Acta Derm Venereol (Stockh) 1986; 66: 316–320

# Dermatitis herpetiformis: Consequences of Elemental Diet

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Zeedijk N, van der Meer JB, Poen H, van der Putte SCJ. Dermatitis herpetiformis: consequences of Elemental Diet. Acta Derm Venereol (Stockh) 1986; 66: 316–320.

The administration of an Elemental Diet to 5 patients with dermatitis herpetiformis, requiring high doses of Dapsone (diaminodiphenylsulphon, DDS), showed a rapid and beneficial effect on the skin lesions within two weeks. This effect was not influenced by simultaneous gluten challenge in one patient. A possible explanation is a reduction in the amount of harmful immune complexes due to the elimination of proteins from the diet. Subsequent introduction of a more comprehensive diet led to an increase of the minimal effective dose of Dapsone. These results underline the importance of dietary influences on the skin activity in dermatitis herpetiformis, other than gluten alone. *Key words: Gluten challenge; Dietary influences.* (Received December 19, 1985.)

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Previously we described two patients with dermatitis herpetiformis (DH) showing a rapid beneficial response to the administration of an Elemental Diet (1). This was done because of high "harmful" doses of Dapsone in these patients, who did not respond to a strictly gluten-free diet. The concept underlying the administration of an Elemental Diet in these patients, was based on a working-hypothesis that an immune complex mechanism is operative in DH.

The aim of this study was to verify these first observations, to convert this diet to more substantial and palatable meals, and to see which substances have deleterious effects. To bypass the systematic procedure of stepwise addition of new food substances to the Elemental Diet, which would be a very timeconsuming and aggravatory procedure, we used a standardized Tubefood containing a limited number of essential food substances. Nutrison® (Nutricia BV., Zoetermeer, The Netherlands), fulfilled these criteria. After a trial had proven that this diet was well tolerated, a further extensified diet was introduced, partly based on the composition of Nutrison®, called Basic Diet.

## MATERIALS AND METHODS

Five patients with active DH requiring high doses of Dapsone are included in this study. The mean duration of disease was 7½ years (range 2 to 15 years). Preceding the study three of the patients adhered to a strictly gluten-free diet during 4, 18 and 42 months respectively, without a favourable effect in skin activity. In all patients the diagnosis of DH was confirmed by the demonstration of suprapapillary microabscesses in early skin lesions and by the characteristic immunohistochemical finding of granular IgA deposits in the uninvolved skin (2, 3, 4). In all patients an intestinal biopsy was taken by a (modified) Crosby capsule under radiographic control 10–20 cm beyond the ligament of Treitz, prior to the administration of the Elemental Diet. The intestinal biopsies were repeated at the end of the Elemental Diet period, which was confined to two weeks. Two patients refused a second biopsy. The microscopic appearance of the jejunal mucosa was graded according to the method of Shuster and co-workers (5).

The minimal effective dose (MED) of Dapsone, defined as the smallest dose sufficient to suppress skin activity completely (6), was determined under clinical control, before and after the institution of the subsequent diets.

The composition of Elemental Diet, Variant 2000® (Nutricia BV., Zoetermeer, The Netherlands) is shown in Table I, indicating that proteins are substituted by aminoacids. The substance was dissolved in tap-water and ingested by mouth. Tea and coffee without milk were permitted. All patients used this diet during two weeks.

Patient 4 was challenged with 25 g wheat-gluten flour daily (Latenstein BV., Rotterdam, The Netherlands), during the intake of Elemental Diet.

After the MED of Dapsone in each patient was established during Elemental Diet a commercially available Tubefood, Nutrison®, was administered to patients 1, 2 and 3, during two weeks as well. Its composition is shown in Table I. The suspension was drunk in its ready to hand form. Since Nutrison® is composed of current food articles, a diet can be "translated" from its constituents. To these constituents some compounds were added to achieve palatable meals and to avoid deficiencies. These included yeast and buckwheat flour, which are indispensable to bake gluten-free bread, and potatoes which form a major element in Dutch feeding habits and are an important source of carbohydrates and ascorbic acid. This diet was given the name "Basic Diet" (Table II). As the Basic Diet had to be taken for a longer period, a dietician evaluated the sufficient intake of essential nutrients. After they finished the 2-week period with the Tubefood diet, patients 1, 2 and 3 were put on the Basic Diet. Patients 4 and 5 immediately switched from the Elemental Diet to the Basic Diet, without an intermediate period with Nutrison®. The observation period with Basic Diet was confined to two months. Patient 4 discontinued the use of Basic Diet after 2 days and was withdrawn from further study. The other patients were seen at regular intervals, adapting the MED of Dapsone to their skin condition.

