## REFERENCES

1. Agnello V. Complement deficiency states. Medicine 1978; 57: 1–23.
2. Rynes R. Inherited complement deficiency states and SLE. Clin Rheum Dis 1982; 8: 29–47.
3. Glass D, Raum D, Gibson D, Stillman JS, Schur PH. Inherited deficiency of the second component of complement. J Clin Invest 1976; 58: 853–861.
4. Gelfand EW, Clarkson JE, Minta JO. Selective deficiency of the second component of complement in a patient with anaphylactoid purpura. Clin Immunol Immunopathol 1975; 4: 269–276.
5. Einstein LP, Alper CA, Block KJ et al. Biosynthetic defect in monocytes from human beings with genetic deficiency of the second component of complement. N Engl J Med 1975; 292: 1169–1171.
6. Rendall JRS. Vasculitis with probable familial C2 deficiency Proc Roy Soc Med 1977; 70: 733–734.
7. Matsuura H, Murai M, Hashimoto T, Matsumoto T, Fukui O. C2 deficiency vasculitis: Complication of enterocolitis, cutaneous ulcers and neuropsychiatric disorder. Am J Gastroenterol 1983; 78: 1–5.
8. Bennett RE, Clough JD, Calabrese LH. Fulminating vasculitis in a homozygous C2-deficient patient. Cleve Clin Q 1985; 52: 213–215.
9. Hyatt AC, Altenburger KM, Johnston RB, Winkelstein JA. Increased susceptibility to severe pyogenic infections in patients with an inherited deficiency of the second component of complement. J Pediatr 1981; 98: 417–419.
10. Sampson HA, Walchner AM, Baker PJ. Recurrent pyogenic infections in individuals with absence of the second component of complement. J Clin Immunol 1982; 2: 39–45.
11. Friend P, Repine JE, Kim Y, Clawson CC, Michael AF. Deficiency of the second component of complement (C2) with chronic vasculitis. Ann Intern Med 1975; 83: 813–816.
12. Soter N. Cutaneous necrotizing venulitis. In: Wolff, K, Winkelmann R, eds. Vasculitis. Lloyd-Luke Ltd, 1980: 173–182.
13. Svensson Å, Edman B, Möller H. A diagnostic tool for atopic dermatitis based on clinical criteria. Acta Derm Venereol (Stockh) 1985; 114: 33–40.


# Relationship of Dietary Gluten Intake to Dapsone Dose in Dermatitis herpetiformis


HÅKAN MOBACKEN,[1] HENRIK ANDERSSON,[2] ERIK DAHLBERG[1] and WENDELA KASTRUP[1]

*Departments of [1]Dermatology and [2]Clinical Nutrition, Sahlgren's Hospital, University of Gothenburg, Sweden*



Mobacken H, Andersson H, Dahlberg E, Kastrup W. Relationship of dietary gluten intake to dapsone dose in dermatitis herpetiformis. Acta Derm Venereol (Stockh) 1987; 67: 267–270.



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 ($p<0.01$, $r_S=0.43$). 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.)



H. Mobacken, Department of Dermatology, Sahlgren's Hospital, S-413 45 Göteborg, Sweden.


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*

Fourty-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, Kvarn 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*

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

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

| | *n* | Dapsone mg/day (range) |
|---|---|---|
| Villous atrophy | 30 | 61±8.0 (0–100) |
| Normal or Inflam. | 11 | 42±12 (0–100) |

ACKNOWLEDGEMENTS

The dietary interviews were performed by dietician A.-C. Björkman. The gastrointestinal biopsies were obtained by Rolf Gillberg, MD and Reinhold Stockbrügger, MD, Division of Gastroenterology, Department of Medicine II, Göteborg.

REFERENCES

1. Katz SJ, Strober W. The pathogenesis of dermatitis herpetiformis. J Invest Dermatol 1978; 70: 63–75.
2. Fry L, Seah P, Riches DJ, Hoffbrand. Clearance of skin lesions in dermatitis herpetiformis after gluten withdrawal. Lancet 1973; i: 288–291.
3. Swain AF, Ahmad RA, Rogers HJ, Leonard JN, Fry L. Pharmacokinetic observations on dapsone in dermatitis herpetiformis. Br J Dermatol 1983; 108: 91–98.
4. Alexander JOD. Dapsone in the treatment of dermatitis herpetiformis. Lancet 1955; i: 1201–1202.
5. Ellard GA, Gammon PT, Savin JA, Tan RS-H. Dapsone acetylation in dermatitis herpetiformis. Br J Dermatol 1974; 90: 441–444.
6. Reunala T, Blomqvist K, Tarpila S, Halme H, Kangas K. Gluten-free diet in dermatitis herpetiformis. I. Clinical response of skin lesions in 81 patients. Br J Dermatol 1977; 97: 1–8.
7. Andersson H, Björkman A-C, Gillberg R, Kastrup W, Mobacken H, Stockbrügger R. Influence of the amount of dietary gluten on gastrointestinal morphology and function in dermatitis herpetiformis. Hum Nutr Clin Nutr 1984; 38 C: 279–285.
8. Björkman A-C, Mobacken H, Kastrup W, Andersson H. Changes in food consumption and its nutritional quality when on a gluten-free diet for dermatitis herpetiformis. Hum Nutr: Appl Nutr 1985; 39 A: 124–129.
9. Arvidsson-Lenner R, Bengtsson C, Carlgren C, Isaksson B, Lundgren BK, Peterson I. The study of women in Gothenburg 1968–1969. Acta Med Scand 1977; 202: 183–188.
10. Steen B, Isaksson B, Svanborg A. Intake of energy and nutrients and meal habits in 70-years old males and females in Gothenburg, Sweden. Acta Med Scand 1978; Suppl 611: 39–86.
11. Gillberg R, Kastrup W, Mobacken H, Stockbrügger R, Åhrén C. Gastric morphology and function in dermatitis herpetiformis and in coeliac disease. Scand J Gastroenterol 1985; 20: 133–140.
12. Fry L, Leonard JN, Swain, F, Tucker WFG, Haffenden G, Ring N, McMinn RMH. Long term follow-up of dermatitis herpetiformis with and without dietary gluten withdrawal. Br J Dermatol 1982; 107: 631–640.
13. van der Meer JB, Zeedijk N, Poen H, van der Putte SCJ. Rapid improvement of dermatitis herpetiformis after elemental diet. Arch Dermatol Res 1981; 271: 455–459.
14. Mobacken H, Andersson H, Dahlberg E, Fransson K, Gillberg R, Kastrup W, Stockbrügger R. Spontaneous remission of dermatitis herpetiformis: dietary and gastrointestinal studies. Acta Derm Venereol (Stockh) 1986; 66: 245–250.

## Methotrexate Treatment of Psoriatic Arthritis

HUGH ZACHARIAE and EVA ZACHARIAE

*Department of Dermatology, Marselisborg Hospital, and the Department of Rheumatology, Aarhus Kommunehospital, University of Aarhus, Aarhus, Denmark*

Zachariae H, Zachariae E. Methotrexate treatment of psoriatic arthritis. Acta Derm Venereol (Stockh) 1987; 67: 270–273.

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, consumption of analgetics, and sedimentation