Patch Testing

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Patch testing is the main investigation in the diagnosis of allergic contact dermatitis. It reproduces, albeit in miniature, the clinical expression (eczematous erythemato-edemato-vesicular response) and the pathogenic mechanism (depicting the elicitation phase of delayed type hypersensitivity). If properly performed and interpreted, it is a direct, practical and scientific diagnostic method. It may seem simple to apply and read but in actual fact, the procedure is fairly complicated and proper performance requires adequate experience [1–8].

First of all, it must be understood that the patch test does not duplicate the clinical exposure to an allergen that occurs in real life. In fact, real-life exposure is quite different: various factors (maceration, sweating, occlusion, repeated application over time) favor skin absorption of a substance. Moreover, the concentration of the allergen, that is rarely known in real-life, is 'adjusted' in patch tests to minimize irritant reactions and any side effects. Despite such mild imperfections, patch tests at set concentrations and applied for standard times are still the best in vivo scientific diagnostic method. Therefore, they should be used much more frequently than they currently are, on condition that the dermatologist performing them has gained adequate experience under the supervision of experienced staff with proper training in the field of skin allergy forms [1, 9–11]. It is sometimes believed that the medical history alone is sufficient to identify cases of contact allergy but this is not always true. Just a simple example is illustrative of this fact: a history of reactions to cheap jewelry, zippers or metal buttons could be clinically attributed to nickel allergy. Instead, this conviction may be false in 53% of cases and may miss true nickel allergy in a further 35% of those surveyed [12].

The reasons why a dermatologist may be reluctant to use, or at any rate advise, patch tests (the time it takes the doctor to perform them, number of visits the patient needs to attend, cost of test materials, risk of side effects) are not usually supported by fact. In fact, it has been shown that the doctor's and patient's efforts in such cases are largely rewarded, demonstrating that patch testing is clearly cost-effective [13], bearing in mind that the costs (in terms of time,

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money and health) for patients would be much higher if their disease and its etiology are not properly diagnosed, and so persists and worsens over time [14].

23.1 Who and When to Patch Test

Apart from in subjects with eczematous contact dermatitis and noneczematous contact dermatitis (erythema multiforme-like contact dermatitis, lichenoid contact dermatitis, purpuric contact dermatitis, lymphomatoid contact dermatitis, primary dischromic contact dermatitis, etc.) [15], patch tests should be done in all cases of other eczematous dermatoses [16–20]. They must also be performed in all cases of worsening of preexisting other dermatoses (stasis dermatitis, leg ulcers, psoriasis, acne, scabies, post-traumatic wounds) when a superimposed contact allergy is suspected, due to topical treatments or occupational chemicals, for example [21–25] (Table 23.1).

Patch tests should be postponed in various cases in which the results might be invalidated (Table 23.2), resulting in false-negative reactions (UV light and tanning, topical medicaments, immunosuppression), or increasing the skin reactivity (active dermatitis).

Table 23.1 Patients who should be patch tested

Patients with eczematous contact dermatitis
Patients with noneczematous contact dermatitis
Patients with other eczematous dermatoses
Atopic dermatitis
Nummular eczema
Pompholyx
Patients with a mucous membranes reaction
Conjunctivitis Stomatitis
Genital mucosa
Patients with worsening of preexisting dermatoses due to topical treatment or occupational chemicals
Stasis dermatitis
Leg ulcers
Psoriasis
Acne
Scabies
Post-traumatic wounds

Table 23.2 Conditions requiring postponement of patch tests

Dermatitis on the upper back or other sites of application of patch tests
Recent use of topical corticosteroids on test sites
Recent ultraviolet exposure of test sites
Generalized active dermatitis
Systemic immunosuppressive treatment in relevant doses
Precautions should be taken in the following cases: Individuals with immunosuppressive diseases Individuals with atopic dermatitis Pregnancy or lactation

