

# The purpuric patch test in patients with allergic contact dermatitis from azo dyes

ANETA LAZAROV<sup>1</sup> AND MARIO CORDOBA<sup>2</sup>

<sup>1</sup>Dermatology Clinic, <sup>2</sup>Department of Pathological Anatomy, Meir Hospital, Kfar Saba, Israel

The histopathological features of the purpuric patch test have been described in individual cases only. We report a series of patients with allergic contact dermatitis, who developed purpuric patch tests at the sites of allergens from the azo dye group. 105 patients were clinically evaluated and tested with the TRUE Test and the textile color & finish series (Chemotechnique Diagnostics) because of suspected clothing dermatitis. Positive results to the latter were found in 31 patients (29.5%). In 9 of these, purpuric patch tests were observed at the sites of the allergens Disperse Blue 124, 106 and 85. 10 biopsies were performed and studied. The histopathological changes of the purpuric patch test included: spongiosis (in 90% of cases), exocytosis (70%), and dilated blood vessels (100%) without signs of vasculitis, surrounded by an inflammatory infiltrate composed mainly of T lymphocytes. Extravasated erythrocytes were seen perivascularly, but also in the interstitium, surrounding the acrosyringium, at the dermoepidermal junction, and in the epidermis. Increased number of mast cells were found in 22.2% of cases. Disperse Blue 124, 106, and 85 are potent allergens that can elicit purpuric patch test reactions. The purpuric patch test in our cases was a manifestation of an allergic reaction, based not only on histopathological changes, but also on evolution and relevance of the patch tests.

**Key words:** purpuric patch test; allergic contact dermatitis; azo dyes; histopathology; erythrocytes; mast cells; clothing; textiles. © Munksgaard, 2000.

*Accepted for publication 15 July 1999*

Purpuric patch tests were first observed after patch testing with apronalide (Sedormid) and quinidine in patients with purpuric drug eruptions from their ingestion (1). Petechial reactions to cobalt chloride 1% pet. are reported in approximately 5% of patients tested (2). Other allergens that have elicited purpuric reactions include: diphenyl-paraphenylenediamine and N-isopropyl-N'-phenyl-paraphenylenediamine (IPPD) 0.1% pet. (3), paraphenylenediamine 1% pet. (4), dimethylolpropylene urea (5), benzoyl peroxide 5% pet. (6), methyl methacrylate 2% pet. (7) and Disperse Yellow 27 (8).

We describe a series of patients with allergic contact dermatitis, who developed a purpuric patch test reaction at the site of allergens of the azo dye group.

## Patients and Methods

105 patients were clinically evaluated and tested with the TRUE Test and a textile color & finish series (Chemotechnique Diagnostics) because of suspected allergic contact dermatitis from cloth-

ing. Patch tests were applied on unaffected skin of the upper back, removed at 2 days and read at day (D) 2, 3, and 7, according to standard patch test definitions.

Patients who developed purpuric patch tests were studied. These patients were not taking any medications affecting the coagulation system. Biopsies from the sites of purpuric patch tests were obtained immediately after the D3 reading. Biopsies were stained with hematoxylin-eosin and prepared for routine histopathological examination for diagnostic purposes. Immunohistological staining was performed with the following monoclonal antibodies: anti-human T lymphocytes UCHL-1 (Dako), anti-human B cells - CD20 (L26 Dako) and anti-human mast cells tryptase - AA1 (Dako). The infiltrating cells, T cell lymphocytes, erythrocytes and mast cells, were evaluated quantitatively according to the following grading system: 1–5 cells per high power field - mild, 6–10 - moderate, more than 11 - severe infiltration.

Blood tests, including blood count and prothrombin time, were made in all such patients.

