pital for this purpose was not thought then to provide the safety margin that is desirable even in a procedure with such small risks as the termination of early pregnancy by this method. Until we had more experience of the method in hospital in Britain we were both of the opinion that safety must come first.—We are, etc.,

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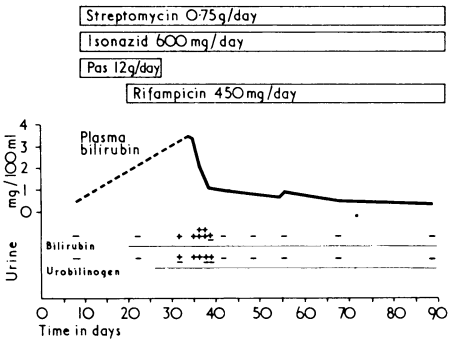
Rifampicin Jaundice

SIR,—I have recently seen asymptomatic jaundice in a 26-year-old female being treated for renal tuberculosis with streptomycin, isoniazid, and rifampicin. The jaundice began about 12 days after the start of rifampicin, lasted nine days, and resolved without change of therapy. The plasma bilirubin was 3·5 mg/100 ml. Transaminases and alkaline phosphatase were normal. The urine contained small quantities of bilirubin and urobilinogen (see Fig.). The patient received no other drugs.



In a report[1] of four cases of jaundice following rifampicin, important features were malaise and elevation of transaminases and alkaline phosphatase. In a French series[2] of 12 jaundiced patients with elevated transaminases associated with rifampicin, symptoms were not mentioned, but four alcoholic patients died of liver failure.

This case is reported to document two points of difference from other cases of jaundice complicating rifampicin therapy. The patient had no symptoms and there was no biochemical evidence of liver cell damage.

The patient was under the care of Mr. J. E. A. Wickham.

—I am, etc.,

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1 Lees, A. W., Asgher, B., Hashem, M. A., and Sinha, B. N., *British Journal of Diseases of the Chest*, 1970, **64**, 90.
2 Lesober, R., Ruffino, J., Teyssier, L., Achard, F., and Brefort, G., *Revue de Tuberculose et de Pneumologie*, 1969, **33**, 393.

Cyclophosphamide and the Bladder

SIR,—Your recent leading article on cyclophosphamide and the bladder (26 June, p. 726), together with a recent circular from W.B. Pharmaceuticals Ltd., prompts me to report two cases of carcinoma of the bladder in patients of Dr. M. Hulbert with lymphomas treated with cyclophosphamide.

The first patient had Hodgkin's disease diagnosed in 1958. Apart from deep *x*-ray therapy he was treated with a variety of drugs, including cyclophosphamide (100-150 mg daily) for two years (1966-8) and prednisolone 20 mg daily. In 1967 he developed troublesome urinary infections and first had haematuria in January 1968, while still on cyclophosphamide. Cystoscopy in December 1968 showed inflammatory areas with ulceration, which were diathermized. In April 1969 at a further cystoscopy a biopsy was taken of a raised area by Mr. K. Owen and reported on by Dr. R. C. B. Pugh as showing papillary transitional cell carcinoma with areas of squamous metaplasia.

The second patient had a lymphosarcoma diagnosed in 1967. He was given local deep *x*-ray therapy to a lesion in his retro-orbital region and because of lesions on his trunk was placed on cyclophosphamide 150 mg daily. He first developed haematuria in November 1970, which stopped when the drug was withdrawn, but recurred when the drug was restarted. Cystoscopy in June 1971 showed the bladder to be ulcerated, biopsy of one area showing the features one sees in cyclophosphamide cystitis. In addition there was a papillary lesion high up on the left side of the bladder, which on resection biopsy proved to be a stage 1 papillary transitional cell carcinoma.

The first patient was 49 and the second 67 when the bladder tumour was diagnosed, and they had been on cyclophosphamide for 2 and 4 years respectively. There is nothing unusual in a bladder tumour in this age group, but it is possible, though by no means certain, that the drug had some part to play in the pathogenesis of the tumour.