There is little information in the literature about immunosuppressive drugs. In practice, when it is not possible to suspend these, patch tests can be performed just the same, but the clinician must be aware of the possibility of false-negative reactions. Some reports have shown, however, that positive reactions can occur despite immunosuppressive treatment, although at lower frequency and intensity [26, 27]. Topical cyclosporin A seems to inhibit reactions in man [28] and animals [29, 30]. Our studies of oral cyclosporin A [31] and those of other authors [32] have shown that the response to patch tests is not inhibited but the intensity is reduced. When using cyclosporin A in excited skin syndrome to distinguish allergic reactions from those of irritant type, we saw that the drug only blocks irritant type reactions [33].

As regards the time between the suspension of such oral treatments and the execution of patch tests, a period of five half-lives of the particular drug is thought to be a reasonable interval from the clinical point of view [1]. In particular, as regards systemic corticosteroids, it has been seen that a dosage of 20 mg of prednisone does not affect the onset of reactions, or at least not of intensely positive reactions [34–36]. All the same, if possible it is advisable to perform patch tests after the drug has been suspended. Treatment with topical corticosteroids on the test site can also give rise to negative reactions [37].

Some antihistamines (cinnarizine administered for one week) affected the intensity of the response in some cases [38], whereas in others

they seemed inert [35]. In this sense, antihistamine treatment as a contraindication to patch tests is not generally accepted. Treatment with disodium chromoglycate and with NSAIDS is not considered to influence the reactions either [1].

Exposure to UVB rays temporarily reduces the elicitation of allergic reactions in sensitized subjects. UVA rays do not seem to pose the same risk [39, 40]; however, combined treatment with UVA rays plus psoralens reduced the positive reactions elicited [41]. Notoriously, UV irradiation reduces the number of Langerhans cells in the epidermis [42].

Some precautions need to be adopted in subjects with atopic dermatitis, who, when regularly patch tested, present the same frequency of positive reactions as non atopic subjects. However, owing to their skin hyperreactivity, it is important to make a particularly careful interpretation of the results because false-positive reactions are possible [17, 18]. Filaggrin mutations, by inducing an altered barrier function, can foster contact sensitization [43, 44].

Subjects with some immunosuppressive diseases, like severe generalized infections or neoplasia, can have a reduced capacity to develop contact allergy, althoug in some cases the onset of sensitization can occur, with positive reactions [45, 46].

Finally, the execution of patch tests during pregnancy or lactation does not seem to be harmful; nevertheless, most dermatologists prefer to postpone the tests as a general precaution.

23.1.1 Patients Information

Patients must be accurately informed about the patch tests procedure and the advantages that they may offer. They must also be aware of the potential adverse effects, since they must give written consent to the performance of the patch tests.

Patients should avoid showering or in any way wetting the test sites; they should avoid activities that give rise to sweating and also physical effort because the test devices could detach, as well as UV irradiation. It is also very important to inform the patient about the possibilities of pruritus and burning at the zone of application of the tests, and that the skin manifestations may worsen and new clinical lesions may appear.

23.2 Patch Test Procedures

Since there are various national legal regulations governing the execution of patch tests, dermatologists should be aware of the national frameworks in their own country.

23.2.1 Materials: Type of Chambers

There are various different test chamber systems, some having circular chamber areas and some square. In some systems the allergen is applied manually before the patch testing and in others it is preloaded. The latter system has some advantages (rapidity of execution of the test, less health care operators needed, standard pre-established quantities of hapten material applied), and also disadvantages (costs, use by insufficiently expert operators, a tendency toward non updated standard series available on the market). Moreover, pre-packaged systems contain a limited number of allergens, that do not in general cover the whole European base line series. In any case, there is no documentation demonstrating that either test system is superior to the other; the choice of test system is based on tradition and experience.

In one common system, the chambers are supplied in strips of 5 or 10, and consist of small aluminium disks mounted on non-occlusive acrylic-based tape, chosen for its adhesive and hypoallergenic properties. Other systems consist of square plastic chambers on hypoallergenic tape.