## Results

Positive reactions to the textile color & finish series were found in 31 out of the 105 patients studied (29.5%). Purpuric patch tests were seen in 9 of the patch-positive patients. 8 of these were female and 1 male, aged from 14 to 62 years. Seasonal rhinitis was observed in 1 female patient. The average duration of skin disease prior to diagnosis was 8.8 months. Allergic contact dermatitis from clothing was suspected in all patients. Clinical features included purpuric patches admixed with erythematous papules and plaques in 4 patients, erythematous squamous patches and plaques in 2 patients, hyperpigmented patches in 2 and punctiform purpura in 1. Lesions were disseminated in 6 patients, localized on the back in 2, and confined to the vulva in 1. Textile articles identified as causal included personal clothing in 5, personal clothing and bedspread in 2, and underwear in 2 patients. The garments and the bedspread were of synthetic material in dark colors. 17 positive results to the allergens in the textile color and finish series were recorded in the 9 patients studied. They included Disperse Blue 106 and Disperse Blue 124, each in 41.2%, and Disperse Blue 85 in 17.6%. In 6 patients, the patch tests that were not subject to biopsy persisted until the D7 reading. Standard series allergens elicited positive reactions to nickel sulfate, black rubber mix, fragrance mix and colophony, each in 1 patient. All positive results had present relevance. Clearing of the skin lesions was achieved on an average in 6 weeks after stopping contact with the causative garments. Hyperpigmented lesions were the slowest to resolve. Most patients remained lesion-free when wearing light-colored apparel.

In all 9 patients, purpuric macules, which evolved to papules, were observed at the sites of the positive allergic reaction to certain of the following allergens: Disperse Blue 124, 106 and 85 (Fig. 1). 10 biopsies from the purpuric patch test site were performed on D3, 1 from Disperse Blue 85, 3 from Disperse Blue 106 and 6 from Disperse Blue 124. In 1 of the patients, 2 biopsies were obtained at the sites of positive reactions to Disperse Blue 106 and 124, respectively. In another patient, a lesional biopsy was performed along with the biopsy from the purpuric reaction at the site of Disperse Blue 124.

The histopathological changes in the epidermis of the purpuric patch test biopsies are analysed in Table 1. The main histopathological features in the epidermis were spongiosis, present in all the cases as generalized (90% of cases) or/and focal spongiosis (50%) and exocytosis (70%). In 3 cases, spongiotic intraepidermal vesicles were seen in relation to the marked spongiosis in the epidermis.

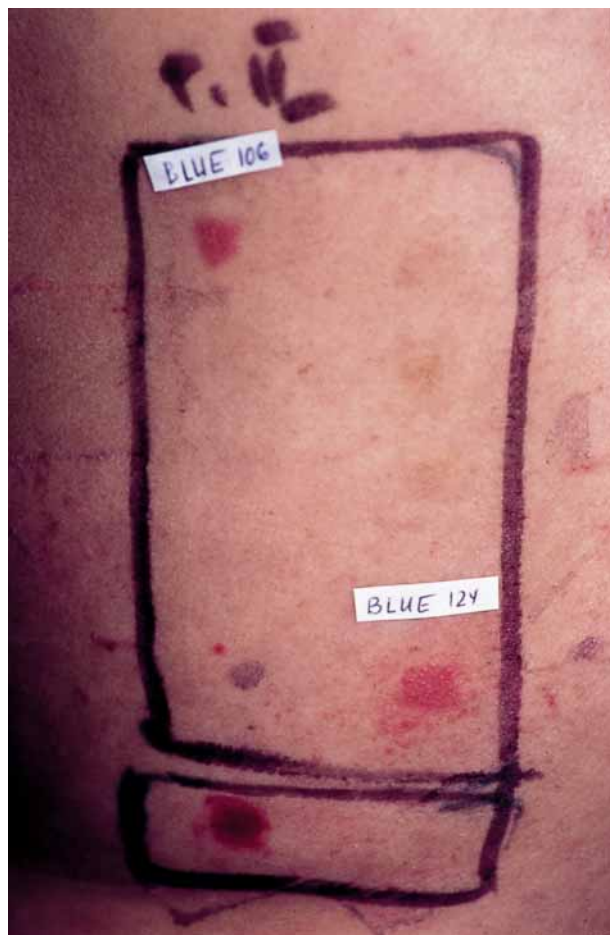


Fig. 1. Purpuric patch test reactions to Disperse Blue 106 and 124 at the D2 reading.

