

## DRUGS CAUSING SKIN ERUPTIONS (An analysis of cases confirmed by provocation tests)

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### Summary

Twenty one patients having drug eruptions are reported. The causative drug(s) were confirmed by provocation tests. Eleven patients had exanthematous eruptions. The causative drugs were thiacetazone (3), para aminosalicylic acid (3), isonicotinic acid hydrazide (1), streptomycin (1), ethambutol (1), carbamazepine (1), and phenytoin sodium (1). In 4 patients having toxic epidermal necrolysis, the causative drugs were para aminosalicylic acid (2), isonicotinic acid hydrazide (1), streptomycin (1), tetracycline (1), and phenobarbitone (1). Two of these patients reacted to two drugs each, namely, streptomycin and para aminosalicylic acid; and tetracycline and phenobarbitone respectively. In 3 patients with exfoliative dermatitis, the causative drugs were isonicotinic acid hydrazide (1), streptomycin (1), thiacetazone (1), and chloroquine (1). One patient reacted to both thiacetazone and chloroquine. In 3 patients who presented as urticaria, the causative drugs were analgin (1), phenylbutazone (1), and dilantin sodium (1).

**KEY WORDS:** Drug eruptions; provocation tests;

### Introduction

Among the various types of adverse reactions due to drugs, allergic skin eruptions are one of the most frequent<sup>1</sup>. Many patients and physicians attribute any symptom or eruption that may appear during the course of treatment to the drug(s) being used at that time. Out of the several *in vitro* and *in vivo* tests, provocation test is generally agreed to be the most reliable test for confirming the cause of the eruption<sup>1-3</sup>. Many physicians, however, are too scared to resort to the provocation test for fear of fatal consequences. Reports which are based on unconfirmed drug reactions, however,

are likely to be misleading, because, it is incorrect to presume that the drug most commonly known to produce a drug reaction is the one responsible in every case. Sometimes, a drug not previously known to produce a drug reaction is found to be the causative drug<sup>1,4,6</sup>. For the sake of accuracy, therefore, it seems important to find out the exact drug responsible for the reaction in each case. The present report deals with the drugs found responsible for the skin eruptions in our patients, by the provocation test.

### Materials and Methods

Patients in whom the cause of the drug eruption was confirmed by the provocation test are included in this report. Most of these patients reported during the acute phase of the eruption. The drug reaction in each

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Received for publication on 14-9-1981.

case was controlled by giving appropriate drugs, usually systemic corticosteroids in adequate doses. After the drug reaction had been controlled and the corticosteroids withdrawn, the patients were subjected to the provocation tests according to the procedure described earlier<sup>7</sup>. On the first day, depending on the type and the severity of the reaction, the patient was given 1/6 to 1/2 of one day's therapeutic dose of the first drug. If there was no reaction during the next 24 hours, the patient was given the same drug in progressively increasing doses on successive days, till one day's full therapeutic dose was reached. If there was no reaction even to one day's full therapeutic dose, the drug was considered safe and testing with the next drug was undertaken in the same manner. In case the patient developed a reaction to any drug, he was examined to confirm the reaction, the drug was withdrawn and the drug reaction was controlled with appropriate treatment. After the eruption had been controlled, provocation with the remaining drugs was resumed. In this manner, each patient was tested with all the drugs being taken at the time of the eruption. Patients who had severe eruptions like toxic epidermal necrolysis were generally hospitalised and provoked under supervision.

### Results

Exanthematous eruptions were seen in 11 cases, the causative drugs being thiacetazone and para aminosalicylic acid in 3 cases each, isonicotinic acid hydrazide, streptomycin, ethambutol, carbamazepine and phenytoin sodium in one case each. Toxic epidermal necrolysis seen in 4 patients was caused by para aminosalicylic acid in 2 cases and isonicotinic acid hydrazide, streptomycin, tetracycline and phenobarbitone in one case each. However, two patients were sensitive to two unrelated drugs i.e. streptomycin and

para amino salicylic acid; and tetracycline and phenobarbitone respectively. Exfoliative dermatitis seen in 3 cases was caused by isonicotinic acid hydrazide, streptomycin, thiacetazone and chloroquine in one case each. One of them was sensitive to two unrelated drugs i.e. thiacetazone and chloroquine. Urticaria seen in 3 patients was caused by analgin, phenylbutazone and dilantin sodium in one case each.

### Discussion

This analysis is based only on those cases in whom provocation tests were undertaken to confirm the causative drug(s), and who completed the test. There were quite a few patients who failed to complete the provocation tests. Thus the figures quoted in this report cannot be strictly considered to represent the true incidence of various types of drug eruptions due to various drugs. Surprisingly, thiacetazone was not found responsible for any case of toxic epidermal necrolysis; in contrast to some earlier reports based on unconfirmed drug reaction<sup>8,10</sup>.

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