Of course, the inert plastic system must be used in cases of suspected contact allergy from aluminium. This chamber gives rise to a reaction only very exceptionally, but if the substance to be patch tested has a pH that facilitates ionization, false-positive [47] or false-negative reactions can be observed [48].

23.2.2 Selection of Materials

The patient's medical history and clinical examination can supply data on the possible allergens involved, and so offer guidance as to which patch test materials to choose. In practice, the "baseline series" of test allergens is applied to all patients with contact dermatitis, but this series should be seen as dynamic and subject to continual evaluation and modifications.

The baseline series includes allergens that result positive in routine patch testing of patients in more than 0.5–1% of cases [49] and are ubiquitous. Naturally, in particular cases allergens with much lower positive reaction rates may be included (e.g. plants), as well as allergens that are locally important in specific areas.

Some allergens, such as fragrances and rubber compounds, are compiled into mixes to save space. In cases of positive reactions to a mix, then all the individual components must be tested singly, so as to be able to offer the patient precise information.

Table 23.3 shows the Italian baseline series of the Italian Society of Allergological, Occupational and Environmental Dermatology. Naturally, this series, that is anyway in continual evolution, can be expanded with other allergens as suggested by the patient's clinical history.

Most allergens are dispersed in petrolatum (white soft paraffin) and supplied in labeled syringes specifying the name and concentration of the substance. Other vehicles include water or ethanol. There are hundreds of test allergens available, and others can be prepared from the patient's own materials or from ingredients supplied by product manufacturers. It is important to check the expiry dates of the test materials, particularly in view of the instability of some vehicles. Patch test materials must be kept at 4 °C and protected from light.

23.2.3 Dosing of Chambers

The dose is exceedingly important, since false positive, false negative and adverse reactions are dose-dependent. Therefore the dose needs to be standardized for each type of test chamber (Table 23.4) [5, 50]. Petrolatum-based allergens are pipetted from the syringe into the chamber; for aqueous-based allergens, small filter papers are placed in the well, and these will hold about 15 μl of liquid dispensed with a micropipette. The use of micropipettes yields the best accuracy and precision as compared to other techniques [51]. Dosing of petrolatum-based allergens requires an experienced operator to minimize variations [52]. Usually, petrolatum-based substances are placed in the chambers just before the application of the patches (not more than a few hours before), while liquids and some volatile allergens (acrylates) are introduced at the moment of application.

23.2.4 Sites of Patch Test Application

The upper back is the preferential site for patch test application for various reasons: the flat surface permitting good occlusion and the ample application surface, generally not affected by diseases, not normally exposed to the sun and less prone to scratching. If necessary, the outer surface of the upper arms or thighs can be used.

Skin reactivity varies from one anatomical region to another: the forearm, for example, is less sensitive than the back to the elicitation of contact allergy to nickel [53]; when executing a repeated open application test (ROAT), the lower arm is less sensitive than the upper arm, while the back is the most reactive [54]. The proposed greater reactivity of the upper back compared to the lower back [55] was not confirmed by other studies [53, 56].

23.2.5 Occlusion Time

An occlusion time of 48 hours is recommended. Allergen dose and occlusion time are, in theory, parameters that will affect the results of patch tests, and are also correlated, since the dose is standardized for an occlusion time of two days. Most textbooks and authors recommend this

Table 23.3 SIDAPA (Italian Society of Allergological, Occupational and Environmental Dermatology) baseline patch test series

