total, 27 g. by mouth. Within 24 hours of starting treatment there was definite subjective improvement, which was maintained. The temperature had settled by the fourth day, and has remained normal up to the present time (July 22). On the first two nights the patient showed mild urticarial skin lesions, and for a few hours there was severe pain in the splenic area, but the spleen did not become palpable. The patient is heavily

Sensitivity to Codeine

The following case is recorded because of the rarity of reactions to codeine in spite of its common use and because of the resemblance of the rash to that of scarlet fever.

CASE REPORT

The patient, a woman aged 24 suffering from pulmonary tuberculosis, stated that one night she had been given two "veganin" tablets (containing $\frac{1}{2}$ gr. (22 mg.) of codeine phosphate) for headache. Next morning she developed an irritation of the whole body and later in the day "a red rash" appeared. On the following day the rash had faded and the irritation had subsided. She also stated that a similar reaction had followed a single dose of 1 dr. (4 g.) of syrup of codeine phosphate (codeine content, 16.2 mg.).

In order to demonstrate the specificity of the reaction, and to study the rash, several months later she was given a test dose of $\frac{1}{2}$ gr. (32.5 mg.) of codeine phosphate at midday. At 5 p.m. she developed irritation of the neck and chest, which rapidly involved the whole trunk and limbs. The irritation was followed by a macular rash, which soon coalesced to give a scarlatiniform appearance. The rash was most prominent on the front of the chest, the abdomen, and lower limbs, but the pruritus was not confined to the area involved by the rash. Both the rash and the irritation were less marked the next day, and during the following day both had disappeared; the irritation, however, remained some hours after the rash had gone.

At no time was there any lesion in the mouth, the patient felt well, and there was no febrile disturbance. Slight desquamation occurred over the lower face only. A blood count at the height of the reaction showed 259 eosinophils per c.mm.

COMMENT

In spite of its widespread use very few cases of sensitivity to codeine have been recorded. Indeed, Seidmann (1943) says that his is the tenth case to be reported.

Scheer and Keil (1934) reviewed the literature and added a further case following 1 gr. (65 mg.) of codeine phosphate. They point out that antibodies cannot be demonstrated by the direct Prausnitz-Küstner method, since codeine itself normally produces an erythematous-urticarial reaction with pseudopod formation when injected intradermally. Using a modified P.-K. technique (serum locally and codeine by mouth), they were unable to demonstrate antibodies in the serum. Scheer and Keil describe the original appearance of the rash as follicular, later taking on a generalized erythematous appearance by coalescence of the broad zone of erythema surrounding the individual follicles. They produced a positive skin-patch reaction with codeine phosphate solution (1 gr. to the ounce), while a similar test with a solution of morphine sulphate was negative, indicating a specific hypersensitivity to codeine, which is all the more significant since the latter differs from morphine only in having a methyl group.

The constant feature of the recorded cases is the pruritus, followed by an erythematous rash, the early phase of which may present as macular or follicular. Usually there are no symptoms apart from the irritation. In Seidmann's case, however, weakness, fatigue, headache, nausea, and redness of the mouth and throat occurred a few hours after ingestion of 15 mg. of codeine phosphate. There was an eosinophilia of 1,080 per c.mm.—a finding also recorded by Dittrich (1926). Desquamation has been reported in a few of the cases.

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Temperature chart of the case.

built, and a moderate enlargement of the spleen could easily go undetected. He also had an unpleasant taste in the mouth after taking the drug, particularly if the 0.25-g. dose was exceeded. We had given instructions that if, in error, a dose were missed during the night the succeeding dose should be increased in compensation. At the end of treatment the patient was easily tired, but otherwise he felt well. Convalescence proceeded uneventfully, and he now seems fit.

COMMENT

This case is described because the treatment seems free from risk and can be carried out at the patient's home, whereas any method employing blood transfusion implies admission to hospital and exposure to the hazards of transfusion. We appreciate that our diagnosis is based on a reasonable supposition (agglutination reaction) rather than on the absolute proof which would be given by a positive blood culture. It is known, however, that in only a small proportion of cases of undulant fever due to *Brucella abortus*, estimated at 10–20% (Topley and Wilson, 1945), can a bacteriaemia be demonstrated. Inspection of the temperature chart shows a fall in temperature exactly coincident with the administration of chloramphenicol. At the present time this method of treatment is not cheap, as 27 g. of the substance costs £30 12s., less 33 $\frac{1}{3}$ % discount to institutions, plus £6 16s. 1 $\frac{1}{2}$ d. purchase tax—a net total of £27 4s. 1 $\frac{1}{2}$ d. The makers inform us that negotiations are proceeding to eliminate purchase tax—an imposition which seems illogical, especially if distribution of the amounts available is restricted to definite prescriptions and specific infections.

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