histopathological changes of erythema nodosum. The histopathological findings changed in the late phase of TA: a granulomatous vasculitis with occlusion of small vessels and giant cells was now detectable at the site of erythema nodosum-like lesions and in the maculopapulous and nodular lesions at the upper extremities and trunk.

Our report shows that nodules which appear early in the history of the disease can be clinically and histologically indistinguishable from erythema nodosum. But later on they may be a sign of true granulomatous giant cell vasculitis. Therefore, histopathological investigation of such nodules is mandatory.

Since granulomatous vasculitic changes reflect persistent activity, histopathological investigations can give additional information about the disease activity of TA. Such changes may be the reason for more intense systemic therapy, especially if combined with necrotizing lesions. All skin lesions in TA should therefore be carefully investigated. On the other hand all erythema nodosum-like lesions and necrotizing skin lesions of unknown origin should lead to the inclusion of TA into the list of differential diagnoses, especially if associated with the histological finding of granulomatous vasculitic changes.

Bullous Pemphigoid and Diabetes Mellitus

Sir,

Bullous pemphigoid (BP) is an immunobullous disorder mainly affecting subjects over 60, and its association with other diseases is controversial for the already critical high incidence of pathologies such as diabetes, neoplasm, cardiopathies, etc., in this age range.

We have studied the possible association between BP and diabetes mellitus in a retrospective case-controlled study.

Sixty-six patients over 60 years of age (mean age 79, range 62–95, 27 men and 39 women) with BP who attended our Institute between 1985 and 1995 were investigated. The diagnosis in all patients had been confirmed by histological examination and direct and/or indirect immunofluorescence test. Each patient was age- and sex-matched with 2 controls recruited from subjects hospitalized in the same period with a diagnosis of contact dermatitis or urticaria. Controls were the first ones whose names appeared in the hospital record books within 3 months before or after the name of each of the BP patients. Controls receiving steroid therapy were excluded from the study.

Diabetes mellitus was assessed through positive past medical history and/or fasting plasma glucose value >140 mg/dl conducted before steroid treatment.

As reported in Table 1, 21 patients (32%) with BP had an associated diabetes mellitus compared to 12 of the control subjects (9%). This difference was statistically significant (p<0.001 with Yates' correction).

The prevalence of diabetes in our patients was also relevant when compared to a large population-based survey of known diabetes mellitus in our town of Verona (1), which found 9% diabetes in 48,580 subjects over 60 (9% in men, 8.5% in women).

There are few reports of BP and diabetes mellitus association with different results.

| Table I. Subjects with diabetes mellitus (DM) compared as to age and sex |
|--------------------------|-----------------|-----------------|-----------------|-----------------|
|                         | Patients with bullous pemphigoid | Controls         |
| Age                     | Male | Female | Male | Female | Male | Female |
| 60–69                   | 3    | 6      | 0    | 2      | 0    | 12     | 1    | 4    |
| 70–79                   | 4    | 12     | 2    | 17     | 2    | 24     | 2    | 34   |
| >80                     | 4    | 9      | 8    | 20     | 3    | 18     | 4    | 40   |
| Total                   | 11   | 27     | 10   | 39     | 5    | 54     | 7    | 78   |
| (40.7%)                 | (25.6%) | (9.2%) | (8.9%) |       |

Downham & Chapel found an adult-onset diabetes mellitus in 14 of 34 (41%) patients (2).

Chuang et al., in a case-controlled study, found an increased frequency of diabetes in their series of 30 patients with 20% diabetes in BP compared to 2% of controls (3).

On the contrary, Taylor et al. did not find a difference for the frequency of diabetes in a series of 108 patients with BP when compared with controls (4).

Further statistical and clinical studies are then required to evaluate whether this association could share a pathogenetic mechanism.