Allergen	Concentration (%)	Vehicle
Nickel sulfate	5	pet.
Neomycin sulfate	20	pet.
Sorbitan sesquioleate	20	pet.
Thiuram mix	1	pet.
Tetramethylthiuram monosulfide	0.25	—
Tetramethylthiuram disulfide	0.25	—
Tetraethylthriuram disulfide	0.25	—
Dipentamethylenethiuram disulfide	0.25	—
p-tert-Butylphenol formaldehyde resin	1	pet.
N-isopropyl-N'-phenyl-*p*-phenylenediamine	0.1	pet.
Fragrance mix I	8	pet.
Cinnamic alcohol	1	—
Cinnamal	1	—
Hydroxycitronellal	1	—
Amyl cinnamal	1	—
Geraniol	1	—
Eugenol	1	—
Isoeugenol	1	—
Oak moss absolute	1	—
Hydrocortisone 21 acetate	1	pet.
Peru balsam	25	pet.
Paraben mix	16	pet.
Methylparaben	4	—
Ethylparaben	4	—
Propylparaben	4	—
Butylparaben	4	—
Mercaptobenzothiazole	2	pet.
p-Phenylenediamine (free base)	1	pet.
Dimethylpropylamine	1	pet.
Budenoside	0.01	pet.
Benzocaine	5	pet.
Methylchloroisothiazolinone/methylisothiazolinone (3:1)	0.02	aq.
Cobalt chloride	1	pet.
Fragrance mix II	14	pet.
Hydroxyisohexyl 3-cyclohexene carboxaldehyde	2.5	—
Citral	1	—
Farnesol	2.5	—
Coumarin	2.5	—
Citronellol	0.5	—
Hexylcinnamal	5	—
Colophony	20	pet.
Potassium dichromate	0.5	pet.
2-Hydroxyethyl methacrylate	2	pet.
Formaldehyde	2	aq.
Wool alcohols	30	pet.
Disperse mix	6.6	pet.
Disperse blue 35	1	—

Table 23.3 (Continued)

Allergen	Concentration (%)	Vehicle
Disperse yellow 3	1	—
Disperse orange 1	1	—
Disperse orange 3	1	—
Disperse red 1	1	—
Disperse red 17	1	—
Disperse blue 106	0.3	—
Disperse blue 124	0.3	—
Epoxy resin	1	pet.
Mercapto mix	2	pet.
2-4-Morpholinylmercaptobenzothiazole	0.5	—
Dibenzothiazyl disulphide	0.5	—
N-Cyclohexyl-2-benzothiazylsulfenamide	0.5	—
Mercaptobenzothiazole	0.5	—
Hydroxyisohexyl-3-cyclohexene	5	pet.
Methylisothiazolinone	0.2	aq.

pet. = petrolatum, aq. = aqueous

Table 23.4 Dose of allergen in the common chamber sizes (modified, by [5])

Chamber	Liquid preparation	Preparation in petrolatum	µl/mg/cm^2
Finn Chamber ® (area 0.5 cm^2)	15 µl	20 mg	30/40/cm^2
Van der Bendt ® (area 0.64 cm^2)	20 µl	25 mg	31/39/cm^2
IQ Ultra ® (area 0.68 cm^2)	20 µl	25 mg	29/36/cm^2

occlusion time, although some centers still prefer 24 h occlusion [57]. A longer occlusion time is not recommended.

23.2.6 Practical Suggestions

Conservation of Haptens. Haptens must be kept in the refrigerator or in cold environments in the dark, because exposure to light and/or high environmental temperatures can modify their diagnostic potential.

Sequence of Haptens. To minimize the excited skin syndrome phenomenon, it is wise to avoid testing haptens that provoke extreme positive reactions or cross react in nearby sites; this precaution is recommended even if the phenomenon is not reproducible [58].

Rimoval of Hairs. To improve the adhesion of the test apparatus to the skin, hairs must be dry shaved, although it should also be borne in mind that the patch applied on a shaved area can provoke irritation.

Removal of Skin Grease. In cases of a greasy skin, it is better to delicately cleanse the site of application of the tests with ethanol, left to evaporate.

