and acute respiratory infections. In fact, however, they did not count all episodes of respiratory infection but only those brought to the notice of general practitioners, assuming—perhaps wrongly—that both sets of parents had the same ideas on when to consult a doctor. This really leaves the question open whether these children suffer more respiratory infections or whether the parents who permit obesity in their children are more prone to consult doctors over any sort of problem, including respiratory disease.—I am, etc.,

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Urinary Tract Dilatation and Oral Contraceptives

SIR,—Dr. P. B. Guyer and Dr. D. Delany (5 December, p. 588) state that "oral contraceptives produce overdilatensibility of the upper urinary tract in some patients." This statement is based on six nulliparous patients who were judged to have overdilatensibility on intravenous urography and who had taken oral contraceptive pills from two to 11 months. All patients had a history suggestive of urinary tract infection; this was considered confirmed in only two.

The distensibility described is apparently identical to that seen in pregnancy—namely, affecting the right side more than the left and ending at the pelvic brim. In other words, these authors imply that some hormone or hormones (not specifically identified) can produce selective dilatation of the upper urinary tract. This therefore goes one step further than the hormonal school of pregnancy dilatation, who usually add "mechanical as well as hormonal factors influence dilatation."¹

I think it is almost certainly largely or totally irrelevant that these women have, at some time, taken a hormone pill; the findings can and should be interpreted on a simple anatomical basis, recognizing that infection may play a contributory and possibly major part. This belief is based on the following: (1) the distribution of pregnancy dilatation is pathognomonic and is due to pressure by the gravid uterus;² (2) the right ureter is more easily compressed than the left ureter at the pelvic brim;² whether this be by the gravid uterus or the Cuthbert Andrews apparatus used by these authors; (3) it is easier to compress the ureter through the softer, more compliant female anterior abdominal wall than the more muscular male; and (4) upper urinary tract infection may produce reversible or persistent ureteric dilatation.^{2,3}

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¹ Fairstat, T., *Obstetrical and Gynecological Survey*, 1963, 18, 845.

² Dure-Smith, P., *Radiology*, 1970, 96, 545.

³ Shopfner, C. E., *American Journal of Roentgenology*, 1966, 98, 172.

Blood Transfusions for Leukaemic Patients

SIR,—We wish to answer the questions posed by Dr. R. A. Cumming and his colleagues (2 January, p. 50) regarding the blood transfusion requirements in our

patients treated for acute leukaemia. We did not discuss this in the paper (28 November, p. 513) since we have no original data to present. The supportive care was standard but we used neither prophylactic antibiotics nor protected environments. Each patient received an average of eight units of packed red cells. A transfusion for anaemia was usually required on admission. A total of 65 units of platelets were given to five patients (one patient had 39 units). Three units of platelets per square metre body surface area were given at each transfusion. A total of 34 units of whole, fresh blood were given to eight patients. Three of these patients also received platelet transfusions. Overall the requirements in this group of patients were not significantly different from the requirements of similar patients treated in the past with less intensive chemotherapy.

All the stored blood and all the platelet concentrates were obtained from the Regional Blood Transfusion Centre at Brentwood, while the fresh, whole blood was provided by Red Cross donors at St. Bartholomew's Hospital. There were problems with the delivery of fresh, viable platelets since our regional blood transfusion centre is about 20 miles (32 km) from the hospital. This was the reason for fresh, whole blood being given on occasions. All the blood products given were ABO and Rhesus compatible with the patients concerned. In view of these difficulties platelet transfusions were not given prophylactically when the platelet count fell below 10,000 mm³. They were reserved for patients with haemorrhage into the urogenital, gastrointestinal, and respiratory tracts.

We hope to have a continuous cell separator available at this hospital in the future and this will ease our problems, since several units of platelets may be obtained from a single donor and road transport will not be required. The donors could be relatives of the patients concerned and this may help to avoid problems of incompatibility.

We agree with Dr. Cummings that there are many advantages in treating such patients at special centres.—We are, etc.,

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Renal Failure and Contrast Media

SIR,—For their recent paper (19 December, p. 717) Dr. J. McEvoy and his colleagues used the somewhat evocative title "Renal Failure after Radiological Contrast Media." It would be well to consider their data carefully before accepting that the four cases which they described provide good evidence of an aetiological association.

Of their cases, one (Case 2) surely did not merit inclusion, for not only was this patient suffering from myelomatosis (usually taken as a contraindication to the use of contrast media) but major surgery in the form of nephrectomy followed angiography, and many factors could have contributed to the postoperative rise in blood urea.

In their renal cases no details of radiological techniques were obtained nor was the quantity or type of contrast specified. Without such information comment must be limited, but clearly these factors would be of major importance in

Case 1 where selective renal angiography was completed to assess a space-occupying lesion in one kidney of an elderly patient with malignant hypertension, impaired renal function, and poor renal blood-flow.

Their other two cases both concerned renal failure following intravenous cholangiography, but in one of these (Case 4) the possibility existed on their own admission that renal failure could have been due to septicaemia; certainly the severe hypotension, tachycardia, and other features described might suggest bacterial shock syndrome, with its well-known risk of renal damage. No necropsy was carried out on this patient—the one death reported—and no renal histology was reported from any of the four patients.

Very large numbers of examinations using contrast media are undertaken all over the world—the numbers must run into many millions annually. There has been a conspicuous lack of reports of renal failure following such investigations and in this respect our own experience is similar. We have in the past reported our experiences with renal angiography, covering some 2,000 patients to that date, without observing evidence of renal failure.¹ We also reviewed much larger series by other authors; Leadbetter and Markland² and Beall *et al.*³ have commented on a total of 12,298 aortograms without observing renal failure.

At the present time in this hospital about 1,600 intravenous pyelograms and 175 aortograms are completed annually. Among the departments requiring these investigations is a large medical renal unit with a dialysis centre and a major surgical renal unit. Contrast procedures are undertaken at all stages of renal failure and we have yet to see any evidence of renal deterioration following the use of contrast material.

Dr. McEvoy and his colleagues make a valid point in the general observation that "the possibility of adverse side effects in any diagnostic procedure must be weighed against the usefulness of the information it may provide," but further evidence is required before accepting that there is any significant risk of renal failure following the orthodox use of contrast material.—I am, etc.

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¹ Robertson, P. W., Dyson, M. L., and Sutton, P. D., *Clinical Radiology*, 1969, 20, 401.

² Leadbetter, G. W., and Markland, C., *New England Journal of Medicine*, 1962, 266, 10.

³ Beall, A. C., Jun., *et al.*, *Annals of Internal Medicine*, 1964, 60, 843.

Trimethoprim-Sulphamethoxazole in Enteric Fevers

SIR,—With our further experience in the use of trimethoprim-sulphamethoxazole in the treatment of acute typhoid fever and chronic urinary salmonella carriers we suggest increasing and standardizing the dose at 10 mg trimethoprim, 50 mg sulphamethoxazole per kg body weight per day. Previously we used the standard dosage suggested for the drug—that is, two tablets per day for patients of less than 30 kg body weight, and four tablets per day for patients with higher body weight. This means that the dose for a 29 kg patient would be one-half that for a 30 kg patient.

Our preliminary results (8 August, p. 323) have been impressive, but further experi-

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 Clintest 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.

Clintest 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