REFERENCES


Acta Derm Venereol (Stockh) 76
known diabetes mellitus prevalence and 5 years all-cause mortality. Dia-
2. Downham TF, Chapel TA. Bullous pemphigoid. Therapy in pa-
patients with and without diabetes mellitus. Arch Dermatol 1978;
114: 1639–1642.
3. Chuang TY, Korkij W, Soltani K, Clayman J, Cook J. Increased
frequency of diabetes mellitus in patients with bullous pemphigoid:
4. Taylor G, Venning V, Wojnarowska F, Welch K. Bullous pemphi-
Accepted March 29, 1996.
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Pseudoallergen-free Diet in the Treatment of Chronic Urticaria

Sir,

In addition to the article by Zuberbier et al. on pseudoallergen-
free diet in the treatment of chronic urticaria (1), we want to
report our own experience. Since 1979 we have studied patients
suffering from chronic urticaria for the relevance of pseudoall-
ergic intolerance due to food additives and aspirin by oral
provocation tests, and in case of positivity we treated them
with pseudoallergen-free diet and followed them up for 6
months. In 1982 we published our first results (2). Thirty-nine
out of 100 patients exhibited intolerance phenomena to one
or more substances. They had avoided drugs strictly and were
on additive-free diet during the oral provocation. Twenty-
three per cent of patients reacted with intolerance to aspirin,
15% to tarrazine, 13% to patent blue and indigotin, 10% to
choline yellow and yellow orange, 8% to sodium benzoate and
8% to potassium sorbate. Forty-four per cent of the previously
positively reacting patients, having been on an additive-free
diet and avoiding aspirin, did not reveal any urticaria in a
6-month follow-up. There was a statistically significant differ-
ence between these patients and those without intolerance
phenomena and without an appropriate diet, only 24% of
whom cleared spontaneously after 6 months.

Since 1982 we have applied this diagnostic and therapeutic
regimen continuously. Details are given in Table I. We com-
pleted the food dyes (e.g. erythrosin E 127) and added sodium
metabisulfit, sodium glutamate, propylgallate and butylhy-
droxylansol to our test battery and interposed placebo gelatine
capsules on two or three occasions of testing. Again, several
patients reacted to more than one test substance. On the other
hand, we may have obtained falsely negative tests due to the
dose-dependency of the additives or even the great number of
additives (2,000–20,000 estimated) (3), which cannot be tested
in detail. In addition, the combined or synergistic effect of addi-
tiva may be required or several pseudoallergens are still
undetected. This may explain the different results reported by
several authors (4–6).

For the last 14 years we have put altogether 412 patients on
pseudoallergen-free diet, and symptoms ceased or were greatly
reduced within 2 to 4 weeks in 73% of them. In 52% of
patients this effect lasted while they were on the diet. Even
patients in whom we could not find any cause or hint for
eliciting factors of the urticaria we applied this diet, and 28%
of them benefited from this regimen. IgE-mediated allergy
had been excluded by a specific RAST test and prick tests as
well. Also chronic infections, e.g. by Helicobacter pylori and
Candida albicans had been looked for (1, 7) and treated
adequately.

However, the same patients admitted that they had not
always followed our recommendations strictly, e.g. when
taking part in social events or parties. It is well known that
the concentration of salicylates changes in plants, fruits or
vegetables according to their growth conditions (8). On the
other hand, it seems clear that such a strict diet requires
reliable compliance by the patient. As shown by our controls,
without intolerance, without diet and without an evident
alternate cause of the urticaria the self-limiting effect in chronic
urticaria is about 24%.

Finally, we want to emphasize that food dyes are also
incorporated in the cover of drugs, even in antihistammines.
The declaration of food for additives and preservatives would
be very helpful for the patients, the more so as the composition
changes in dependency on the dye required.

By all means, even when pseudoallergic intolerance or other
eliciting factors for chronic urticaria cannot be identified, the
use of a pseudoallergen-free diet for about 4 weeks is recom-
mended as a diagnosis ex iuvantibus.

REFERENCES
1. Zuberbier T, Chantraine-Hess S, Hartmann K, Czarnetzki BM.
Pseudoallergen-free diet in the treatment of chronic urticaria. Acta
Derm Venereol (Stockh) 1995; 75: 484–487.
2. Kirchhof B, Haustein UF, Rytter M. Azetyhalazysäure-Additiva-

Table I. Six-month follow-up of patients with chronic urticaria while on a pseudo-allergen-free diet

<table>
<thead>
<tr>
<th>Patients</th>
<th>Number</th>
<th>Free of skin lesions</th>
<th>Improvement</th>
<th>No improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with positive oral provocation, on the diet</td>
<td>98</td>
<td>43</td>
<td>29</td>
<td>26</td>
</tr>
<tr>
<td>Patients without positive oral provocation, without diet</td>
<td>143</td>
<td>34</td>
<td>47</td>
<td>62</td>
</tr>
</tbody>
</table>

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