23.3 Reading Times

Patch tests are applied on day O (DO) and removed on D2. In the literature, the best solution is considered to be 3 readings at different times. The first reading should be at D2, 15–60 minutes after removal, being the time necessary for resolution of pressure effects. A second reading at D3 or D4 is a must [59]. A further reading between D5 and D10 is necessary at least for some allergens, since about 7–30% of positive reactions would otherwise be missed [60–62].

In some countries, the first reading is made at D3 or D4. A single reading at D4 is absolutely not recommended. In one study in which reading was done several times between D2 and D9, it was noted that most of the positive reactions were observed at D4, but various other reactions were

Table 23.5 Positive reactions to nickel at D1–D5 in 577 patients

	D1	D2	D3	D4	D5
N° patients	250	296	21	8	2
% Positive reactions	43.3	51.3	3.6	1.5	0.3

Table 23.6 Reading times of patch tests after 48 h occlusion: 3510 positive reactions among 3312 patients

Positive reactions at D2	90.7%	98.2%
Positive reactions at D3	7.5%	
Positive reactions at D4	1.5%	
Positive reactions at D5	0.2%	
Positive reactions at D6	0.1%	

still evident at D7 [60]. A single reading at D2 is not therefore appropriate [63]. In conclusion, at least two readings of patch tests reactions are recommended: at D2/D3 or D4, and around D7 [64].

Our unpublished data on patch tests reading times demonstrated that at the reading on D2 the incidence of positive reactions was about 90%; this incidence increased at subsequent readings until D7. "Delayed" positive reactions are observed after D3/D4, related in particular to neomycin, nickel, wool alcohols, paraphenylenediamine, corticosteroids, and aminoglycoside antibiotics. In 577 patients with clinical manifestations and a medical history definitely related to nickel allergy, we performed 5 patch tests with nickel sulfate 5% pet., and made daily readings from D1 to D5: at D1, 43.3% of the subjects already showed a positive response; at D3 the positive responses had reached 98.2% of the cases; a further 1.8% of positive responses was observed at D5 (Table 23.5). In another study conducted in 3312 patients patch tested with the standard European series, making daily readings from D2 to D6 we observed that over a total of 3510 positive reactions, 98.2% were observed at D3, 1.5% at D4, and a further 0.3% between D5 and D6 (Table 23.6).

23.4 Reading Scale

The quali-quantitive assessment of allergic reactions takes into account the reading parameters reported in Table 23.7, namely erythema, edema, infiltration, papules and vesicles. Other parameters are the fine skin structure, reaction surface and area involved [3–9]. Unequivocally, allergic reactions and those of irritant type are generally well defined.

Instead, a problem of interpretation arises in the presence of reactions featuring only erythema, and so reported as "?+" or "±". Erythema is an intensity parameter and so cannot discriminate alone between an allergic and a non allergic reaction. Edema is also essentially an intensity parameter. A reaction with just erythema, or doubtful, must be checked at a later time by repeating the patch test, if necessary with a different antigen concentration or by applying the use test.

The fine structure of an allergic reaction, that is also appreciable at superficial digitopalpation, consists of minute vesicles and/or papules and must be homogeneous all over the test area: the reaction will tend to spread beyond the test area, with indistinct borders (Fig. 23.1), although some antigens (Kathon CG, fragrance mix, thiuram mix) often induce well-demarcated reactions circumscribed to the test area (Fig. 23.2).

The readings of patch tests must be done by a dermatologist with adequate experience, and even in this case inter-observer variability has been demonstrated, when discriminating irritant and doubtful reactions and distinguishing between doubtful and weak positive reactions [65, 66]. It has also been observed that some substances (corticosteroids) in a liquid vehicle can give rise to a ring-shaped test reaction, and that clearly allergic reactions are then elicited at higher concentrations of the same allergen [67]. A continual process of standardization of reading parameters is therefore desirable [65].

23.4.1 Irritant Reactions

The irritant reaction has typical morphological characteristics, although it may sometimes be difficult to differentiate from a "one plus" reaction.

