for one week but flared up again on stopping treatment. His skin eventually returned to normal with the topical application of a fluorinated steroid for several weeks. The second patient was a 21-year-old woman who developed a severe eczema of the hands and neck which started on the day after her chemistry examination. She was sure that no caustics had spilt on her skin but thought that the DNCB solution might have come into contact with her hands. She was treated with potassium permanganate soaks, a steroid cream, and prednisone 20 mg daily for 4 days, but despite this the condition became more severe. It eventually responded to prednisone 50 mg daily for one week, which was then rapidly withdrawn, and her skin has since been normal. In view of the severity of the reaction produced we felt it inadvisable to perform patch tests on either patient.

Both patients worked in chemistry laboratories and believed they might have handled DNCB in the past and neither had been warned of its sensitising potential. An inquiry at the institution which organised the examination revealed that none of the organic chemists on the staff knew that DNCB is a sensitiser and the fact is not mentioned in the standard practical textbooks of organic chemistry.

We feel it unlikely that a dermatologist would overlook the possibility of DNCB sensitivity in a chemist or laboratory technician presenting with a contact dermatitis, but it may not be so well known that DNCB cross-reacts with chloramphenicol.¹ The preparation of DNCB on one or more occasions could presumably therefore sensitise a person to chloramphenicol, with the subsequent provocation of a severe eczematous reaction following systemic or topical exposure to the drug. In view of the increasing use of topical chloramphenicol we feel that the potential hazards of handling DNCB should be widely publicised to doctors and chemists.

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¹ Schwank, R, and Jirasek, L, *Hautarzt*, 1963, 14, 24.

Reactions to current influenza vaccine

SIR,—For some years the Medical Officers of Schools Association has supported the belief that boarding-school children should be among those offered annual influenza vaccination. This has been supported by evidence of its efficacy.^{1 2} One of the assumptions behind this policy is that the rate of systemic reactions to influenza vaccine is low. For some years the rate has been below 1%.

This year there have been reports of high rates of reaction to the vaccine, which contains influenza A/New Jersey/76 for the first time. From my contacts with members of this association I have obtained data from 14 schools which have given one of the two commercially available (and antigenically identical) vaccines to over 4600 pupils. The overall rate of systemic reactions is 15%. This is clearly a crude figure as rates of reporting and criteria of diagnosing reactions must vary. Nevertheless, the picture differs so markedly from previous years that I feel it is worth bringing to your attention.

The reactions described include pyrexia, reaching 39.4°C in some cases, headache, nausea, vomiting, faintness, and myalgia. In most schools they have been more frequent in the younger pupils, even when the under-13s

have been given half the adult dose. None of the reactions lasted longer than 36 h and no sequelae have been reported to me.

This unexpectedly high reaction rate must lead to a reassessment of vaccination policy, including reconsideration of the intradermal route recommended by Payler and Skirrow.³

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¹ Hoskins, T W, *et al*, *Lancet*, 1973, 2, 116.

² Hoskins, T W, *et al*, *Lancet*, 1976, 1, 105.

³ Payler, D K, and Skirrow, M B, *British Medical Journal*, 1974, 2, 727.

Side effects of prazocin

SIR,—The recent short report by Professor Clive Rosendorff (28 August, p 508) indicates that, at least symptomatically, commencement of prazosin therapy for hypertension with a 0.5-mg dose instead of the previously recommended 2 mg may be accompanied by a lower incidence of side effects a short time after taking the first dose. However, there are several points in the paper which I feel are worthy of comment and clarification.

