

## Purpuric dermatosis due to house-dust mite (*Dermatophagoides* spp.) allergy: a case report

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### Summary

A case of pigmented purpuric dermatosis is reported. The patient was a fit young girl subject to recurrent, generalized, transient purpuric capillaritis appearing 36–55 hr after systemic absorption of house-dust mite antigen. Her serum contained IgG and IgE antibodies to house dust and to mite antigens. Skin from a test site had IgE on the mast cells, and half of the cells showed anaphylactic degranulation. However, this case was not a typical example of anaphylactic (atopic) sensitivity, and did not resemble any of the classical types of allergy.

### Introduction

Cutaneous capillaritis or pigmented purpuric dermatosis has been caused by drugs, for example Carbromal, Meprobamate, and Carbamazepine, and as a contact dermatitis to khaki clothing and optic whiteners. In most cases a cause is not found. The child reported here developed generalized pigmented purpuric dermatosis provoked by systemic absorption of house-dust mite antigens.

### Case history

The patient (A.H.330598), now aged 7, is a shy, healthy girl with no past or present serious illness but with a family history of eczema, psoriasis, asthma and hay fever. Her rash, which first appeared in February when she was 4½ years old, came in crops lasting 4–6 weeks and re-appeared without relation to the stage of the preceding crop. It involved the trunk and limbs (Fig. 1), varying in severity at each site from crop to crop, but preserving bilateral symmetry and showing a tendency for the long axis of lesions to follow skin creases. Once the rash had cleared from a site of maximal involvement this region was less severely affected by immediately succeeding crops. There was no relationship to clothing, but exposure to sunlight speeded clearing of the rash. The rash generally appeared as minute red macules which enlarged over 5–10 days to produce red, not indurated, plaques 0.5–1 cm in size (Fig. 2). These spots resolved spontaneously in about 4 weeks. During very severe manifestations spots of

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2–8 cm were common, and crusted lesions which took 12–14 weeks to heal were also present. There was no evidence of involvement of systems other than the skin.

The duration of the rash was shortened fourfold with topical steroids; clearing appeared to be speeded by ascorbic acid (50 mg/day), and by hydroxyethylrutoside (Paroven 250 mg t.d.s.). Daily ultraviolet irradiation (3 min) resulted in rapid resolution of the rash on exposed areas and slower resolution on the less exposed sides of the trunk. Neither Triprolidine hydrochloride, 20 mg at night, nor disodium cromoglycate, 20 mg three times daily, by inhalation, affected recrudescence or resolution of the rash.