Irritant reactions are, of course, more likely when testing the patients' own materials or

Table 23.7 Qualitative/quantitative evaluation of allergic reactions

? +	Doubtful reaction: faint erythema only
+	Weak positive reaction: homogeneous erythema, infiltration, possible papules or vesicles
++	Strong positive reaction: erythema, infiltration, papules and vesicles
+++	Extreme positive reaction: erythema, edema, infiltration, coalescing vesicles
IR	Irritant reaction
–	Negative reaction
NT	Not tested

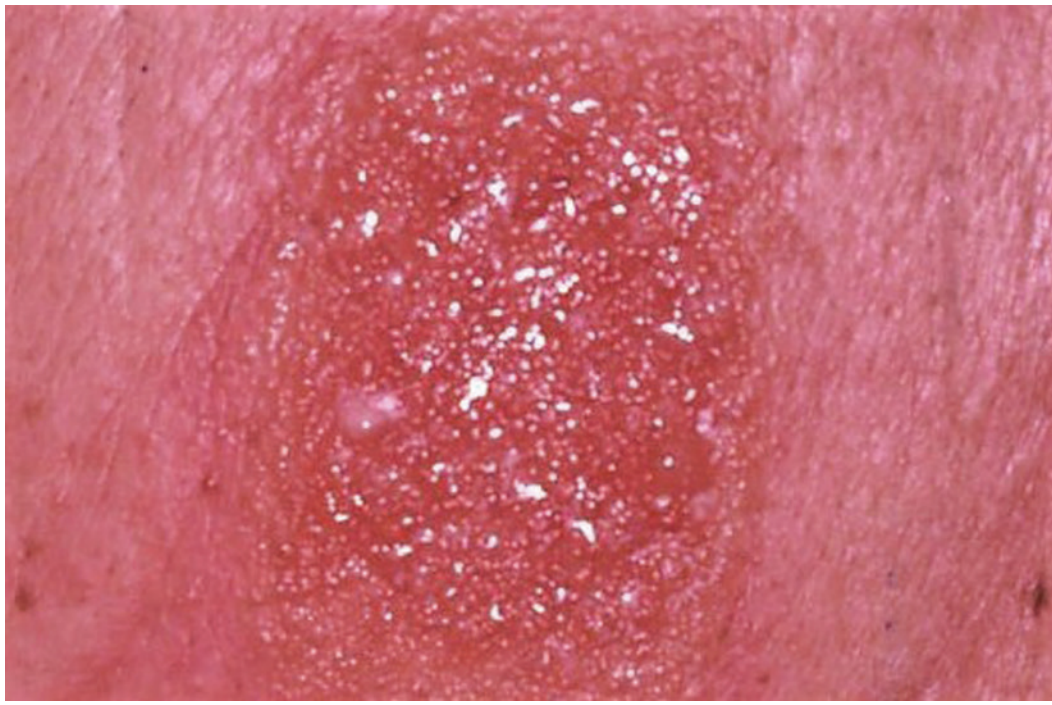

Fig. 23.1 Positive patch test reaction with indistinct borders (Reproduced with permission by Nettis and Angelini [8])

substances that are not well known, so their concentration is not standardized. Even within the baseline series there can be problems of this type, as with formaldehyde, for example. When doubts arise, a dilution series should be performed: in the presence of a true allergen, there will be a positive reaction in several dilutions, whereas this will not occur in cases of an irritant reaction.

