state for treatment, which might include penicillin. Above all, patients who have been given penicillin in any form should, for their own safety, be told even though no adverse reaction ensued. Swift⁴⁸ has shown the value of careful documentation in a clinic where penicillin is widely used.

For the benefit of all concerned, publicity from manufacturers could be increased by the adoption of "manufacturers' slips of caution"⁴⁹ displayed on the bottles or included in the packages of all penicillin preparations. Further publication of case reports and/or their submission to a central agency collating such data would permit a true assessment of the frequency of these reactions. Since most injections of penicillin are given by nurses they should be informed that these anaphylactoid reactions require prompt recognition and treatment. As an additional safeguard they should re-question the patients about previous courses or applications of penicillin and ascertain if any apparently related adverse effects had occurred. Here needless confusion is avoided by speaking the simple language of the patient and inquiring if anything went wrong previously rather than using the terms "sensitivity" or "allergic reactions."

Summary

The literature on anaphylactoid reactions from penicillin is briefly reviewed. A further case is reported to emphasize that moderately severe reactions can follow the use of penicillin lozenges and that there are occasional instances of severe reactions even when no history of previous administration of the drug can be elicited. A detailed description of a subsequent profound anaphylactoid shock in this patient is presented. A scheme for reducing the frequency and degree of these catastrophes is outlined.

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Medical Memorandum

Reactions to Intramuscular Iron

A new iron-dextran complex ("imferon") has recently been described (Baird and Podmore, 1954; Cappell *et al.*, 1954; Scott and Govan, 1954). It is reputed to be less toxic and more stable than saccharated iron oxide ("ferrivenin"). The dosage administered is 2 to 5 ml. (100 to 250 mg. of iron) as compared with the usual maximum dose of 5 ml. (100 mg. of iron) of intravenous saccharated iron oxide. Adequate serum concentrations have been obtained after the administration of the iron-dextran complex, the maximum absorption occurring in the first one to two days and the serum iron level falling to normal about the seventh day. Toxic reactions were not observed, but discomfort at the site of injection lasting up to twelve hours and staining of the skin were noted.

Dempster *et al.* (1954) obtained satisfactory results, but encountered local reactions in several patients and had to stop treatment in 2 of their 16 patients. Callender and Smith (1954) encountered four severe reactions in a limited period; two of these occurred soon after injection and two showed a delayed reaction of an allergic character. They gave the patients iron and dextran separately without producing any reaction, and suggest that the combination of iron and dextran may result in a sensitizing compound. Jennison and Ellis (1954) state that all their patients attained a satisfactory haemoglobin concentration. They report a few cases of local reaction; but mild general reactions, including nausea, vomiting, depression, fainting, and skin rash, occurred in 20% of their patients. Ross (1955) reports a delayed allergic reaction in a man of 55 and an early reaction after 1.5 ml. given intravenously to a youth of 17.

Reactions due to intravenous saccharated iron oxide fall into two main groups, early and late. The early consist mainly of cardiovascular collapse and of pain in the chest, back, and limbs possibly due to ischaemia. These occur even after doses of 100 mg. or less. The late (delayed) reactions are uncommon and occur after larger doses, usually 300 mg. or more. Nissim (1954) found only 13 cases of late reaction in the literature, of which only two had suffered an early reaction.

Librach (1953) considers allergy to be an important factor, especially in the production of early reactions, and believes they may be due to a natural hypersensitivity.

It seems as though the new iron-dextran complex may present us with combined early and late (delayed) reactions, the main symptoms of which have been observed previously. The accent is, however, upon symptoms hitherto uncommon. This is to be expected, as the mechanism of toxicity varies with the other properties of the whole molecule injected (Nissim, 1954).

CASE REPORT

On September 22, 1954, a married woman aged 46 was admitted to hospital for total hysterectomy. She had suffered from menorrhagia for two years, and on examination the uterus was enlarged by fibroids to the size of a

16-weeks pregnancy. On the 24th total hysterectomy was performed by Mr. Dickinson. There was very little loss of blood and the patient's condition was satisfactory.

The immediate post-operative course was uneventful. The haemoglobin, which was 62% on admission, had fallen to 58% on the 27th. Intravenous iron therapy was begun the next day. Saccharated iron oxide ("ferrivenin") was given daily up to a total of 34 ml. ($\equiv$ 680 mg. of iron) in eight days, the last dose, 5 ml. ($\equiv$ 100 mg. of iron), being given on October 6.

At 2.30 p.m. on October 7, 2 ml. of iron-dextran complex was given intramuscularly into the left buttock. The injection was slightly painful, but the patient did not complain at the time. Ten minutes after the injection she had a feeling of tightness in the chest and nausea. At 3 p.m. she felt faint and giddy, and also complained of a pricking sensation in the palms of her hands which she likened to severe "pins and needles." She felt cold, began to shiver, and was given an extra blanket and a hot-water bottle; she then slept from 3.30 to 5 p.m. On waking she had a mild generalized headache. Her temperature was 99.6° F. (37.6° C.), and her pulse, which had not risen during the rigor, remained between 80 and 90. The B.P. was 120/70.

