COMMENTS

Kiistala & Mustakallio (2) showed that the blisters in normal skin splits below the basal membrane. In psoriatic lesions we also found the rupture at the dermal-epidermal junction. The surface of the basal cells in non-treated psoriatic lesions showed a striking difference from non-lesional skin or treated lesions. The reason is not clear.

The intercellular bridges seen in treated and normal appearing skin are probably cytoplasmic extensions containing tonofilaments ending at desmosomes. They are absent in non-treated psoriatic lesions. This might be associated with the presence of intracellular oedema and/or the rapid proliferation in the basal cells in active psoriasis. The absence of elongated processes and desmosomes can also explain why blisters on psoriatic lesions easily rupture as soon as they are formed and that only a moderate subpressure can be used (1). That partly healed lesions rarely rupture could be explained by the existence of normal structures. One could have expected that the blisters form more rapidly in psoriatic lesions. The reason that no marked difference in time for appearance of blisters was seen between normal and lesional skin could possibly be due to that the increased thickness of the plaques gives a decreased suction force in the deeper layers of the epidermis.

REFERENCES


Minimal Effect of Complete H1 Receptor Blockade on Urticaria pigmentosa

LIONEL B. KRAUSE and SAM SHUSTER

University Department of Dermatology, Royal Victoria Infirmary, Newcastle upon Tyne, England


The effect of complete H1 receptor blockade on urticaria pigmentosa was studied in 6 patients. Astemizole 10 mg tds was given for 6 weeks to achieve complete H1 receptor blockade and the response measured by change in force-weal response measurements using two different forces on a dermographic stylus and measuring response as weal diameter. Weal and flare reactions to 8 µg histamine were completely abolished by the astemizole but dermographic weal-force responses were reduced only by 12-15% indicating that histamine acting at the H1 receptor plays only a small part in the wealing of urticaria pigmentosa. (Received January 22, 1985.)

S. Shuster, Department of Dermatology, The Royal Victoria Infirmary, Newcastle-upon-Tyne, NE1 4LP, England.

Skin mast cells are greatly increased in number in urticaria pigmentosa and the clinical features of itching and wealing are attributed to histamine release. Our recent finding that prolonged administration of a large dose of astemizole will completely inhibit the histamine weal and flare (1) allowed us to test this view.
Table 1. Diameters of dermographic weals produced by two forces before and after astemizole 40 mg tds for 6 weeks in 6 patients with urticaria pigmentosa

<table>
<thead>
<tr>
<th>Stylus force (g/cm²)</th>
<th>Weal diameter</th>
<th>Pre-treatment</th>
<th>Post treatment</th>
<th>Difference</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>56</td>
<td></td>
<td>3.6±0.4</td>
<td>3.4±0.4</td>
<td>11.6±4</td>
<td></td>
</tr>
<tr>
<td>85</td>
<td></td>
<td>4.0±0.5</td>
<td>3.7±0.4</td>
<td>14.7±4</td>
<td></td>
</tr>
</tbody>
</table>

MATERIALS AND METHODS
Six patients with urticaria pigmentosa were studied, 2 men and 2 women aged 40-60, 1 girl of 5 and 1 boy of 2. The diagnosis had been made clinically and histopathologically and all had dermographic wealing. Dermographic wealing was induced by a spring-loaded stylus and the response measured as weal diameter as previously described (2) using forces of 56 and 85 g/cm² on the stylus head before and after astemizole 10 mg tds for 6 weeks. We have previously shown this regimen to produce total inhibition of the histamine weal and flare response (1). Continuation of this effect was sought in 3 of the adult patients using 8 µg histamine in 0.1 ml NaCl with 0.1 ml saline as control, measuring weal area at 10 min with a planimeter (3).

RESULTS
Before treatment all 6 patients gave a brisk dermographic response with both stylus forces (Table I). After 6 weeks of astemizole 10 mg tds there was little clinical change and only the small reduction in weal-force potency of 12-15% (Table I). At this time there was no weal and flare response to 8 µg intradermal histamine.

DISCUSSION
Our findings are that astemizole in a regimen which inhibits histamine weal and flare potency by more than 98% (1) produced only 13% inhibition of the dermographic weal response in patients with urticaria pigmentosa. Likewise there was little clinical improvement. We therefore conclude that the clinical features of urticaria pigmentosa are due only in small part to H1 active histamine. This presumably explains the poor response of urticaria pigmentosa to antihistamines and drugs which modify histamine metabolism. The involvement of substances other than histamine, e.g. mast cell proteases, would also explain the occurrence of bullae from dermo-epidermal separation since we have never produced blisters by experimental injection of histamine in many hundreds of subjects. The response of idiopathic dermographism and urticaria to H1 antihistamines is considerably greater (4) but in these disorders likewise H1 histamine only explains part of the wealing (1; Krause & Shuster, in preparation). The nature of the unknown additional vasoactive agent in these diseases is not clear and the definition of these mast cell products now appears essential for improved therapy of the urticarias.

ACKNOWLEDGEMENT
We are grateful to Janssen Pharmaceuticals Ltd.

REFERENCES
Separate Effects of Topical Indomethacin on the Itch Response and on the Flare Reaction Induced by Histamine in Human Skin

Mona Ståhle and Östen Hägermark

Department of Dermatology, Karolinska Hospital, Stockholm, Sweden


The effects of topical indomethacin on histamine responses and histamine release were studied in 15 healthy volunteers. Three hours before testing, the indomethacin solution was applied under occlusion on one arm and the corresponding vehicle on the other. Solutions of histamine and the histamine releasing compound 48/80 were injected intradermally in both arms. Indomethacin treatment inhibited the flare reactions induced by histamine and compound 48/80 to about 50%, whereas no influence was seen on the itch responses. Our results indicate that indomethacin has no effect on the release of histamine, but it selectively suppresses the histamine-induced flare reaction leaving the itch duration unaffected.

Key words: Histamine release; Compound 48/80.

In a previous investigation (1) we concluded that topical glucocorticoid treatment could suppress histamine release in human skin. The mechanism for this inhibition was unexplained. However, the possibility of interference in the arachidonic acid metabolism was considered, since arachidonic acid formation is known to be suppressed by glucocorticoids (2), and products of the arachidonic acid cascade might be essential for the histamine release process (3, 4, 5). Arachidonic acid is a precursor both to cyclo-oxygenase products such as prostaglandins and thromboxanes and to lipoxygenase products such as leukotrienes and HETE’s.

As a first step in the evaluation of the role of arachidonic acid products in cutaneous histamine reactions, we studied the effects of the cyclo-oxygenase inhibitor indomethacin on histamine responses in human skin. Although indomethacin was not found to inhibit histamine release, we made the interesting observation that it selectively decreased the flare reaction induced by histamine without affecting the itch response. Such a selective influence on the histamine flare reaction is not a rule, but a similar pattern has previously been observed after treatment with the local anaesthetic lidocain (unpublished, Hägermark).

MATERIALS AND METHODS

Fifteen non-atopic, drug-free volunteers (age 18–57 years) took part in this investigation. Clearly outlined areas, 14 cm x 5 cm on the lateral aspect of the upper arms, were used for the experiment. We applied 0.3 ml of indomethacin solution (2.5% w/w in a vehicle of ethanol: propylene glycol: dimethyl