In irritant type reactions the fine structure is not homogeneous all over the test area and the margins are in most cases clearcut. There are various types of irritant reactions (Table 23.8). Among those most frequently observed, purpuric reactions (Fig. 23.3) are generally induced by cobalt chloride. Pustular reactions, with elements in follicular sites or the sweat gland outlets, sometimes on a poorly erythematous base, are generally linked to metals (chromium, cobalt and, in particular, nickel) (Fig. 23.4) and are most often observed in children and atopic subjects; cytodiagnostic examination of the pustules reveals neutrophils. Exclusively papulous reactions in follicular sites are not significant either. Blisters are uncommon if optimal hapten materials are used; if they appear, or there is necrosis,

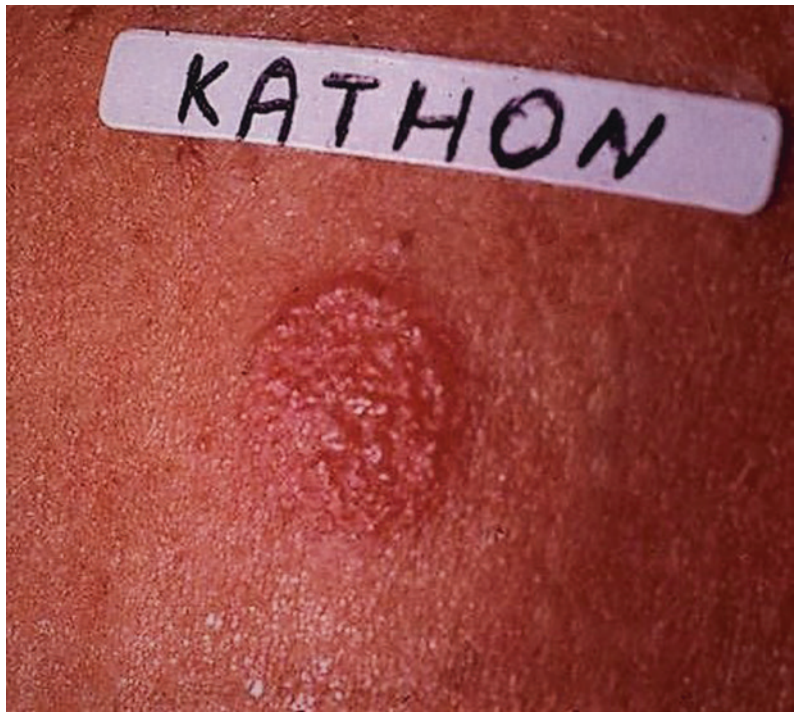

Fig. 23.2 Positive patch test reaction with demarcated borders (Reproduced with permission by Nettis and Angelini [8])

Table 23.8 Irritant reactions

Non homogeneous faint erythema
Purpuric reaction
Pustular reaction (sometimes with weak erythema)
Papular elements with a follicular pattern
Shampoo or soap effect
'Cigarette paper' skin
Bullous reactions
Necrotic reactions
Excited skin syndrome

an artefact should also be suspected, consciously induced by a simulator for illicit purposes (e.g. to gain recognition of an occupational disease) (Fig. 23.5).

The soap or shampoo effect, in which the skin is weakly erythematous, the skin folds are accentuated and the margins of the lesions are clearcut, is due to substances with a tensioactive power (soaps, shampoos, quaternary ammonium salts, triethanolamine). Owing to the poor viscosity of vaseline or other vehicles, the hapten material can accumulate at the periphery of the test area, at a relatively increased concentration, thus causing erythemato-purpuric and/or bullous lesions ("edge effect") (Fig. 23.6).

The excited skin syndrome, or "angry back", is a skin hyperreactivity phenomonen whereby an intense positive reaction to one or more substances (e.g. those whose concentration in use for patch tests is near to the irritant threshold: formaldehyde, wool alcohols, parabens, paraphenylenediamine) can give rise to false positive reactions to nearby haptens, even if to a lesser degree. This can also occur when patch tests are executed in the active disease phase, and when cross reacting substances are tested nearby. If this phenomenon is observed, all the substances that elicited positive responses must be retested, one at a time, at intervals of one week between each.

