drapes; (2) high relative humidity in the room; (3) preoperative dehydration; (4) atropine and other anticholinergic drugs.

Heatstroke is a highly fatal disease unless promptly treated. But it is also a preventable disease. Surgeons and anaesthetists should consider what can be done to alter the conditions in the operating-room and the condition of the patient. As a single important way to prevent fatal heatstroke in the operating-room, I suggest monitoring of body temperature during operation. This is easily done, and, because the patient is unconscious, can provide the only clue to diagnosis in time.—I am, etc.,

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Outpatient Anaesthetics

SIR,—Dr. R. K. Gilbert (8 March, p. 637) draws attention to the necessity of considering the anaesthetic problems of outpatient operating, and thereby does a service to anaesthesia. However, we can assure him that for the series in question (Mr. J. A. Williams and Dr. D. Dean and Dr. B. R. Wilkinson (18 January, pp. 174 and 176)),

surgeon and anaesthetist have been in the closest possible liaison from the beginning of the study.

Anaesthetic aspects of outpatient operating were not included in the original publication because we, as the consultant anaesthetists associated with the team, have found that these aspects do not constitute a problem, and no departure from our usual practice is necessary or desirable. Modern anaesthesia makes possible prompt awakening of the patient, and a great freedom from postoperative vomiting and "hangover," provided the traditional opiate premedication is avoided. We do not think the traditional opiate premedication is desirable for inpatients either, for a variety of reasons which are also relevant to the outpatient.¹

Of course, success in outpatient operating is greatly dependent upon a careful selection of the patients, attention being paid particularly to their general health and their social conditions. This selection has been performed most successfully by the surgeon and the general practitioners. The decision to allow the patient to return home the same day rests with the anaesthetist. In no case has it been necessary to retain the patient in hospital.—We are, etc.,

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REFERENCE

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Fresh Onions and Blood Fibrinolysis

SIR,—*Allium cepa*, the common onion, has been investigated by several workers¹⁻⁶ and has been found to contain a hypoglycaemic agent. However, the active principle responsible for the hypoglycaemic effect was found to be very unstable.⁷

Recently my colleagues and I⁸ demonstrated that fried or boiled onions increased the blood fibrinolytic activity. The study reported below is a follow-up of our previous findings, and was undertaken to discover if the property which causes this increase in fibrinolysis was present in the raw onion or brought about by the process of heating (boiling or frying).

Effect of Fresh Onions and the Water in which Onions were Boiled on Fibrinolytic Activity

Euglobulin Lysis Time (in units)

Sub-jects	Day 1			Day 2			Day 3			Day 4		
	Breakfast Only			Breakfast + Liquidized Fresh Onions			Breakfast + Liquidized and Strained Fresh Onions			Breakfast + Water in which Fresh Onions were Boiled		
	9.30 a.m.	11.30 a.m.	12.30 p.m.	9.30 a.m.	11.30 a.m.	12.30 p.m.	9.30 a.m.	11.30 a.m.	12.30 p.m.	9.30 a.m.	11.30 a.m.	12.30 p.m.
1	15.6	13.2	13.0	18.2	27.0	27.6	14.9	24.1	24.4	16.4	12.3	12.1
2	13.3	3.2	3.4	14.2	22.9	21.7	18.1	31.2	31.1	16.6	12.1	12.2
3	65.9	37.9	36.2	77.2	116.7	103.3	73.7	110.9	117.7	74.7	50.6	47.9
4	35.9	25.7	25.8	45.8	77.0	74.6	38.9	64.5	62.1	31.7	22.9	21.6
Mean	32.7	20.0	19.6	38.9	60.9	56.8	38.9	57.8	58.8	34.9	24.5	23.5

Four volunteers were included in the study. On day 1, after fasting, samples of blood were collected for the estimation of the euglobulin lysis time using the method described by von Kaulla⁹ slightly modified.¹⁰ The fibrinolytic activity has been derived from these lysis times and expressed in units by multiplying the

reciprocal of these lysis times in minutes by 10,000.¹¹

After the withdrawal of the blood samples mentioned the volunteers were given a breakfast (at 9.30 a.m.) containing a total of 39.8 g. of fat and new samples of blood were collected after two and three hours. On day 2 the procedure was repeated, but this time 60 g. of liquidized fresh onions were added to the meal. On day 3 the method was identical with that outlined above, the only difference being that this time the 60 g. of fresh onions were liquidized and strained to discard big lumps and fibres and the rest was added to the meal. On the fourth day 60 g. of onions were boiled for more than two hours and then the water in which they were boiled was added to the meal. The volunteers

were made to rest throughout the experiment, since a previous study had shown that moderate exercise increases the fibrinolytic activity.^{12 13} Smoking was not permitted.

The Table shows the fibrinolytic activity of the four volunteers. The results indicate

that after ingestion of breakfast the fibrinolytic activity is decreased. The addition of fresh onions not only prevented this reduction but caused a marked increase. The water in which the onions were boiled had, however, no effect on the fibrinolytic activity.

The results show that the property which causes an increase in the fibrinolytic activity is inherent in the fresh onions and not brought about by heating. The results also confirm that the factor responsible for the increase in fibrinolytic effect is not water-soluble. In the previous study⁸ we had shown that the factor is not only heat-stable but probably not water-soluble.—I am, etc.,

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"Cold" Cures and Monoamine-oxidase Inhibitors

SIR,—Prompted by the recent article (15 February, p. 404) warning of the potential hazard from the use of monoamine-oxidase inhibitors and phenylpropanolamine contained in various "cold" remedies, we thought it of interest to report the following case.