Since no bladder tumour has previously been described in association with cyclophosphamide cystitis I feel it is important to report these two cases and to advocate that bladder biopsies should always be carried out if suspicious areas are seen.—I am, etc.,

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Viper Bites

SIR,—Dr. A. W. J. Houghton (12 June, p. 650) queries the value of antivenom in poisoning from the bite of *Vipera berus* and mentions troublesome side effects. He also states that ". . . the rapidly beneficial effects of chlorpheniramine combined with hydrocortisone are undoubted." Although benefit from antihistamines and steroids in patients with viper bite poisoning has been claimed, to a critical mind the evidence is not convincing. The results of animal experiments using American viper venoms showed no benefit from steroids,[1 2] and suggested that antihistamines were contraindicated as they might aggravate hypotension.[2] A controlled therapeutic trial in patients with poisoning following bites of the Malayan pit viper showed no significant benefit from prednisone.[3] Personally, I agree with Chapman[4] that the sole benefit in snake bite from steroids or antihistamines lies in the control of sensitivity reactions to antivenom. And in my experience the most effective drug in combating anaphylaxis is adrenaline (provided it is promptly injected).

The controlled clinical trial in Malayan viper bites[3] showed that specific antivenom was very effective in combating systemic (though not local) poisoning. Provided antivenom is reasonably potent and specific for the poisoning being treated, and if it is given in sufficient dose by the intravenous drip route, it should be highly effective in reversing systemic poisoning. In the case described by Dr. Houghton the victim was bitten some years ago. At that time antivenom stocked in Britain was "Serum antivenimeux Aspis-Berus" made at the Pasteur Institute in Paris. Although labelled Aspis-Berus, it was made solely with *V. aspis* venom as antigen and I know of no evidence supporting its effectiveness in combating *V. berus* venom. In 1969 the Standing Medical Advisory Committee agreed that this antivenom should no longer be held at designated centres in Great Britain.[5] The matter is somewhat confused by the availability of a different antivenom made at the Pasteur Institute in Garches (not Paris) using as antigens the venoms of *V. aspis*, *V. berus*, and *V. ammodytes*. This should be more effective than the Paris antivenom in neutralizing *V. berus* venom but it is unrefined and thus more likely to cause sensitivity reactions than refined antivenom.

The Zagreb antivenom made with *V. ammodytes* venom as sole antigen is both highly refined[5] and remarkably effective in neutralizing *V. berus* venom. By the customary potency tests in mice, 10 ml of the Zagreb antivenom neutralizes 25 mg of *V. berus* venom (Lj. Higy-Mandić, personal communication, 1969). The venom yield of *V. berus* has been recorded as 10-18 mg dried weight.[6] In my opinion Zagreb antivenom, obtainable from the Institute of Immunology, Rockefellerova 2, Zagreb, Yugoslavia, should be stocked in a central hospital in each regional board area or in each county where adder bite is a possibility (virtually every county in England, Scotland, and Wales). This could obviate the nuisance, fuss, and delay of obtaining antivenom urgently from a distance when required for a patient with *severe* adder bite poisoning.[5] In such cases, as the Zagreb antivenom is so potent, the contents of one or at most two ampoules given by intravenous drip should suffice.—I am, etc.,

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1 Russell, F. E., and Emery, J. A., *American Journal of Medical Science*, 1961, **241**, 507.
2 Schöttler, W. H. A., *American Journal of Tropical Medicine and Hygiene*, 1954, **3**, 1083.
3 Reid, H. A., Thean, P. C., and Martin, W. J., *British Medical Journal*, 1963, **2**, 1378.
4 Chapman, D. S., in *Venomous Animals and Their Venoms*, ed. W. Bücherl, E. Buckley, and V. Deulofeu, Vol. 1, p. 523. London, Academic Press, 1968.
5 *British Medical Journal*, 1969, **3**, 370.
6 Minton, S. A., and Minton, M. R., *Venomous Reptiles*, p. 215. New York, C. Scribner, 1969.

Health Centre Design—a Criticism

SIR,—I refer to Dr. J. R. James's statements in his article "Health Centre Design—a Criticism" (15 May, p. 389). As the only general practitioner to have been on the Somerstown Health Centre Working Party since its inception I would like to say that certain of his statements may be misleading and others are a matter of opinion.

Among other matters, Dr. James states quite incorrectly that "In our case there has