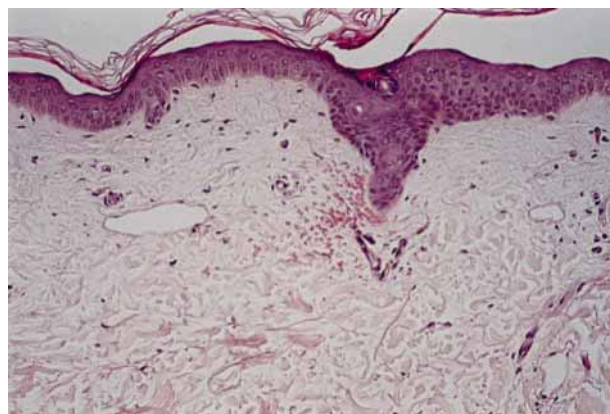


Fig. 2. Extravasated erythrocytes surrounding the acrosyringium and a dilated lymphatic vessel are seen in the dermis. H&E  $\times 40$ .

There were no karyopyknotic or necrotic changes in the epidermal cells. Parakeratosis and hyperkeratosis were not present. Mild to moderate dilatation of the blood vessels was observed in all cases. Edema of the endothelial cells was present

Table 1. Histopathology of the purpuric patch test – epidermal changes

| Biopsy no. | Acanthosis | Exocytosis | Spongiosis focal | Spongiosis generalized |
|------------|------------|------------|------------------|------------------------|
| 1          | 0          | +3         | +3 and vesicles  | 0                      |
| 2          | 0          | +2         | 0                | +1                     |
| 3          | 0          | 0          | 0                | +2                     |
| 4          | 0          | +1         | 0                | +2                     |
| 5          | +1         | 0          | 0                | +1                     |
| 6          | +1         | +1         | +2               | +1                     |
| 7          | +2         | +3         | +3 and vesicles  | +2                     |
| 8          | +1         | +1         | +3               | +2                     |
| 9          | +1         | +2         | +3 and vesicles  | +2                     |
| 10         | 0          | 0          | 0                | +1                     |

1: mild; 2: moderate; 3: severe.

in 50% of cases. The edema never led to occlusion of the vessel's lumina. In 3 cases, dilatation of the lymphatic vessels in the upper dermis was observed (Fig. 2). Changes compatible with vasculitis were never seen. Edema of the papillary dermis was present in 50% of biopsies. Melanin, free and in macrophages, was noted in 1 case. A summary of the main histopathological changes in the epidermis and dermis is made in Table 2.

The inflammatory infiltrate had a mainly perivascular distribution in the superficial dermis in 1/2 the cases and surrounded the superficial and deep vessels in the other 1/2. In 70% of cases, the inflammatory infiltrate was composed of mononuclear cells, mainly lymphocytes, in 20% of lymphocytes and eosinophils, and in 10%, some neutrophils were seen in admixture to the lymphocytes. The mononuclear infiltrate was mild in 50% of cases, moderate in 40% and severe in 10%. Immunostaining revealed moderate infiltration with T lymphocytes in the inflammatory infiltrate. Im-

munostaining with antibodies against mast cells demonstrated mild infiltration, which did not appear to differ from the quantity of mast cells seen in normal skin in 77.8%. In the remaining 22.2% of cases, a moderate infiltration with mast cells was found. The T-lymphocytes and the mast cells were seen in a mostly perivascular distribution, with the exception of 1 case in which T lymphocytes were also found around adnexal structures and 2 cases in which mast cells were observed in a predominantly periadnexal distribution.

In all cases, extravasated erythrocytes were seen along with the inflammatory infiltrate, their pattern of distribution being shown in Table 3. In most biopsies, extravasated erythrocytes were seen perivascularly in the superficial or superficial and deep dermis. In individual cases, extravasated erythrocytes were seen in the interstitial area, surrounding the acrosyringium (Fig. 2), at the dermoepidermal junction and in the epidermis. In 3 cases, blood vessels were dilated and congested with rolled erythrocytes. Mild extravasation of erythrocytes was seen in 52.6% of cases, moderate in 36.8% and severe in 10.5%. A striking similarity between the pathological findings in a lesional biopsy and in the biopsy of the purpuric patch test reaction, in a patient with purpuric allergic contact dermatitis, was seen.

Blood tests were all within normal limits.