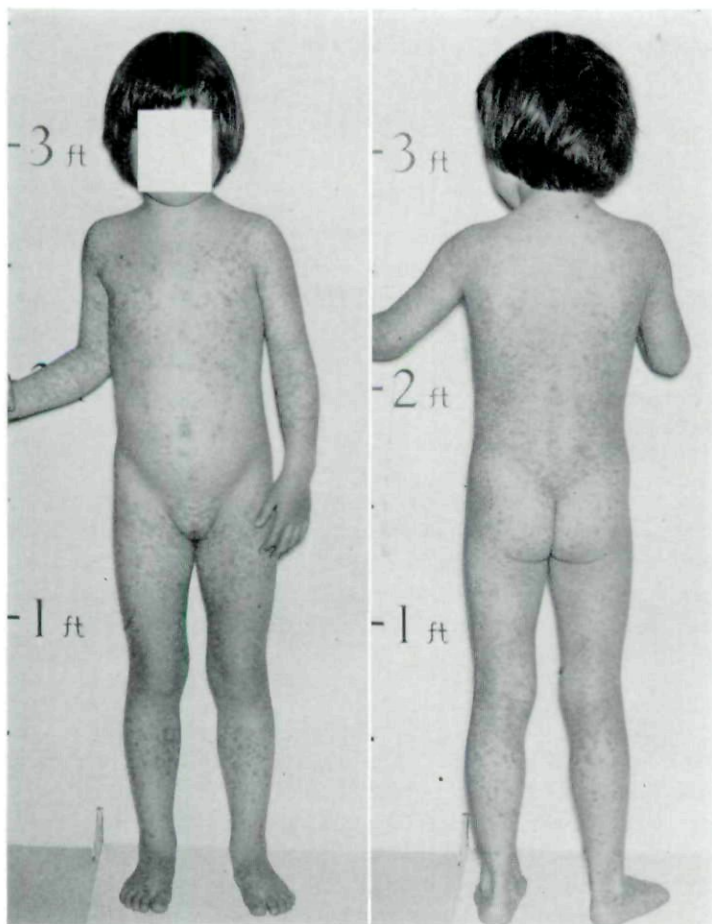


Fig. 1. Distribution of the rash—limbs and trunk are involved.

The distribution and intensity of the rash were recorded from its initial appearance in February 1969. It did not spread at random but progressed from one discrete area of the body to another. These areas were the arms, legs, buttocks, back, chest, abdomen and face. The sum of areas bearing new spots was recorded, 1 to 7 on the vertical axis of Figs. 3 and 4, level 8 indicated that widespread scaling was also present.

Initial investigations excluded some possible causes, such as systemic drugs, sulph-



**Fig. 2.** Detail of rash: (a) early lesions on dorsum of feet, showing red macular lesions; (b) intermediate lesions on trunk, showing pale brown, oval macules or plaques which tend to lie with long areas parallel to skin creases; (c) late lesions on forearm, showing fine scaling and one area of very superficial necrosis—the lesions heal without scarring.

acetamide eye drops, clothing, optical whiteners and several items of food. The behaviour of the rash during the first year seemed to suggest that, if of allergic origin, the allergen must be continuously present in the patient's environment, but subject to considerable fluctuations in concentration. Attempts to correlate the changes in the rash with ubiquitous allergens, such as fungi and yeasts, were unsuccessful. Finally, it was noticed that an increase had followed (Fig. 3) 48 hr after sleeping in a different bed, on seven separate occasions. Microscopical examination of the bedding concerned on these seven occasions revealed that it was heavily infested with *Dermatophagoides pteronyssinus*, whereas her own bed was not.

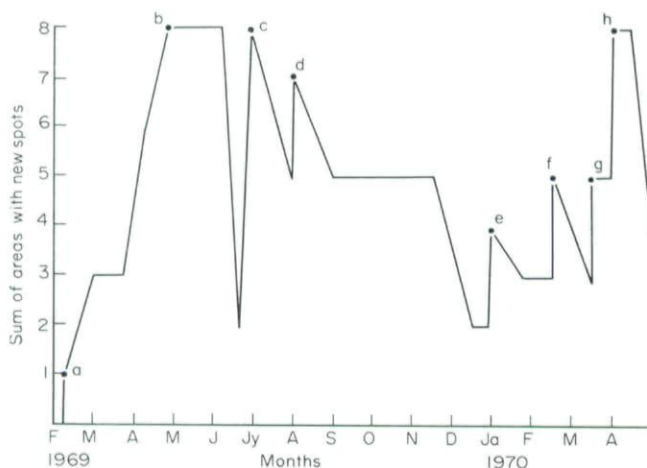


Fig. 3. Progress of rash, February 1969 to April 1970. a, First record; b, h, holidays away from home; c, d, e, f, g, contact with infested blankets at home.

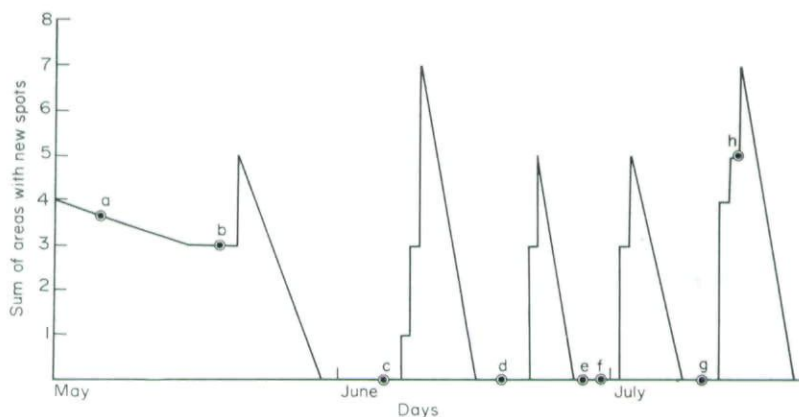


Fig. 4. Distribution of the rash during challenge testing. a, Patch test; b, prick test; c, g, intradermal challenge (*D. culinae*); e, intradermal challenge (placebo); d, f, challenge with natural source of antigen; h, biopsy.

