Serious complications following primary vaccination in adults are known to be rare, but systemic reactions with fever, general malaise, and headache are common. Many of our patients felt unwell for one or two days but only eight were so incapacitated that they asked to be visited at home. One of these had generalized eczema vaccinata which necessitated admission to the university sanatorium. This patient had a history of mild eczema and had still wished to be vaccinated.

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Anaphylactic Reactions to Hydrocortisone Injections

The injection of a suspension of hydrocortisone acetate either into the synovial cavity of a joint or into the soft tissues for the treatment of rheumatic diseases is now a well-established method of treatment. It may be of interest to record three severe reactions which have occurred during the past two years out of a total of approximately 4,000 hydrocortisone injections.

The reactions appear to be of two differing types. The first patient developed a general urticarial reaction. In the other two cases the anaphylactic reaction was accompanied by a purpuric rash.

CASE REPORTS

Case 1.—A woman aged 49, suffering from bilateral plantar fasciitis, had 2 ml. of hydrocortisone acetate suspension injected into the soft tissue of each heel. Four hours after the injection she complained of constriction in the throat, became hoarse, and had difficulty in speaking. There was pain in the knees, ankles, elbows, and shoulders. An intramuscular injection of 50 mg. of promethazine hydrochloride was given. An urticarial rash soon appeared on the face, limbs, and trunk, and there were large weals on the hard palate. Twelve hours later there were effusions in both knee- and ankle-joints. The rash began to subside in 24 hours, and after three days she was completely free from signs or symptoms. Patch tests using the hydrocortisone acetate suspension were performed on the third day and produced a large area of erythema underneath the test strip. Six months later skin tests were carried out with separate suspensions of pure hydrocortisone acetate and vehicle obtained from the manufacturers. The intradermal injection of 0.1 ml. of hydrocortisone suspension produced a weal 1 cm. in diameter and there was no reaction to the vehicle.

Case 2.—A man aged 29, suffering from unilateral plantar fasciitis, had an injection of 2 ml. of hydrocortisone acetate suspension into the soft tissues of the heel. This was followed by a manipulation of the foot under general anaesthesia. Four hours later he complained of tightness in the throat and dyspnoea, and there was oedema of the face. An hour later a petechial rash developed on the chest, abdomen, buttocks, and upper thighs. The rash became confluent particularly over the buttocks. He was given 4 mg. of chlorpheniramine hydrogen maleate by mouth, and this dose was repeated at six-hourly intervals for 48 hours. The rash gradually subsided in four days. The haemoglobin was 16.4 g./100 ml., the bleeding-time 1 minute 8 seconds, the prothrombin index 100, the E.S.R. 2 mm. fall in the first hour (Wintrobe), and the platelet count 120,000/c.mm. A repeat of the platelet count two days later showed 190,000/c.mm. An intradermal injection of 0.1 ml. of the same batch of hydrocortisone acetate suspension produced no reaction. Three months later skin-sensitivity tests were

carried out to pure hydrocortisone acetate and to the vehicle: 0.1 ml. of these suspensions was injected intradermally but produced no reaction.

Case 3.—A man aged 39, suffering from a right tennis elbow, had an injection of 2 ml. of hydrocortisone acetate into the soft tissues close to the lateral epicondyle of the right humerus. Four hours later he complained of a tight feeling in the chest and difficulty in breathing. This was followed by vomiting of altered blood and by melaena. A petechial rash developed over the chest and base of the neck, spreading to the abdomen and buttocks later, and becoming confluent over the buttocks. An intramuscular injection of mepyramine hydrogen maleate was given immediately, and this was followed by 100-mg. doses by mouth six-hourly for 48 hours. The patient's condition rapidly improved and the rash faded within three or four days. Three months later sensitivity tests were carried out to pure hydrocortisone acetate and vehicle. There was no reaction to either of these or to the test injection of sterile water until 24 hours later, when a small weal of 1.5 cm. diameter developed around the point of injection of the vehicle. The bleeding-time taken on the day after the injection was 1 minute 37 seconds, the clotting-time 3 minutes 15 seconds, the haemoglobin 15.1 g./100 ml., and the platelet count 175,000/c.mm. and 204,000/c.mm. 10 days later.

DISCUSSION

Urticarial reactions to the injection of suspensions of hydrocortisone acetate have been reported by several authors. Kendall (1958) reported the occurrence of generalized urticaria in eight cases out of a total of 6,700 injections. Procaine was used concomitantly in some of these cases and it could not be ruled out as a cause of the reaction. Hollander (1953) reported four cases of urticaria out of a total of 10,000 intra-articular injections of hydrocortisone. King (1960) reported an anaphylactoid reaction to hydrocortisone after the injection of 5 ml. of hydrocortisone suspension into the shoulder. In this case the patient developed a purpuric rash and vomited altered blood and had melaena. Sensitivity test showed a late development of an erythematous plaque 24 hours after an injection of the hydrocortisone acetate suspension.

The cases described above fall into two groups. Case 1 appears to be a true allergic reaction to the hydrocortisone suspension with a positive reaction to an intradermal injection of this pure suspension of hydrocortisone acetate. Cases 2 and 3 developed a purpuric type of reaction and there was no definite evidence of sensitivity to either the hydrocortisone or the vehicle, although in one case an erythematous area developed 24 hours after intradermal injection of 0.1 ml. of hydrocortisone acetate. In none of these cases was procaine or other local anaesthetic used accompanying the injection. The cases of purpuric reaction to hydrocortisone acetate injection bear a clinical resemblance to the milder type of fat embolism, and it is possible that these reactions are due to the entry of tiny emboli of hydrocortisone acetate into the circulation.

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