and usually, as in the present case, constructional apraxia will be detected with or without ideational apraxia, alexia, or sensory agnosia.

Interpretation of Gerstmann's syndrome as an easily demonstrated and memorable pointer to diffuse cerebral damage accords well with this case, where there is no reason to suspect a highly focal lesion. Gerstmann's syndrome does not seem to have been reported in association with penicillin anaphylaxis. There can be little doubt that in this case the curious neurological manifestations were secondary to hypotension and cerebral oedema associated with anaphylactoid shock.

Summary

An anaphylactoid reaction to oral penicillin in a 46-year-old woman is described: after hours of unconsciousness and weeks of confusion she was left with a residual Gerstmann's syndrome. These reactions are less rare than is generally supposed. Symptomatology, treatment, diagnosis, and mechanism are discussed, and some of the relevant literature is briefly reviewed.

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Skin Sensitization to Remiderm and Cross-sensitization to Hydroxyquinoline Compounds

C. F. ALLENBY,* M.R.C.P.

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The use of local corticosteroid preparations on the skin is increasing, and to counter skin infection antibiotics and antiseptic preparations are being added more frequently. Because of epidermal sensitization to antibiotics, exemplified by the increase in neomycin sensitivity (Kirton and Munro-Ashman, 1965), and the development of antibiotic resistance, "antiseptic preparations are becoming more popular" (Vickers, 1964), and the chief of these is the hydroxyquinoline group.

This paper reports the cases of three patients who showed skin sensitization to Remiderm, which contains a new antiseptic, halquinol (Quixalin), 0.75%, with 0.025% triamcinolone in either a cream or Plastibase.

In addition to sensitization to halquinol they showed cross-sensitivity to related hydroxyquinoline compounds. The possibility that sensitivity may be present should be borne in mind whenever these or new related compounds are used on the skin or systemically.

Case Reports

Case 1.—A woman aged 24 showed sensitization dermatitis to Remiderm after the second application of ointment to gravitational ulcers. She had used Vioform ointment six months previously, which produced irritation.

Case 2.—A woman aged 31, after using Remiderm for gravitational dermatitis, immediately had acute exacerbation with generalized spread of dermatitis. She had used Vioform two years previously.

* Department of Dermatology, the Radcliffe Infirmary, Oxford.

Case 3.—A man aged 58 had gravitational dermatitis which was made worse by Remiderm. He had used Vioform two years previously.

Investigations.—Halquinol contains three derivatives of hydroxyquinoline. Two of these, 5,7-dichloro-8-hydroxyquinoline and 5-chloro-8-hydroxyquinoline, were skin-tested, and all three patients showed strongly positive patch tests to them and to halquinol after 24 hours (see Table). The third constituent (less than 4%), 7-chloro-8-hydroxyquinoline, was not available.

Results of Patch-testing

	Case 1	Case 2	Case 3
Halquinol	++++	+++	++
5,7-dichloro-8-hydroxyquinoline	++++	+++	++++
5-chloro-8-hydroxyquinoline	++++	+++	++++
Steroxin (chlorquinaldol)	+++	++	++
Vioform	+++	+++	++
Diodoquin (di-iodohydroxyquinoline)	+++	++	++
Quinolol	++++	+++	++++

All compounds 0.75% in hydrous eucerin, except Quinolol. Grading of result according to Schwartz *et al.* (1957).

No patient had a history of infantile eczema, and patch tests to Plastibase, cream base (Squibb), 0.025% triamcinolone, tincture of iodine, and hydrous eucerin (Smith and Nephew) were negative at 48 hours and showed no delayed results.

Cross-sensitization to related compounds was also demonstrated, the structure of 8-hydroxyquinoline (see Formula) being the common factor.

Formulae are: Diodoquin, 5-7-di-iodo-8-hydroxyquinoline; Vioform, 7-iodo-5-chloro-8-hydroxyquinoline; Steroxin

(known abroad as Sterosan), a hydroxyquinaldine with two chlorine radicals in positions 5 and 7 and a methyl radical at 2; Quinolol, an amorphous mixture of 8-hydroxyquinolines with chlorine radicals at 5 and 7.