At 6.30 p.m. she vomited 10 oz. (280 ml.) of altered food, after which the headache was more severe and mostly frontal. She complained of swelling of the eyelids and said that she felt "quite ill," but was pleased that the tight feeling in her chest had gone. Her eyes showed only slight swelling of the upper lids.

At 9 p.m. the headache, which was much worse, was frontal and occipital, with most of the increasing pain at the back. She complained of pricking in both eyes and required considerable persuasion before she would open them, as that made the pricking sensation much worse. The eyes were watering profusely, the lids were swollen, and a mild conjunctivitis was present. Sight was unimpaired. Chlorcyclizine hydrochloride, 100 mg., was given orally every four hours.

She spent a restless night, being awakened by the pricking sensation in her eyes. Next morning she had a mild frontal headache, which was relieved by aspirin, 10 gr. (0.65 g.). The pricking sensation in the hands and the faintness and giddiness had gone. The pulse remained at 70-80, the B.P. was 130/80, and the temperature was normal.

There was no photophobia, but the pain in the eyes became much more unpleasant when the eyes were opened. She had developed diplopia, and blurring of vision prevented her from reading newspaper headlines. There were no other symptoms. The eyelids were more swollen, the conjunctivitis more marked, and the watering more profuse.

On October 9 there was tingling in the eyes only, but the pricking returned when they were opened. The diplopia improved throughout the day, and had gone by 6 p.m.; the blurred vision also improved enough to allow her to read newsprint. The eyelids remained very oedematous, but the conjunctivitis and excess lacrimation were just as severe.

Next day the eyes were greatly improved and watered only slightly. There was no diplopia and only slight blurring of vision. On the 11th the sight was normal, but there was some tingling at the inner canthus of both eyes. Only very slight conjunctivitis remained. The next day the eyes appeared normal, but the patient complained of tingling and slight blurring of vision after reading for 20 minutes. On October 13 the eyes were normal and the patient was discharged.

At no time did the patient have a rash. The optic disks and fundus oculi were normal throughout. She had never previously shown any allergic manifestations. Adrenaline would probably have controlled the reaction, but was not given, as the patient had developed a marked dislike of injections and we wished to study the course of the reaction under treatment of an oral antihistamine. Two months later an intradermal injection of iron-free dextran and an injection of ferrivenin were given without any ill effect.

COMMENT

Local reactions of pain, tenderness, and staining are fairly common, as is some small rise of temperature and headache a few hours after injection (Jennison and Ellis, 1954). General reactions, both early and late, seem to occur, and, whilst the early reactions are not usually severe, several cases of fainting have been reported. If the allergic theory is correct, these reactions should be controlled by adrenaline, and there is some evidence to support this view (Callender and Smith, 1954).

It is the late reactions, however, that give rise to concern, because many of the patients have returned home before the symptoms develop. These delayed reactions, most of which occur from two to twelve hours after injection, are mostly allergic in nature and can be quite severe or even dangerous. Adrenaline may control these symptoms, but, as one would expect, antihistamines have little or no effect.

It has been found that 40 to 50 mg. of iron-dextran complex intramuscularly raises the haemoglobin level by 1% (Jennison and Ellis, 1954; Baird and Podmore, 1954; Scott and Govan, 1954) as compared with 25 mg. of intravenous saccharated iron oxide; the lower utilization ratio of iron-dextran complex offsets to a great extent the advantage of injecting a larger amount of elemental iron. Furthermore, the maximum response from intramuscular iron-dextran complex occurs in from four to nine weeks, compared with three to five weeks after saccharated iron oxide given intravenously.

The *British Medical Journal* (1954) and Ross (1955) are correct in asking that this iron-dextran preparation should be given a much more extensive trial before its general use is advocated, and meanwhile it should be given to out-patients only after very careful consideration. It should not be used in the routine treatment of anaemia in pregnant women until further trials have been completed.

I wish to thank Mr. J. R. Dickinson for permission to publish this case.

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About 20% of men reaching their late fifties in a reasonable state of working efficiency are compelled by their age or its infirmities to seek lighter work, and a further 10% are incapacitated for all but the easiest tasks, states *New Jobs for Old Workers*, a Nuffield Foundation report by F. Le Gros Clark and Agnes C. Dunne. Study of the 1951 census returns showed 16 occupations in which the proportion of older men is unusually high, and where, out of the total body of men, 37.7% are 55 and over. 71% of watchmen are in this age group—before 1951 some 20,000 older people moved to this job—61.1% of office cleaners, 43.7% of lift attendants, and 37.4% of gardeners. Some work, such as caretaking, seems to have a somewhat restricted field of recruitment, attracting chiefly ex-Army or police pensioners. Of the 16 occupations, only a few seem likely to increase their intake of older people. Progressive mechanization means men can replace women as office cleaners; and more local authorities are using older gardeners to mow lawns and cut hedges; while the occupation of lift attendant has now been reserved for the disabled. The factories and transport provide manpower for alternative jobs; mining, agriculture, and the docks can provide light or part-time work for their ageing employees.