## Discussion

Data on skin biopsies from petechial/purpuric patch tests is scarce, and reported only in individual cases. The comparatively large number of affected patients in our series points to the fact that the purpuric patch test may be a more common phenomenon than reported. The purpuric reaction with a conspicuous livid blue color evoked by the allergens Disperse Blue 124, 106 and 85 may be overlooked, relating it to the color of the allergens rather than to purpura. In such cases, performing a biopsy may be of diagnostic value.

Table 2. Frequency of the main epidermal and dermal histopathological changes in the purpuric patch test

| Epidermis                   | % (n=10) |
|-----------------------------|----------|
| acanthosis                  | 50%      |
| spongiosis – focal          | 50%      |
| spongiosis – generalized    | 90%      |
| Dermis                      |          |
| edema papillary dermis      | 50%      |
| dilatation of blood vessels | 100%     |
| edema endothelial cells     | 50%      |

Table 3. Pattern of distribution of the extravasated erythrocytes

| Pattern                                                     | % (n=10) |
|-------------------------------------------------------------|----------|
| perivascular                                                | 40%      |
| perivascular+interstitial                                   | 10%      |
| perivascular+acrosyringium                                  | 10%      |
| perivascular+interstitial+epidermis                         | 20%      |
| perivascular+interstitial+dermoepidermal junction+epidermis | 10%      |
| epidermis                                                   | 10%      |

The histopathological changes of purpuric patch tests described in the literature include: perivascular lymphocytic infiltration, swollen endothelium, extravasation of erythrocytes without signs of vasculitis (2, 4), vascular changes compatible with selective toxic damage of the capillary endothelium, without epidermal alterations (6), accumulations of lymphocytes and polymorphonuclear neutrophils around the superficial and deep dermal venules with marked extravasation of erythrocytes, and minimal spongiosis of the epidermis (7), or in summary "as the pattern of allergic contact dermatitis associated with red cell extravasation" (8).

Our series demonstrated the essential findings of purpuric lesions namely: dilated blood vessels, edema of the endothelial cells and extravasated erythrocytes without vasculitis, as described by others (2, 4, 7). In addition, there was marked spongiosis and exocytosis in the epidermis, with formation of vesicles in some cases, edema in the papillary dermis, and an inflammatory infiltrate composed of lymphocytes and lymphocytes admixed with eosinophils. All these features are seen with greater frequency in allergic patch test reactions, although differentiation between allergic and irritant patch test reactions is not possible using only histopathological criteria (9).

The presence of extravasated erythrocytes mainly surrounding the blood vessels but also at other levels of the dermis, close to the acrosyringium at the dermoepidermal junction, and in the epidermis is of interest. It might be speculated that the influx of erythrocytes along with mononuclear cells follows a chemotactic gradient and could be related to penetration of the allergen through the pilosebaceous unit and the acrosyringium. Alternatively, the vasodilatation and extravasation of erythrocytes could be due to the action of cytokines released from keratinocytes and the dendritic cells after exposure to an allergen. An example of such a cytokine is vascular endothelial growth factor (VEGF) released from the keratinocytes, which induces endothelial cell permeability and IL8 – which, along with other actions, also stimulates the release of histamine (10).

Another interesting finding was the presence of mild infiltration with mast cells (1–5 cells per high power field) in 77.8% of cases, which resembles the amount of mast cells present in normal skin (11). The rôle of mast cells in allergic contact hypersensitivity is debatable. Some studies claim that early mast cell activation occurs in the allergic patch test, on the grounds of histological evidence of mast cell degranulation (12). In our cases, degran-

ulation of mast cells was not observed. The increased number of mast cells seen in 22.2% points to the fact that, in some cases, mast cells participate functionally in the early stages of the allergic patch test.

The purpuric patch tests were provoked by Disperse Blue 124, 106, and 85. These azo dyes, particularly 124 and 106, are potent allergens that can elicit purpuric patch test reactions. We believe that the purpuric reaction at the site of the patch tests, in our cases, was a manifestation of an allergic reaction, based not only on the histopathological changes, but also on the crescendo pattern of the patch test reactions and the persistence of the patch tests until D7. Moreover, in all of our patients, a present relevance for the positive patch tests to the textile color and finish series was established.

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Address:

Aneta Lazarov  
Dermatology Clinic  
Sapir Medical Center  
Meir Hospital  
44281 Kfar Saba  
Israel