance Tests

SIR,—Dr. A. J. Handley (25 July, p. 203) in following phenytoin concentrations after oral and intravenous administration of phenytoin found a biphasic plasma phenytoin disappearance curve in four patients who had been given 250 mg phenytoin intravenously. After initial high levels plasma phenytoin decreased to values below 3 µg/ml one to two hours after administration, followed by a secondary rise to values between 10 and 17.5 µg/ml.

During the last five years we have determined the phenytoin half-life in blood after

intravenous injection of 100 mg phenytoin to which 20µCi ¹⁴C-phenytoin was added. Thin-layer chromatography was performed on all serum extracts to ensure that all radioactivity was located in the phenytoin spot. The procedure has been described in detail elsewhere.¹ The radiophenytoin determination was usually done on blood samples taken 3 to 12 hours after the injection, because these values give a linear disappearance in a semilogarithmic system.² In 24 patients, however, we also determined the two-hour values and these were in all cases considerably higher than the three- and four-hour values. In the Figure the mean values of ¹⁴C-phenytoin in serum after intravenous injection in 24 patients are shown (A). In an additional four patients the disappearance curve was studied during the first two hours. These patients were given doses between 25 mg and 250 mg phenytoin intravenously. The mean values of these four cases are shown (B).

In no cases have we found biphasic curves as those reported by Dr. A. J. Handley. We have no explanation of this discrepancy.—We are, etc.,

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¹ Hansen, J. M., Kristensen, M., and Skovsted, L., *Epilepsia*, 1968, 9, 17.

² Hansen, J. M., Kristensen, M., Skovsted, L., and Christensen, L. K., *Lancet*, 1966, 2, 265.

Combination Chemotherapy in Acute Myeloblastic Leukaemia

SIR,—We read with great interest the report of Dr. D. Crowther and his colleagues (28 November, p. 513) on their favourable results in the therapy of acute myeloblastic leukaemia using intermittent chemotherapy. They rightly stress the advantages of multiple drug therapy (increased remission rates and drug synergy) and the disadvantages (the dangers of marrow hypoplasia). Hypoplasia occurs commonly in this disease, possibly because all marrow elements are abnormal. To avoid increasing these risks the drugs they use are carefully chosen and used only when bone marrow hypoplasia is not present.

More gentle therapy, designed to achieve more gradual elimination of the tumour