

# Dapsone for the Treatment of Bullous Pemphigoid\*

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The use of dapsone for the treatment of bullous pemphigoid (BP) was successful in three out of six cases in our study.<sup>1</sup> In another study, Person and Rogers reported that less than 15 per cent of the cases responded to dapsone or sulphapyridine therapy.<sup>2</sup> The patients were younger in the latter study and their histopathology showed a predominance of polymorphonuclear leucocytes rather than eosinophils.

This report reviews a series of 28 cases of various types of BP, 21 cases of which were treated with dapsone.

## MATERIALS AND METHODS

The series consisted of 28 patients (21 males and 7 females) presenting various types of BP. The patients were treated between 1979 and 1981 on an in-patient basis at the Institute of Dermatology, Bangkok. Positive diagnosis was confirmed by both histopathological and immunopathologic techniques. In each case, subepidermal bullae were present; these were filled with a mixture of neutrophils and eosinophils. In 25 of the cases, neutrophils predominated. Because of the absence of neutrophilic-eosinophilic abscesses at the tip of the dermal papillae (biopsies were taken at an early stage from tiny vesicles, especially those of the vesicular type<sup>3</sup>) the

**SUMMARY** Thirteen cases (45.4% of the total) of bullous pemphigoid out of 28 were successfully controlled by the administration of dapsone alone. In most cases the initial dosage was 200 mg per day. The onset of favourable response in most cases was noted within two or three weeks. Thereafter, the dosage was gradually reduced over an interval of two or three weeks. Each patient was maintained for several months on a dosage of 50-100 mg/day. On this regime there were no side effects. Patients under the age of 60 years who demonstrated clinical features of the pure vesicular or vesiculobullous type of pemphigoid responded just as well as those with the Brunsting-Perry type, which is characteristically seen among older age groups. Patients over the age of 60 with the classical bullous type pemphigoid showed no response to dapsone.

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diagnosis of dermatitis herpetiformis (DH) was very unlikely. All lesions exhibited a linear or tubular pattern of IgG and complement deposited at the dermoepidermal junction. The antisera used were fluorescein isothiocyanated tagged antihuman IgG, IgA, IgM, C3 and fibrinogen (Hyland Laboratories). Granular deposits of IgA were not observed in the dermal papillae with the exception of Case No. 10, which was a case of mixed bullous disease.<sup>4</sup> In some cases (see Table 1), IgG antibasement membrane zone (BMZ) antibodies were present. Indirect complement immunofluorescent technique<sup>5</sup> was performed in five cases in which the IgG anti-BMZ antibodies were negative. In each case the results were negative. In all cases, G-6-PD was normal. The dosage of dapsone used was 2-4 mg/kg (in 21 cases) according to the severity of the disease and the age

of the patient. Concomitantly 300 mg per day of vitamin C was given. In the remaining seven cases of classical BP, dapsone was not used therapeutically.

## RESULTS

The patients were divided into four groups according to treatment response:

### Group I - Responders

The administration of dapsone alone controlled 12 cases of BP (four with the pure vesicular type, five with the vesiculo-bullous type, one with mixed bullous disease and two with the Brunsting-Perry type<sup>6</sup>). The dosage was 100-200 mg/day; a

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Table 1. Summary of the responders.

Case No.	Age	Sex	Clinical features	Immunofluorescent tests		Dosage of dapsone (mg/day)	Response (weeks)
				Direct, Igs	Indirect		
1	35	M	E, V, B	G, C3	Negative	200	3
2	18	M	E, V	G, C3	Negative	200	2
3	80	M	E, V, B	G, C3	Negative	200	3
4	40	M	E, V, B (hepatoma)	G	1 : 40	100	1
5	57	M	E, V, B	G, A, M, C3	Negative	200	2
6	50	F	V, B (mild)	G, C3	Negative	100	2 days
7	51	M	V	G, C3	Negative	150	2
8	58	M	V	G, C3	Negative	200	3
9	6	M	V	G, A, M, C3	1 : 1	50	3
10	51	M	E, V (Mixed bullous disease)	Tubular G; Granular A	Negative	100	2
11	75	M	V, S (Brunsting-Perry)	G, A, M, C3	Negative	100	2
12	60	F	V, S (Brunsting-Perry)	G, M, C3	1 : 40	100	2
13	60	M	E, B	G, C3	Negative	100 plus prednisone 60 mg; finally, dapsone alone	1  16

E = erythema or urticaria; V = vesicles < 1 cm usually about 0.5 cm; B = bullous > 1 cm; S = Scar

favourable response was obtained in two to three weeks. In fact, one case, which demonstrated only a comparatively mild degree of involvement, responded within two days. The patients in this group were given maintenance doses of 50-100 mg/day of dapsone and after several months on this regimen, no side effects were demonstrated. Response to dapsone was good in Case No. 4, despite the fact that the patient had concomitant hepatoma (Table 1).