## RESULTS

In all 5 patients a rapid and favourable response to the administration of Elemental Diet was obvious (Table III). Although Dapsone could be discontinued completely within 2 weeks in patient 1, the other 4 patients still needed this medication, however, in a much smaller dose than before the experiment.

Of special interest are the results in patient 4, who showed a substantial improvement in

Table I. *Analysis of Elemental Diet[a] and Tubefood[b]*

| | Amounts per day | |
|---|---|---|
| | Elemental Diet | Tubefood |
| Proteins | – | + (80 g) |
| Aminoacids | + (50 g) | – |
| Fats | + (6 g) | + (80 g) |
| Carbohydrates | + (436 g) | + (226 g) |
| Iodine | + (120 µg) | + (120 µg) |
| Energetic value | 8 400 kJ | 8 400 kJ |

[a] Variant 2000® and [b] Nutrison®, made by Nutricia, Zoetermeer, The Netherlands.

Table II. *Composition of Basic Diet*

| Derived from the constituents of Nutrison® Tubefood | Added compounds |
|---|---|
| Cowmilk | Rice |
| Maize oil | Potatoes |
| Beef | Chicken egg |
| Carrots | Yeast |
| | Buckwheat flour |

his skin condition, despite the concurrent gluten challenge (Table III). This gluten challenge was initiated at the start of the Elemental Diet.

The substitution of Elemental Diet by Tubefood maintained the remission of skin activity without sulfone therapy only in patient 1 (Table IV). In patients 2 and 3 some days of remission alternated with days of itching and vesiculation. To suppress these symptoms completely the MED of Dapsone had to be established at 60 mg daily in both patients. The observation period of Tubefood was confined to 2 weeks as well, because within this period a stabilization seemed to be attained (Table IV).

The results of Basic Diet were rather variable. In patient 1 recurrence of skin lesions within 2 weeks necessitated the reintroduction of 50 mg Dapsone daily, increasing to 75 mg after 2 months (Table IV). Patient 2 showed a slight worsening of his skin condition resulting in a rise of the MED of Dapsone from 60 to 75 mg within two months. In patient 4 a rapid outburst of itching and vesiculation was seen within two days after switching from Elemental Diet to Basic Diet. His skin lesions disappeared after increasing the dosage of Dapsone to 225 mg. After one week of Basic Diet patient 5 showed a rapid worsening of her skin condition, necessitating increase of the Dapsone dosage from 25 to 100 mg. In the following two months her MED of Dapsone rose to 300 mg. Reintroduction of a normal unrestricted diet in patient 1 and a gluten-free diet (GFD) in patients 2 and 3, resulted in an increase of the MED of Dapsone within 2–10 days, followed by a rapid improvement again after a repeated observation period with Elemental Diet.

The jejunal biopsies taken before and after two weeks Elemental Diet showed various grades of atrophy in all patients, without a consistent relation to use and duration of a

Table III. *The effect of Elemental Diet on skin activity*

| Patient | MED of Dapsone at onset of disease (mg) | MED of Dapsone after GFD (duration) (mg) | MED of Dapsone after 2 weeks Elemental Diet[a] (mg) |
|---|---|---|---|
| 1 | 250 | 250 (4 mths) | 0 |
| 2 | 300 | 300 (3½ yrs) | 50 |
| 3 | 250 | Never GFD | 25 |
| 4 | 300 | Never GFD | 75[b] |
| 5 | 200 | 200 (1½ yrs) | 25 |

[a] Note that three patients used already a GFD preceding the start of Elemental Diet. Hence the effect of Elemental Diet cannot be attributed to gluten withdrawal as a side effect.
[b] Besides Elemental Diet this patient was challenged with 25 g gluten daily.

Table IV. *Minimal effective dose of Dapsone after the institution of Elemental Diet, Tubefood and Basic Diet respectively (in mg per day)*

| Patients | Elemental Diet after 2 weeks | Tubefood after 2 weeks | Basic Diet after 1 week | 2 weeks | 4 weeks | 8 weeks |
|---|---|---|---|---|---|---|
| 1 | 0 | 0 | 0 | 50 | 50 | 75 |
| 2 | 50 | 60 | 60 | 60 | 75 | 85 |
| 3 | 25 | 60 | 60 | 60 | 60 | 60 |
| 4 | 75 | Not done | 225[a] | – | – | – |
| 5 | 25 | Not done | 100 | 100 | 200 | 300 |

[a] MED of Dapsone after 2 days. Discontinuance of the study at this moment.

