maximum level of 17 l. of urine daily, 70 mOsm/l., with a free water clearance of 9.09 ml/min. The maximum therapeutic effect of Pitressin-tannate in oil twice daily and, subsequently, intranasal vasopressin (up to 70 drops daily; 1 ml=50 IU) reduced urine output to only 5-6 l./day. The specific gravity of the urine never rose above 1.006 and the patient was not relieved of symptoms of thirst and depression. Shortly after each administration there were strong, painful, and very prolonged uterine contractions. Because of the contraction she was switched over to intranasal drops of aqueous DDAVP. A dose of 15 µg DDAVP (three drops) was given eight hours into the nose. Her daily urine output immediately came down to 2 l. a day and urine specific gravity increased to 1.010-1.027, maximum 900 mOsm/l. There was no uterine or other reaction to this dosage, and thirst and depression disappeared. When antithyroid drugs were omitted the daily urine output on the same DDAVP dosage increased to 3 l. a day.

A fortnight before her calculated term, the patient gave spontaneous birth to a fully-developed baby. The patient continues to be maintained on DDAVP at her own insistence, and shows no signs even of local mucosal irritations in the nose. The results are summarized in the Figure.—I am, etc.,

D. ORAVEC

IIIrd Clinic of Internal Medicine,
The Comenius University,
Bratislava, Czechoslovakia

B. LICHARDUS

Institute of Experimental Endocrinology,
Slovak Academy of Sciences,
Bratislava, Czechoslovakia

- 1 Zaoral, M., Kolc, J., and Sorm, F., *Collection of Czechoslovak Chemical Communications*, 1967, 32, 1250.
- 2 Andersson, K. -E., and Arner, B., *British Medical Journal*, 1971, 3, 111.
- 3 Vavra, I., et al., *Lancet*, 1968, 1, 948.

Pyrexia with Cytosine Arabinoside

SIR,—Fever is stated to be an unusual side effect of cytosine arabinoside.¹ We have recently treated a 67-year-old man with acute myelomonocytic leukaemia in whom a remarkable febrile reaction occurred. We were initially unaware that this could be attributed to cytosine and contemplated a variety of explanations which we were unable to substantiate. Blood and urine cultures, viral studies, serological tests for brucellosis, and chest radiographs were all normal. The

following report is submitted to draw attention to this complication.

The patient's first symptom was severe pain in the abdomen over a grossly enlarged spleen. Acute myelomonoblastic leukaemia was diagnosed from blood and bone marrow features. The blood film and haemoglobin electrophoresis were also characteristic for β -thalassaemia trait. Though the blood contained 30,000 blast cells per μ l the patient was neither neutropenic nor thrombocytopenic. In view of his curious mode of presentation we considered that the acute leukaemia may have supervened on an undiagnosed pre-existing chronic myeloproliferative disorder, but we have no objective evidence to support this.

Treatment was started with intravenous daunorubicin (110 mg on the first day only) and cytosine arabinoside (72.5 mg 12 hourly for five days). The temperature is shown in the Chart. From the start of the treatment the patient had periodic severe rigors. It can be seen that the fever subsided after the completion of the course of treatment. The next schedule of treatment 12 days later employed half as much daunorubicin and cytosine as the previous course. The patient developed an erythematous itching skin rash over his trunk which subsided after 10 days.

When the third therapeutic course was begun one week later at full dosage the patient had been afebrile for a fortnight. Within a few minutes of administration of the first dose of both drugs he developed a rigor and the temperature rose to 39°C. Subsequent doses of cytosine were given with 100 mg hydrocortisone and no further reactions have taken place.

It is intriguing that after it had been concluded that cytosine arabinoside was responsible for the hectic exacerbation of

pyrexia the result of a toxoplasma dye test was received which was strongly positive. The initial titre was 1:2,000, rising to 1:4,000 after three weeks. Perhaps a previously quiescent toxoplasma infection became active with the development of the acute leukaemia and may have been responsible for the less striking pyrexia which flanked the cytosine therapy.

We are grateful to Professor M. H. Lessof for permission to publish this report of a patient under his care.—We are, etc.,

M. S. ROSE
D. N. BATEMAN

Guy's Hospital,
London S.E

1 Upjohn Ltd., Literature on Cytosan.

Potentialiation of Barbiturate by Ouabain

SIR,—In view of the current concern over the unexpected marked increase in bioavailability of digoxin present in Lanoxin tablets I should like to draw attention to the possible clinical significance of some experiments I have been conducting concerning a barbiturate-cardiac glycoside interaction.

These experiments, performed in mice, have shown that a pronounced increase in barbiturate potency can be brought about by ouabain through a direct interaction at the level of the central nervous system. Since the ratio of therapeutic dose to toxic dose is small for the cardiac glycosides, and since their toxicity is made manifest by central nervous symptoms, the possibility of unexpected increases in barbiturate potency in patients receiving combined cardiac glycoside and barbiturate therapy should be borne in mind, particularly when a change of dosage form results in increased bioavailability of the cardiac glycoside.

These findings have been submitted in extenso for publication in *Archives Internationales de Pharmacodynamie et de Thérapie*.—I am, etc.,

N. S. DOGGETT

Department of Pharmacology,
University of Wales Institute of Science and
Technology,
Cardiff

Neurological Deficits in Primary Polycythaemia

SIR,—We wish to report a similar case to that of Dr. M. Kremer and others (22 July, p. 216).

In 1969 a man aged 58 with chronic schizo-