#### Group II – Partial responders

This group consisted of three cases of classical BP, two of which had a high titre (1:160 and 1:320 respectively). In one case, the vesicular form was present; in the other, cicatricial mucous membrane BP. In these cases, prednisone was added to the dapsone and this combination produced excellent response. After prednisone was discontinued at the end of the fourth month of

therapy in one case with classical BP, dapsone alone controlled the disease.

#### Group III – Non-responders

In three cases, a dose of 100 mg/day of dapsone was given for one week; in one case a dose of 200 mg/day, for one week; and in a child, 25 mg/day, for four days. In each case there was no response to dapsone therapy, which was discontinued; prednisone, 60 mg/day, was substituted with dramatic results. The average age in this group was 65 years with the exception of the two-year-old child. At the commencement of this study the effective dose of dapsone and the time required for its efficacy were unknown, also the doubling of the dapsone dosage had not yet been attempted.

#### Group IV – Non-dapsone therapy

During the study, experience was gained with the utilization of dap-

sone. It was found that in elderly patients with large tense bullae displaying classical BP, there was no response to dapsone alone. Thus, in the seven cases comprising this group, (average age was 66.3 years), therapy was initially commenced with prednisone together with or without cytotoxic drugs.

No serious side effects were observed in this study. Anti-BMZ antibodies, in cases that were previously positive, became negative after the initial treatment. The period required for this to occur was two to five months.

#### DISCUSSION

This study demonstrates that dapsone alone controlled 13 cases (12 cases in group I and one in group II) out of the total of 28 BP cases. There were no side effects. Dapsone's mechanism of action has recently been reviewed<sup>7</sup> and is there-

fore not discussed in this paper. Serious side effects from dapsone, particularly when used in high dosages and for long periods of time are well documented.<sup>7-9</sup> Methaemoglobinaemia was not observed in this series, possibly because of the administration of vitamin C;<sup>10</sup> however, it was noted in our previous report.<sup>4</sup> In this series, the dosage of dapsone was gradually reduced after an interval of two to three weeks. A maintenance dose of 50-100 mg/day was used to control vesicular eruptions. The onset of response was noted after two to three weeks had elapsed, which is one week longer than the time from observed in cases of DH; further, the dose was more than doubled in these cases. The schedule of treatment suggested as a result of this study (see Table 2) follows.

In our experience, a dosage of 100 mg/day of dapsone is safe, although it is not effective in severe cases of BP. When 200 mg/day is used, the risk of complication increases, these patients should be carefully observed. The selection of patients is most important; patients younger than 60 years of age, particularly those of the middle-aged group with the pure vesicular, vesiculo-bullous or mixed bullous disease, responded well to dapsone. Patients with the Brunsting-Perry type of disease, which is found in patients older than 60 years of age, also responded to dapsone in a manner similar to those with cicatricial BP as reported by Kingman et al,<sup>11</sup> Roger et al<sup>12</sup> and Bean.<sup>13</sup> However, patients with classical BP who were over the age of 60, particularly those with large tense bullae, seemed to be unresponsive to dapsone. The reason for this failure to respond among patients in the older age group is unknown since the pharmacokinetics of dapsone has not been thoroughly studied in these patients. This report, therefore, confirms the age group which responds to dapsone as found in a previous study.<sup>2</sup>

We were unable to correlate the

Table 2. Schedule of dapsone treatment.

Severe	Dosage (mg/day)		Duration (weeks)	Onset of response (weeks)
		Moderate cases		
200		100	2-3	2-3
150		—	2-3	—
100		—	2-3	—
50-100		50-100	maintenance	—

relative predominance of neutrophils or eosinophils with responsiveness to dapsone. However, in most of our cases, the lesions were neutrophil-rich. The anti-BMZ antibodies in our series were negative in many cases, probably due to their nature<sup>14,15</sup> or to previous treatment. Many of the cases were referred to the Institute of Dermatology when clinical features became exacerbated. Anti-BMZ antibodies do not reflect the clinical status.<sup>16-19</sup> On the other hand, the clinical status is reflected by the presence of indirect complement-fixing pemphigoid antibodies.<sup>20</sup> In this series, they could not be used as a guideline in therapy since it was not possible to obtain positive results. However, clinical remission was associated with the disappearance of anti-BMZ antibodies in cases which were previously positive. This confirmed a previous study.<sup>14</sup>

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