GFD, or the disease activity, before and after the Elemental Diet. After two weeks of Elemental Diet the second jejunal biopsy revealed improvement, no difference and worsening of the villous atrophy respectively in the 3 patients concerned.

## DISCUSSION

From the above observations the effect of an Elemental Diet in DH seems evident and substantial in all patients. In 3 patients its reproducibility was established.

The concept underlying the administration of an Elemental Diet in DH patients was based on the working hypothesis that an immune complex mechanism is operative in DH (3). In short, the normal diet supposedly contains substances which through genetic predisposition act as antigens in DH, i.e. lead to antibody formation by the gut associated lymphoid tissue. Hence, IgA class antibodies are formed, which react with these antigens to form immune complexes. The gluten induced villous atrophy of jejunal mucosa may facilitate the passage of antigen-excess to form soluble immune complexes, which are transported by the circulation and deposited at the dermo-epidermal junction. Chemotactic factors induce the micro-abscess formation in these areas, which in turn elicitate the skin lesions.

According to this hypothesis, various substances could act as antigens. If the bulk of such antigen(s) is eliminated from the diet, no new ("harmful") immune complexes are formed and rapid improvement of the skin lesions can be expected. Since most antigens leading to a humoral immune response are proteins, a diet which does not contain full proteins supposedly does not contain major antigens and, therefore, may be expected to be highly effective in DH. Elemental Diet fulfills these criteria, since it contains aminoacids in stead of proteins. The rapid beneficial effect of this diet is in agreement with our hypothesis. At present the essential antigens are still to be determined. Gluten (gliadin) as a potential antigen does not seem a likely candidate here as has been discussed previously (7, 8). This is supported by the beneficial effect of Elemental Diet in patient 4, obtained despite gluten challenge. This makes a direct relationship between gluten and skin lesions in DH unlikely. Moreover, the strictly gluten-free Basic Diet was able to induce DH skin lesions (Table IV), which indicates that harmful dietary substances other than gluten alone do occur. The observation, nevertheless, that a GFD may be very helpful, can be explained by the fact that a consequential improvement of the jejunal mucosa at the same time restores the intestinal barrier for the excessive passage of antigens and thus prevents the formation of harmful immune complexes. In line with this idea is the observation of Kumar et al. (9) that the incidence of serum antibodies to a variety of dietary proteins in patients with DH and adult coelic disease fell with morphological improvement of jejunal abnormalities after prolonged GFD. The jejunal improvement after GFD seems to occur gradually (10, 11, 12), which might account for the long recovery period of the skin lesions after gluten withdrawal. In our opinion, therefore, a GFD seems to have only an indirect effect on the skin disorder in DH. Nevertheless, a GFD remains an essential step in the management of DH.

The effects of Elemental Diet on the jejunal mucosa were conflicting and difficult to evaluate. This was partly due to the short observation period and the small number of patients. On the other hand several investigators pointed on the patchiness of the jejunal atrophy in DH causing variable histological pictures within one patient (13, 14).

It is known that iodine has a deleterious effect on DH skin lesions. Since the iodine concentrations of Elemental Diet and Tubefood (Table I) are not below the average iodine intake of the Dutch population (15), the effect of Elemental Diet on DH cannot be attributed to a possible reduction of iodine intake.

With respect to possible influences of Elemental Diet on the abnormal small intestinal flora in DH (16, 17), the question of bacterial toxins on DH deserves further examination.

An Elemental Diet offers the opportunity for a systematic search for the harmful dietary factor(s) fundamentally involved in the pathogenesis of DH. The observation, that in some patients an Elemental Diet is not fully effective in the prevention of skin lesions, indicates that the aetiopathological factors in DH are very complex.

## ACKNOWLEDGEMENTS

We are grateful to Prof. Dr W. A. van Vloten, J. Toonstra, dermatologists, Department of Dermatology, State University Hospital of Utrecht and Dr M. C. J. M. de Jong, immunologist, Department of Dermatology, State University Hospital of Groningen, for their helpful advice and criticism. We thank Miss M. van den Ingh and Miss M. H. de Jonge, dieticians, for their valuable technical assistance.

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