Discussion

All three patients showed sensitization to Remiderm very soon after it was applied, and as all had previously used Vioform it is reasonable to assume that Vioform was the primary epidermal sensitizer. Skin irritation with Vioform was reported by Martin Scott (1949), and James and Baird (1958) found three cases of epidermal sensitivity among 597 patients. Tronstein (1949) reported five cases in which sensitization was probably due to the base or iodine content of the Vioform; three of these had no reactions to Steroxin. Jadassohn *et al.* (1944), however, in the first report on Steroxin, described a case cross-sensitized by Vioform.

Leifer and Steiner (1951) investigated three patients showing cross-sensitization to the hydroxyquinolines, the sensitizing substance being Vioform or Diodoquin. Their results suggest that hydroxyquinolines might be converted to carboxylated

pyridines, which act as the actual antigenic complex. One of their patients produced a severe dermatitis with 210 mg. of Diodoquin orally. Because of this we did not feel justified in testing our patients to oral halquinol.

We have proved only epidermal sensitization, but feel it would not be justified to give these patients hydroxyquinoline compounds in the future in any form.

Summary

Three cases are described with sensitivity reactions of the skin to Remiderm. Halquinol was the actual substance to which they were sensitized, and cross-sensitization was demonstrated to Vioform, Steroxin, Diodoquin, and related hydroxyquinoline compounds.

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Preliminary Communications

Plasma Insulin: a Correlation Between Bioassay and Immunoassay

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The levels of insulin-like activity measured by bioassay have usually been found to be higher than plasma-insulin concentration measured by the more specific radioimmune techniques.

Only part of the insulin-like activity in plasma measured with adipose tissue bioassays can be neutralized or "suppressed" by anti-insulin serum, whereas crystalline insulin can be completely neutralized (Slater *et al.*, 1961; Froesch *et al.*, 1963). This suggests that the higher figures obtained for insulin-like activity are the result of stimulation of the tissue by something other than insulin.

It might be anticipated that the fraction of plasma insulin-like activity neutralized by anti-insulin serum is the same as that measured by the immunoassay technique, but no such correlation has as yet been conclusively demonstrated.

This preliminary communication describes modifications of the rat epididymal fat-pad technique with which it is possible to obtain a highly significant correlation between plasma insulin measured by immunoassay and the "suppressible" insulin-like activity of the same sample.

METHOD

The following modifications of the method of Martin *et al.* (1958) are used:

Glucose-1-¹⁴C is added to the flasks in solution and then evaporated to dryness, thereby allowing assay of undiluted plasma.

A pooled assay design is used. The fat pads are dissected in buffer, and the peripheral portion of each pad is divided into 12 pieces. One piece from each rat is then added to each of 24 incubation vessels. Six rats are used, and each flask therefore contains six pieces of adipose tissue totalling 15-25 mg. dry weight.

To ensure equal glucose concentration in all solutions, the plasma samples and the albumin-containing buffer required for the preparation of the standard solutions are dialysed against Krebs's bicarbonate buffer containing 3 mg. of glucose per ml. for 18 hours at 4° C.

Guinea-pig anti-insulin serum is used at a final dilution of 1:200. At this dilution it is capable of completely neutralizing 5,000 μ u./ml. of crystalline insulin without displaying any insulin-like activity of its own. The carbon dioxide liberated from the medium is absorbed in Hyamine and counted in a toluene scintillator solution. A standard curve is obtained by plotting the counts per minute of ¹⁴CO₂ per square root of fat-pad dry weight against the insulin dose. The insulin-like activity of an unknown sample can then be calculated from the standard curve. The insulin-like activity of each unknown sample is obtained in the presence and absence of anti-insulin serum, the difference between the two being the "suppressible" insulin-like activity.

The standard solutions of insulin are made up in Krebs's bicarbonate buffer containing 2 mg./ml. crystalline human albumin instead of the usual gelatin. It has been found (in studies to be reported elsewhere) that albumin is more effective than gelatin in preventing loss of insulin from standard solutions.

The albumin used in the preparation of the standard solutions is fraction AP₃, prepared from human plasma by the method of Kekwick and MacKay (1954). It contains no insulin-like activity of its own in concentrations up to 40 mg./ml., nor does it contain insulin by immunoassay.

The immunoassay used in these experiments is based on that described by Hales and Randle (1963).