showed crystal clear fluid under normal pressure. Microscopic examination showed no cells, and the protein content was 35 mg./100 ml.

It was postulated that the hypertensive crisis might be a consequence of the drug therapy. In case the administration of pethidine was a contributory factor, she was treated with a forced acid diuresis and a minimal urine pH of 4.8 was obtained. The blood pressure started to fall and by 10 hours after the ingestion of Meprobamate the level of 130/70 had been reached. The blood pressure remained normal during the rest of her stay in hospital, and on follow-up one month later she was normotensive and asymptomatic with minimal headache.

Sympathetic amines contained in preparations for the symptomatic relief of nasal congestion are made up in free- or slow-release forms. Tonks and Lloyd referred to two cases taking monoamine-oxidase inhibitors in whom the use of a slow-release form of phenylpropanolamine resulted in the development of a severe headache, and in one case status epilepticus, but only slight elevation of blood pressure. A marked rise in blood pressure was shown experimentally by Dr. Curtberr and colleagues, using phenylpropanolamine in the free form in subjects taking monoamine-oxidase inhibitors. The present patient supports their suggestion that severe hypertensive crises may be seen commonly with amines in their free form than with slow-release preparations. On the other hand there may be little difference in the incidence with which both types give rise to severe headache.—We are, etc.,

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REFERENCE

Hypertension from Cold Remedies

A 36-year-old man was admitted to a hospital with a history of severe headache of sudden onset the hour previously. This was associated with vomiting and photophobia; in addition, she had had a fit while still at home, after which she remained drowsy and confused, but was still complaining frequently of the headache, which was frontal and vertical. She had some neck stiffness and a positive Kernig's sign. The plantar responses were extensor, but there were no focal signs in the nervous system, although a learning to develop a transient right hemiparesis. She was normotensive, and full physical examination did not reveal any further abnormalities. A lumbar puncture contained subarachnoid haemorrhage, and cerebral angiography suggested the possibility of a left posterior communicating aneurysm. She was managed conservatively, and a positive uncertainty in the x-ray findings and because of her long-standing somewhat hysterical personality. There were frequent attacks of recurrent bleeding, and she made a complete recovery.

Questioning revealed that she had been taking phenylzine 30 mg. daily for six months, and that a few hours before her subarachnoid haemorrhage she had taken two Mucron tablets. This proprietary nasal decongestant contains 30 mg. phenylpropanolamine in each tablet, plus vitamin C, phenacetin, and ipecacuanha.

Although we (like Tonks and Lloyd in their cases) consider that hypotension in similar circumstances) did not observe the blood pressure to be raised, it seems likely that sudden severe hypertension caused by the interaction of phenylzine and phenylpropanolamine is a frequent occurrence in ays like this. About three hours passed before the onset of the headache after taking the Mucron and a further three hours before the blood pressure was taken. It is feasible that the rise for the blood pressure to have risen to dangerously high levels and fallen again. Dr. Cuthbert's experiments on himself with a monoamine oxidase inhibitor and phenylpropanolamine were quite rightly cut short with phenolamine, and so we do not have any evidence as to how long to expect the blood pressure to remain raised in such circumstances.

I would like to thank Dr. R. N. Tattersall for his permission to publish the details of this case history.—I am, etc.,

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REFERENCE

Amanzipm and Urticaria

Sir,—I read with interest the papers dealing with adverse reactions to drugs in your issue of 1 March (p. 527), and, in particular, that by Dr. Nathan and Professor O. L. Wade (p. 531). In their summary the authors suggest that "larger surveys of adverse reactions in relation to drug usage in the hospital" might contribute to the problem." In common with most other pharmaceutical manufacturers, we maintain extensive coverage of the international medical and allied scientific literature on all drugs, including studies of adverse reactions and side-effects. I feel, therefore, that it may be of general interest to present our findings with ampicillin, which was reported by Dr. Hurwitz and Professor Wade as having produced eight maculopapular pruritic rashes in 103 patients treated, an incidence of 7.8%.

Our most recent figures show that a total of 13,638 patients treated with ampicillin as been reported in the literature. Of these, 383 (2.8%) experienced skin reactions of various kinds. The description and incidence of rashes varies from observer to observer; careful observation of the patient and post-treatment follow-up tends to produce a higher reported incidence. Of the rashes recorded in the literature 58 cases were described as urticarial, 23 as macular, and 114 as maculopapular (including the so-called "multiform" type); the remaining were classified in other types of rash, and 169 skin reactions were of an unspecified nature.

The rashes reported during ampicillin therapy fell into two broad categories—that is, urticarial and "other dermatological" reactions. These categories are regarded as a sign of true penicillin hypersensitivity, and there is no evidence to suggest that ampicillin is associated with a higher incidence of this type of rash than other penicillins. The majority of the erythematous rashes are apparently ampicillin-specific and do not indicate true penicillin hypersensitivity. They commonly start as a faint erythema, often with a centrifugal distribution. They are usually associated with a maculopapular rash, which is often confluent. It may be difficult to decide how many cases of rashes in the literature were ampicillin-related; in some patients it may even disappear without discontinuation of the antibiotic. In a few cases, however, it becomes a generalized severe erythema, sometimes with swelling and tenderness. The rash may arise during the course of therapy, sometimes as late as after the drug has been stopped for several days after the end of treatment, and for this reason it has been called the "5-day rash." Subsequent courses of the antibiotic may not necessarily reproduce the reaction.

In a limited number of patients with this type of rash, investigation so far have been unable to demonstrate circulating antigenic antibodies in the serum. It is now well established that...