Provocative tests with *D. farinae* (syn *D. culinae*) (Dome Laboratories Allergen extract for prick or scratch testing) were carried out. Patch tests for a delayed response and a prick test for an immediate response, were negative, but the prick test was followed in 48 hr by the appearance of a fresh crop of typical rash (Fig. 4, a and b).

During the period of provocative testing the child was closely supervised to prevent contact with natural sources of the allergen which, fortunately, were below normal because of the exceptionally low humidity during May and June 1969 in Cambridge. She slept on a new mattress, under a nylon quilt and with a synthetic pillow, left the house during bed-making, avoided soft upholstery and soft toys, and did not visit friends' houses. With these strict precautions crops of the rash did not appear spontaneously.

Once the crop of spots had subsided, an intradermal injection of 0.02 ml of *D. farinae* extract was followed by a larger crop in 48 hr (Fig. 4, c). Then a control solution of glycerol and saline (Dome) was injected. No rash appeared (Fig. 4, e). The 0.01 ml of mite extract was injected and the rash reappeared after 48 hr (Fig. 4, g). These intradermal injections did not produce the rash locally. Nasal insufflation (a 0.005 ml puff)

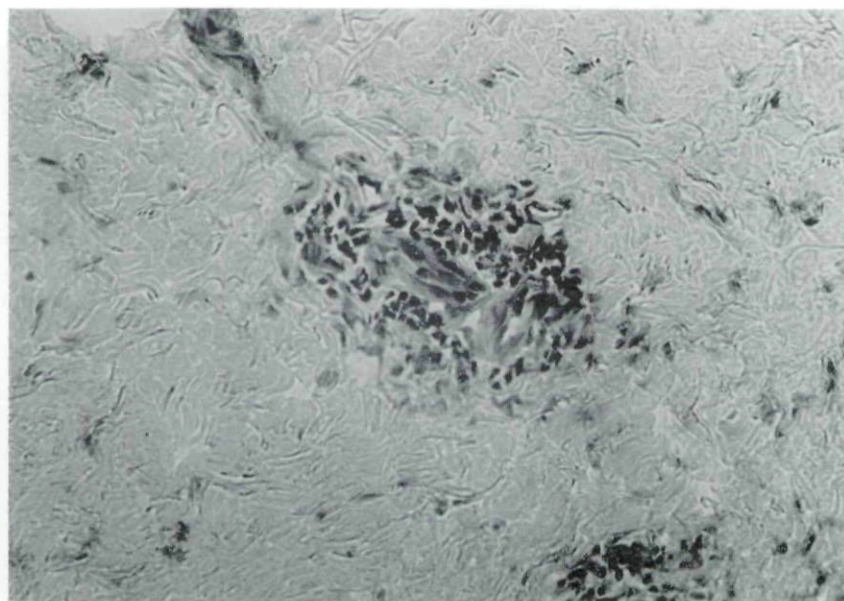


Fig. 5. Skin biopsy. The upper dermis contains small blood vessels with swollen endothelium and a perivascular round cell infiltrate.  $\times 140$ .

of a dilute solution giving a dose of  $5 \times 10^{-5}$  ml of mite extract was followed by a fresh crop of rash, beginning on the trunk in 48 hr and spreading to involve the legs by the fifth day. The rash was more intense than that following intradermal injection of  $1 \times 10^{-2}$  ml of mite extract. Nasal insufflation of a control solution did not provoke the rash.

Because one of us (S.H.) was the patient's mother, it was possible to supplement clinical investigations with continuous observation and tests using a natural source of allergen under controlled conditions. On two occasions when the patient was free of spots she was allowed to bounce on a heavily infested mattress, and each time a rash developed after 48 hr (Fig. 4, d and f).

