

had probably contributed to his emotional state but also recognised that the drug might only have exacerbated an underlying anxiety condition. Further counselling and continued use of the diuretic has alleviated many of the original anxiety symptoms and reduced his blood pressure to 132/84 mm Hg.

Since catecholamine-containing neurons in the central nervous system (CNS) may be involved in mood regulation it is not surprising that drugs which alter noradrenergic activity may produce the opposite effect (i.e., depression). It would therefore be desirable for non-CNS-acting agents to be the first choice drugs. Where centrally acting β -antagonists are to be used, a brief assessment should be made to see if psychological side-effects might be especially disturbing. For example, the drug might exacerbate symptoms in a patient who reports feelings of anxiety or depression and a patient with a previous history of emotional problems might be susceptible to such side effects. Where β -blockers are used, the patient must understand the possible side-effects. Our patient did not ascribe the mood changes to the use of the drug, a finding recorded by others.^{5,6} This could be dangerous for the patient who seeks other advice without mentioning the use of the drug or who tried drastic measures to alleviate his emotional condition.

A single case does not prove a point, and there are other possible explanations for our patient's condition—e.g., spontaneous depression (unlikely, in view of the time course) or a diuretic-induced mood change (unlikely, since he was on a potassium supplement). Nonetheless we hope that our experience will help fellow clinicians to use β -blockers more carefully.

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GENERALISED ALLERGIC REACTION WITH SYNTHETIC HUMAN INSULIN

SIR,—Generalised reactions to insulin are rare. We have seen a patient who reacted in this way to highly purified beef and pork insulin and to synthetic human insulin.

A 28-year-old housewife acquired gestational diabetes during her third pregnancy 18 months ago. 'Hypurin' isophane insulin (highly purified beef; Weddel) 8–10 units daily was required from 30 weeks until delivery. She then remained well until she presented with thirst, polyuria, and a blood glucose of 29.1 mmol/l (524 mg/dl). She has a history of urticaria and penicillin allergy.

She was treated with hypurin neutral insulin (highly purified beef; Weddel) 6 units twice daily, and, 12 days later, had a generalised urticarial rash 15 min after an injection. This reaction got worse with each dose but 'Velosulin' (highly purified porcine; Nordisk) caused a similar reaction and human insulin (emp) ('Human Actrapid'; Novo) 6 units resulted in a severe exacerbation of her urticaria and swelling of her hands and feet.

Skin-patch testing was done with hypurin neutral, velosulin, human actrapid, soluble insulin, 'Neusilin', actrapid, and human insulin (crb) ('Humulin'; Lilly) with a specially prepared solution of *m*-cresol 0.16% w/v plus phenol 0.065% w/v; and with a solution of zinc sulphate 0.0006% w/v. Zinc, which has been implicated as a cause of insulin allergy,¹ is not in the formulation of short-acting insulins but is present entrapped in insulin at a concentration of 12–16 μ g per 100 U. A positive reaction with a weal and flare of at least 5 mm was obtained with all the insulins but subjectively there was less irritation with humulin. No reaction was obtained with *m*-cresol/phenol or zinc.

Desensitisation was started with humulin 0.5 unit daily increasing to 3 units twice daily over 7 days. Each dose was given

mixed with dexamethasone 0.05 mg. The first injection was uncomplicated but the remaining injections resulted in a weal and flare. Desensitisation was continued without dexamethasone, the dosage increasing to 6 units twice daily, over 5 days with a gradual reduction in the local reaction.

The clinical manifestations of insulin allergy resemble those produced by foreign proteins, and there is usually a history of interrupted insulin treatment. Skin-patch testing suggested that the allergen in our patient was the insulin rather than any additive. This case report indicates that a highly atopic individual may have a generalised allergic response to synthetic human insulin after previously being sensitised to beef insulin.

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ALPHA₁-ANTITRYPSIN AND OCULAR SENSITIVITY TO CROMOGLYCATE

SIR,—Dr Price (Sept. 11, p. 606) reported on a child with the combination of alpha₁-antitrypsin (α_1 -AT) deficiency, asthma, and sensitivity to disodium cromoglycate ('Intal'). In some instances, the attacks of asthma appeared to be precipitated by the drug. Earlier this year I described two patients who had an acute chemotic reaction of the conjunctiva following the topical administration of disodium cromoglycate after they had previously discontinued its use for a short time.¹ Although I did not conclusively demonstrate homocytotropic antibodies, the rapid onset of the reaction and its favourable response to topical adrenaline suggested that it was an anaphylactic type of response in which the "shock organ" was the conjunctiva instead of the bronchiolar tree.

Continued use of disodium cromoglycate relieved the symptoms and signs of one of the patients, suggesting that, when he used medication after being without it for a period of time, the drug acted as an allergen and induced degranulation of the mast cells. Continued use of the drug stabilised the mast cells resulting in relief of the symptoms and signs.

I have now measured serum α_1 -AT levels in these patients and have found them to be normal (150–240 as compared with a normal range of 111–270 in our laboratory). Although the level of α_1 -AT was not determined in the tears, we have previously found it in the tears in the presence of normal serum levels.² The findings indicate that in my two patients, a deficiency of α_1 -AT was playing no role in the reaction.

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FIRE HAZARD OF NITROGLYCERIN AEROSOL

SIR,—A manufacturer's representative has shown me a new product ('Nitrolingual Spray'; Rona Laboratories) which is an aerosol preparation of nitroglycerin designed for spraying under the tongue for the relief of angina. I was told that headache was less common with this preparation than with sublingual tablets, and tried the preparation myself to test this claim. I was struck by the ethereal smell of the preparation, and cautiously tested whether it was inflammable by aiming a dose at a lit match one foot away. The result was a sheet of flame. Should such an inflammable preparation be available for oral use in patients some of whom might be holding a lighted cigarette during an angina attack?

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