Though the author states that supine and standing blood pressures were recorded before and at intervals after administration of prazosin, the only results given are for standing pressures. Hypotension as a result of antihypertensive therapy is often a relative phenomenon. It may manifest itself with change in posture from the lying to the standing position. Also in previously hypertensive patients, although lowering of the blood pressure may not result in typically hypotensive levels, a degree of lowering may be achieved that for that patient may produce symptoms of hypotension—this depending on the state of the cerebral vasculature and the rate at which the blood pressure is lowered. Though the dose of drug used was small, the depression of systolic blood pressure in one patient (case 12) was dramatic at $\frac{1}{2}$ h (62 mm Hg). This implies that for certain patients the drug is still very potent even in small dosage. In all, four of the seven patients who were rechallenged had standing systolic pressures lowered by more than 30 mm Hg within $1\frac{1}{2}$ h of administration and in three of these four the fall was in excess of 45 mm Hg, again attesting to the potency of the drug in some patients. Consequently in the context of this paper it is difficult to assess the meaning of the statement, "The standing blood pressure fell in all cases, but in no patient was this fall to anything that could be described as a hypotensive level."

In spite of the low incidence of side effects (only two patients had transient mild dizziness) only three of the seven patients were continued on prazosin for 1-12 weeks (whatever that means). If these seven patients were hypertensives in need of treatment by the criteria used in the clinic, why was prazosin not continued in more of them after a small starting dose had apparently been well tolerated? And which of the seven patients were continued and for how long?

Why, of the twelve patients who had first-dose reactions, did only seven volunteer for rechallenge with a smaller dose of the drug? One must assume that either the side effects were so severe on the first exposure that the medical staff felt it unwise to request further

exposure or that the symptoms were of such severity that five patients felt unable to give further consent for taking part. By either criterion these patients must be regarded as failures and this consequently makes nonsense of the predicted incidence of first-dose reactions in the original population of 74 patients as being 4.6%. In fact the incidence taking into account these five patients would be at least 6.9%, and taking into account the two patients who had reactions on the smaller dose and those who were not continued after the challenge with a smaller dose the incidence of the first reaction may be as high as 10%. This is clearly unacceptable.

I fear that this paper does little to allay the concern regarding prazosin. Although only two patients experienced mild dizziness, it is unwise to extrapolate the findings from this small, randomly selected group of patients being studied in a controlled clinical situation for a relatively short period of time to that pertaining to the usual circumstances of commencement of antihypertensive therapy—that is, outpatients leading normal active lives. Its routine use in the treatment of mild and moderate hypertension is far from established when there are other preparations with less, or potentially less, catastrophic side effects which have been used for a number of years and are trusted, in so far as one can trust any drug, by a large number of physicians. Its general acceptance must await adequate clinical trials with a 0.5-mg starting dose in which it is compared with other, established, antihypertensive agents.

I also feel that the decision to rechallenge these patients with a drug known to have severe initial side effects and in whom the drug has already produced such an initial reaction, is ethically unacceptable.

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* * * We sent a copy of this letter to Professor Rosendorff, whose reply is printed below.—
Ed, *BMJ*.

SIR,—I am grateful to Dr Bendall for raising some points which were impossible to cover in the "short report" format.

An excessive fall in blood pressure on changing from the supine to the standing position obviously may cause dizziness. For the seven patients in the study the mean pretreatment postural fall in blood pressure was $6/2 \pm 7/4$ (SEM) mm Hg. Corresponding values for the period after 0.5 mg prazosin were: $\frac{1}{2}$ h, $12/4 \pm 9/2$ mm Hg; 1 h, $2/2 \pm 10/4$ mm Hg; and $1\frac{1}{2}$ h, $12/2 \pm 4/4$ mm Hg. The pre- and post-treatment values were not significantly different, nor were the post-treatment values significantly different from zero, on paired *t*-testing. In other words we were unable to demonstrate a consistent or significant postural fall in blood pressure in the study. This is not to say that in individual cases there was not a large postural drop; the two patients who did show some dizziness had quite large postural falls of blood pressure. In one case the systolic blood pressure fell from 194 mm Hg supine to 160 mm Hg erect and in another from 168 mm Hg supine to 128 mm Hg erect. This underlines the need for caution in the use of this drug; there are patients who are sensitive to its effects and some patients are more sensitive than others. Prazosin is a potent antihypertensive (isn't that what we are after?),