As a pre-school child the patient was present during Tuesday bed-changing, and

consequently had new spots each Thursday. This ceased and the overall level of the rash fell when she started school. The basic level of the rash, i.e. that which developed when the patient stayed at home, showed the same seasonal variation as that characteristic of house-dust mite populations (Spieksma, 1970). During winter the level was 2; there was a gradual rise to 6 between May and September, and then a sharp drop to 2 in November. The winter decline followed the start of central heating which, by lowering the humidity, reduces the house-dust mite population (Spieksma, 1970).

The general level of house-dust mite infestation was reduced by treating favoured habitats such as blankets, mattress covers and soft upholstery, with benzyl benzoate. The materials were meticulously cleaned and then sprinkled, in the open air, with a 5% solution of benzyl benzoate in chloroform.

### Investigations

Blood count and X-rays of chest and teeth were normal.

*Immunological studies* (Dr W. E. Parish) on a skin biopsy from the thigh, obtained 4 days after intradermal injection of house-dust mite antigen and on serum obtained at the same time.

### Histology

Cytoplasmic and nuclear vacuolation of epidermal cells. Oedema, particularly in the upper dermis. Perivascular accumulation of small numbers of mononuclear cells in mid and upper dermis (Fig. 5). About half of the mast cells had shed their granules and were surrounded by a haze of metachromatic material.

### Skin immunofluorescence tests

Immunofluorescence of unfixed, washed sections. No IgG, IgA, IgM, IgD or  $\beta$ IC was found. An occasional, thin, linear deposit of albumin lined some collagen fibres in the oedematous area of the dermis. Eight mast cells contained, or had absorbed, IgE globulin, and occasional, small, well-defined specks of IgE were also found in the perivascular mononuclear cells, and in others diffusely spread in the dermis. The mononuclear cells were not identified.

Fixed skin (acetone) had diffuse IgG and much albumin in the oedematous area of the dermis, and fine speckles of IgG in the dermis and in a few of the epidermal cells. On the surface of the stratum corneum was a thin layer rich in albumin and IgG. These features commonly occur in eczematous skin. There were also small, discrete particles of IgD in the upper dermis in the non-oedematous areas, and in a few of the perivascular mononuclear cells. There was much less IgE visible in the fixed than unfixed sections. No IgA or IgM was found.

### Antibody to skin

No antibody was found to extracts of whole skin by agglutination. No antibody was found to skin by immunofluorescence when the patient's serum was added to sections of skin from the patient or from other persons. Incidentally, mast cells in sections of skin did not absorb IgE from the serum.

### Agglutination and precipitation tests

A crude lipo-polysaccharide extract of house dust was used to coat sheep red cells for

agglutination tests. The patient's serum caused no direct agglutination, but had an antiglobulin titre of 512 for IgG, but nothing for IgA, IgM or IgE.

Precipitation tests in agar gels showed no macroscopic precipitation with extracts of house-dust mites (*D. pteronyssinus*), timothy, and cocksfoot pollen. However, by using  $^{131}\text{I}$  radioisotope-labelled rabbit anti-IgG to detect invisible precipitation, a single IgG band was found with house dust, one, possibly two, IgE bands with extracts of house dust and mites, and a faint band with timothy pollen.

#### *Disappearance of the rash*

In August 1971 the patient, although vaccinated, developed whooping cough. At the end of the acute stage of the infection the rash disappeared spontaneously and has not, so far, returned.

#### **Discussion**

The rash shows purpuric staining of the skin, and has some features of two of the more precisely defined purpuric dermatoses, Schamberg's disease and itching purpura, but it lacks the predilection for the legs of Schamberg's disease, and is too persistent for itching purpura. Thus it is morphologically and histologically a pigmented, purpuric dermatosis not corresponding to any of the eponymous variants (Farrokhzad & Champion, 1970).

