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Relationship of Dietary Gluten Intake to Dapsone Dose in Dermatitis herpetiformis

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The gluten intake was quantitated utilizing a dietary history method in 43 patients with dermatitis herpetiformis on non-restricted diet. The mean daily gluten intake was 15 g. The individual intake of gluten was related to the maintenance dose of dapsone. It was significantly higher in patients on 100-150 mg dapsone daily than in those taking 0-25 mg daily. There was a significant correlation between amount of gluten in the diet and the dapsone dose (p<0.01, r=0.43). Villous atrophy was not related to the dapsone dose. It is suggested that the gluten-sensitive enteropathy changes the intestinal permeability and thus contributes to the development of blisters. Key word: Dapsone treatment. (Received August 15, 1986.)

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Virtually all patients with dermatitis herpetiformis (DH) have a coeliac-like enteropathy (1). The skin lesions are also gluten-dependent and clear following a gluten-free diet (2).
The link between the small intestinal mucosal lesions and the rash is supposed to be immunological (1). Dapsone (diaminodiphenylsulphone) has a beneficial symptomatic effect solely on the skin lesions. Its mechanism(s) of action is unknown as are the factors determining the dapsone dose (3). It has thus not been possible to relate the maintenance dapsone dose to the severity of disease, the plasma concentration of dapsone and its main metabolite or the occurrence of villous atrophy (3-6).

We have recently used a dietary history method to calculate the amount of dietary gluten in patients with dermatitis herpetiformis on non-restricted or gluten-free diet (7, 8). In the present study we relate the daily gluten intake to the dapsone dose necessary to control the rash.

PATIENTS AND METHODS

Patients
Forty-three consecutive patients with DH on non-restricted diet were investigated. All had granular IgA in the dermal papillae in uninvolved skin biopsies. There were 27 males and 16 females. Their mean age was 43 years (range 16-74) and mean duration of disease 10 years (range 2 months-42 years).

Dapsone
Twelve patients had mild and/or intermittent skin symptoms and required no dapsone treatment. The mean daily dose of dapsone in the remaining 31 patients was 76 mg (range 25-150). The patients had been repeatedly asked to try to reduce the dapsone dose to the minimum required to control skin symptoms.

Evaluation of gluten intake
A dietary history method including cross-checking using a special questionnaire was used (9, 10). The patients were interviewed in detail about their dietary habits. For every food item, the patient was asked about the frequency of consumption (per day, week and month) and also about the size of the portions in order to estimate the average daily consumption. Individual intake of energy, protein, carbohydrates and fat was calculated from food consumption tables (Swedish National Food Administration, 1978) using a macrodata system.

Gluten intake was especially scrutinized in the interviews. Based on the analyses of different flours (Product Development Laboratory, Kvam och Bageri AB, Juvel) the gluten content was calculated to be 80% of cereal protein.

Morphology of small bowel mucosa
Small bowel mucosal biopsies were obtained either endoscopically from the second part of the duodenum and/or as a capsule biopsy from the duodenojejunal junction (11). The classification was based on the dominant finding in this group of biopsies. Small-bowel mucosal findings were graded as normal, inflammatory reaction only, partial villous atrophy, or subtotal villous atrophy (11).

Statistics
Statistical comparisons between two groups was performed with the Chi-square test and the Student's t-test. Correlations were assessed using Spearman's rank correlation coefficient ($r_s$). A $p$-value $<$0.05 was considered significant.

RESULTS

The mean daily gluten intake of the 43 patients was 15 g. The daily gluten consumption was significantly higher in patients requiring 100-150 mg dapsone daily than in patients taking 0-25 mg daily ($p<$0.001) (Table I). There was a significant but weak correlation between the amount of gluten intake and the dapsone dose ($r_s=0.43$, $p<$0.01). The frequency of villous atrophy was not significantly higher in patients on 100-150 mg dapsone daily than in 0-25 mg daily (0.10$>p>0.05$). Likewise there was no significant
difference between the mean dose of dapsone of patients with villous atrophy and of those with normal or inflamed intestinal mucosa (Table II).

DISCUSSION
The maintenance dose of dapsone required to control the skin lesions is a commonly used parameter to evaluate the severity of the rash in DH though its metabolism and mechanism of action are unknown (3). In the present study the daily consumption of gluten was higher in patients taking more dapsone to control their skin rash. However, a considerable overlap occurred. We have previously shown that there is a dose–response relationship between the gluten intake and the morphological abnormalities of the small intestinal mucosa (7). However, there was no significant difference between the dapsone requirement in patients with villous atrophy compared to patients with normal or inflamed small bowel mucosa, which is in accordance with previous reports (6). The enteropathy and the rash are both gluten dependent, though the relationship may not necessarily be direct (12). This might indicate that gluten per se may not necessarily predispose to the occurrence of the rash. Instead it may exert its actions by inducing the bowel lesions and thus allowing other factor(s) to cross the abnormally “leaky gut” (13) or exclude a compound(s) necessary for maintaining the integrity of the basal membrane zone region of the skin. There has recently been a reawakened interest in the possibility of dietary iodine to be such a factor (14).

ADDENDUM IN PROOF:
Pharmacological, clinical and immunological aspects of dapsone treatment in dermatitis herpetiformis have recently been studied (Sanders SW, Zone JJ. Arzneim.-Forsch./Drug Res. 1986; 36: 146–149).

Table I. The daily gluten consumption (mean ± SEM) and small intestinal mucosal villous atrophy in relation to the maintenance dose of dapsone in 43 patients with dermatitis herpetiformis

<table>
<thead>
<tr>
<th>Dapsone (mg/d)</th>
<th>0–25</th>
<th>50–75</th>
<th>100–150</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>14</td>
<td>14</td>
<td>15</td>
</tr>
<tr>
<td>Gluten (g/d) (range)</td>
<td>11.5±0.8 (6.9–19.0)</td>
<td>15.7±1.4 (6.0–24.2)</td>
<td>16.7±1.8 (7.8–34.1)</td>
</tr>
<tr>
<td>Small bowel villous atrophy (positive/examined)</td>
<td>8/13 (62%)</td>
<td>10/13 (77%)</td>
<td>12/15 (80%)</td>
</tr>
</tbody>
</table>

Table II. Maintenance dose of dapsone (mean ± SEM) in relation to the severity of small bowel pathology

<table>
<thead>
<tr>
<th>n</th>
<th>Dapsone mg/day (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Villous atrophy</td>
<td>30</td>
</tr>
<tr>
<td>Normal or Inflam.</td>
<td>11</td>
</tr>
</tbody>
</table>
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Methotrexate Treatment of Psoriatic Arthritis

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A prospective study was carried out over 12 months involving twenty-eight patients with psoriatic arthritis. Almost all patients improved dramatically with regard to both pain and function. Clinical assessment including evaluation of number of swollen joints, joint tenderness score, and morning stiffness was performed by external observer without any knowledge of previous evaluation data. These data together with patients' assessment of pain and assessment of general condition, analgetics, and sedimentation...