A 38-year-old woman had been treated for three months with phenelzine (Nardil) 15 mg. t.d.s. At the end of November last year she developed a "head cold" and one evening took one Mucron tablet (containing 32 mg. phenylpropanolamine) at approximately 10.15 p.m. About 15 minutes later she experienced the sudden onset of a throbbing frontal headache intense enough to cause her to cry out. She was seen by a doctor at 11 p.m., who found her to be in severe pain and recorded her blood pressure as 210/100 mm. Hg. A subarachnoid haemorrhage was suspected; the patient was given 100 mg. of pethidine intramuscularly and transferred to hospital.

On admission to this hospital at about midnight she was found to be disorientated but responding to simple commands. The pupils were widely dilated and reacted sluggishly to light. Her fundi were normal. The reflexes were brisk and equal with bilateral extensor plantar responses. There was no neck stiffness, and Kernig's sign was negative. The pulse rate was 80 per minute and regular, and the blood pressure was 200/100. No other abnormal findings were detected. Lumbar puncture

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

It was thought 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 Mucron it had reached a level of 130/70. 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 apart from a mild depression.

Sympathetic amines contained in preparations for the symptomatic relief of nasal congestion are made up in free- or slow-release forms. Tonks and Lloyd¹ reported 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. Cuthbert 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 more 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

- ¹ Tonks, C. M., and Lloyd, A. T., *Brit. med. J.*, 1965, 1, 589.

Hypertension from Cold Remedies

SIR,—The paper published by Dr. M. F. Cuthbert and others (15 February, p. 404) prompts me to report the case history of a patient seen recently in Leeds.

A 36-year-old woman was admitted with a history of severe headache of sudden onset three hours previously. This was associated with vomiting and photophobia; in addition, she probably had a fit while still at home, after which she remained drowsy and confused, but was still complaining frequently of the headache, which was mainly 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 later she developed a transient right hemiparesis. She was normotensive, and full physical examination did not reveal any further abnormal signs. A lumbar puncture confirmed subarachnoid haemorrhage, and cerebral angiography suggested the possibility of a left posterior communicating aneurysm. She was managed conservatively in view of some uncertainty in the x-ray findings and because of her long-standing somewhat hysterical personality. There was no evidence of recurrent bleeding, and she made a complete recovery.

Questioning revealed that she had been taking phenelzine 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 ippecacuanha.

Although we (like Tonks and Lloyd in their cases of encephalopathy in similar circumstances¹) did not observe the blood pressure to be raised, it seems likely that sudden severe hypertension caused by the interaction of phenelzine and phenylpropanolamine resulted in the rupture of a berry aneurysm. 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 six hours is long enough 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 phentolamine, 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

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Awareness during Anaesthesia

SIR,—In this day and age of light anaesthesia, any reminder that the patient receiving a general anaesthetic expects to be unaware of the surgical procedure, and have no recollection of it, is welcome. However, perhaps the picture is not so gloomy as Drs. J. Wilson and D. J. Turner (1 February, p. 280) suggest.

A reported study¹ described 20 consecutive cases anaesthetized using atropine 0.6 mg., thiopentone 1.0–2.0 mg./lb. bodyweight, nitrous oxide 3.5 l./min.; oxygen 1.5 l./min. into a semiclosed circle absorber system, relaxants, and artificial ventilation 50–150% in excess of the Radford Nomogram value. Words of established emotional significance, in the form of a story, were tape recorded and repetitively applied to the patients through insulated earphones at times varying from 10–90 minutes after the induction of anaesthesia. On the second or third postoperative day the patients were visited by an experienced interviewer who was unaware of the precise details of the study. The interview was designed to annotate a predesigned protocol. No evidence indicating recall of auditory stimuli could be obtained, nor did any patients provide evidence of distress.

The difference between these results and those recently reported in your journal may be explained by differences in experimental method and by the environment of the patients. Important factors in any consideration of awareness and recall associated with surgery are the sounds available to the patients, their interpretation of them, and the significance of that interpretation to the patient. As the authors indicate, if patients are anaesthetized the problem doesn't arise. However, if the surgical situation demands particularly light anaesthesia, perhaps partial isolation of the patient from auditory stimuli is of value during the operative period. Also the appropriate auditory stimuli provided by

good nursing care immediately the patients are even dimly aware of their environment will have a lasting effect on their overall impression of the surgical experience.—I am, etc.,

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REFERENCE

- ¹ McIntyre, J. W. R., *Canad. Anaesth. Soc. J.*, 1966, 13, 495.

Ampicillin 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. Natalie Hurwitz and Professor O. L. Wade (p. 531). In their summary the authors suggest that "larger surveys of adverse reactions in relation to drug usage would make a useful contribution to the problem." In common with most other pharmaceutical manufacturers, we maintain extensive coverage of the international medical and allied scientific literature on our drugs, including a continuous survey 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 have been reported in the published clinical 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 were described as urticarial, 23 as macular, and 114 as maculopapular (including the so-called "morbilliform" type); 19 patients exhibited 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 erythematous. Urticaria is generally 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 macular or maculopapular, and are less irritant than urticaria and often controlled with antihistamines. In many cases the rash fails to develop further and usually disappears quickly when ampicillin is withdrawn; 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 slight fever. Though the rash may arise during the course of therapy, sometimes as early as the first day, it often develops about five days after the end of treatment, and for this reason has been called the "fifth-day rash."¹ Subsequent courses of the antibiotic may not necessarily reproduce the reaction. In a limited number of patients with this type of rash investigated so far we have been unable to demonstrate circulating reaginic antibodies in the serum. It is now well established that