Allergic reactions to house-dust mite have been increasingly documented since the discovery (Voorhorst *et al.*, 1967) that the mite provides the main, if not the only, antigens of house dust. Further investigations showed the similarity of allergic responses provoked by the mites of *D. pteronyssinus* and *D. farinae* (Voorhorst & Spieksma, 1969). Similarly, in our patient the same rash appeared after natural exposure to *D. pteronyssinus* during bed-making as after systemic administration of *D. farinae* extract.

Provocation of the rash by systemic administration of mite extract was repeated on five occasions and, each time, was followed by widespread rash in 48 hr without any local increase in severity at the injection site. This is clear evidence of an altered responsiveness to mite antigen.

Previously described house-dust mite allergy produces asthma and rhinitis; in these patients, skin prick tests produce an immediate weal, nasal challenge tests an immediate rhinitis, and bronchial challenge tests an immediate or delayed (4–12 hr) attack of asthma (McAllen, Assem & Maunsell, 1970). None of these patients showed an Arthus-type skin reaction. IgE (reaginic) antibodies against house-dust mite were found in the serum and leucocytes of the patients examined by Assem & McAllen (1970). Also, a local allergic eczema to house dust antigen at the site of desensitizing injections has been reported by Derbes & Caro (1957).

The allergic response in our patient was very different. It is, however, difficult to identify the type of allergy responsible. The generalized cutaneous, small vessel vasculitis appearing 36–55 hr after administration of the antigen, without any local reaction, is an unusual phenomenon. Normally, a reaction is elicited at the test site, even if followed by a generalized response, as occasionally occurs in tests on patients with contact dermatitis.

It is not, primarily, an anaphylactic reaction because of the absence of the usual weal and flare skin test response, the long delay before the appearance of the generalized signs, and the failure to control the rash with triprolidine hydrochloride or di-

sodium cromoglycate, which effectively control histamine-mediated atopic disorders. Nevertheless, the participation of IgE-mediated anaphylaxis in inducing the rash cannot be ruled out, because the patient had serum IgE antibodies to house dust and to mites, and IgE in mast cells and a few other mononuclear cells in the skin sample. Moreover, half the mast cells in the sample had shed their granules. This change occurs in anaphylaxis in human mast cells from actively sensitized persons (Parish, 1964), and accompanies release of histamine and slow-reacting substance of anaphylaxis from human lung (Parish, 1967).

The response also lacked the usual characteristics associated with an Arthus sensitivity. The IgG antibody to mite antigen was mainly of the non-precipitating type (detected by antiglobulin tests), the skin sample did not contain aggregated IgG or the  $\beta$ IC complement component, and there was no neutrophilia of the test site or blood, such as would be anticipated in a local Arthus or serum sickness type response.

Several theories can be offered to account for this phenomenon, but they remain interesting conjectures with no evidence to support them. The rash could be a manifestation of a delayed hypersensitivity, with an inexplicable lack of response at skin test sites. No laboratory tests for delayed sensitivity were made. A second possibility is that the allergen was not native mite substance, but in a form changed by partial degradation or by coupling to some other protein or cell which then reacted with the IgG antibody. Related to this is a third possibility that the mite allergen diffused from the site and formed complexes of one allergen molecule with one or more of the 'univalent' IgG antibodies. These complexes then involved platelets which released the substances inducing the rash. Due to the 'univalent' nature of the IgG antibody, the formation of complexes and involvement of cells was slow. The IgE antibodies may have participated in the rash, but this form of anaphylactic response had not reached the importance that it normally assumes, as, for example, shown by Assem & McAllen (1970).

The spontaneous remission of the rash coincided with the period of maximum antibody production of the whooping cough infection. It seems possible, therefore, that non-specific stimulation of antibody formation resulted in a persistent beneficial alteration in the antibody balance.

### Acknowledgments

We wish to thank Dr McAllen of University College Hospital, London, for advice about nasal provocation tests, and Dr W. E. Parish of the Lister Institute for Preventive Medicine, Elstree, for immunological studies and comments. Dr Champion gave permission for publication of details of the patient who was under his care. Dr J. Brady, of Imperial College Field Station, Ascot, identified the mites. Also praise is due to the young patient who bore with fortitude many discomforts and restrictions.

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