Reading patch tests on D3/D4 can be useful also in order to differentiate positive from irritant reactions: in fact, the former tend to show

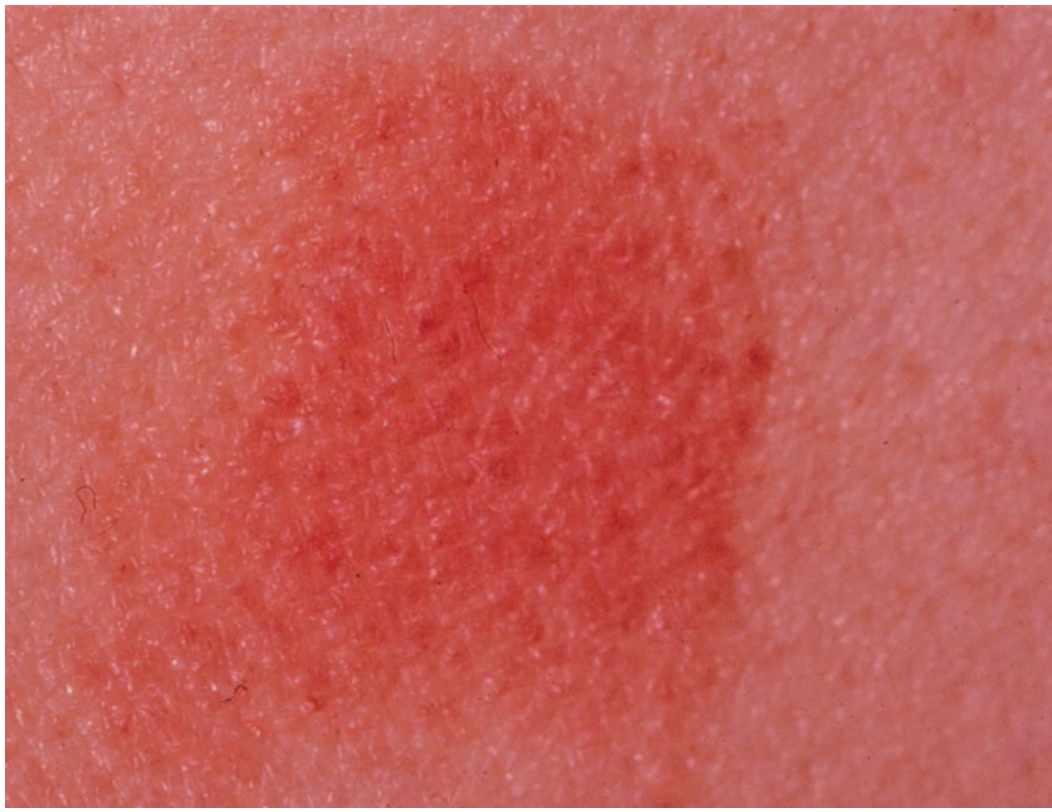

Fig. 23.3 Irritant purpuric patch test reaction to cobalt chloride

an increased intensity over time whereas the latter generally decline or resolve over time.

23.5 False-Positive Reactions and False-Negative Reactions

Most common causes of false-positive and false-negative reactions are reported in Tables 23.9 and 23.10.

Some causes of false-positive reactions are controllable but others cannot be monitored. It may sometimes be useful to execute control tests using a blank patch or one containing just vaseline.

Among uncontrollable causes of false-negative reactions, the following are the most common events: the execution of the patch tests during a refractory or "anergic" phase; the test does not reproduce the real clinical conditions (e.g. multiple applications of the etiological agent in favoring conditions, such as sweating, pressure, damaged skin, friction); the possibility that the transcutaneous penetration is less in the test application site than in the clinical exposure (axillae, eyelids). In the latter event, scratch-patch tests or pretreatment of the site with stripping can be made, or else enhancers of skin absorption can be used (e.g. transcutol) [68].

23.6 Testing with the Patient's Own Products

Guidelines for patch testing with the patient's own products have been reported in the literature [1, 69–71]. These tests are particularly important in cases of occupational contact dermatitis, because many substances present in working environments are not available in

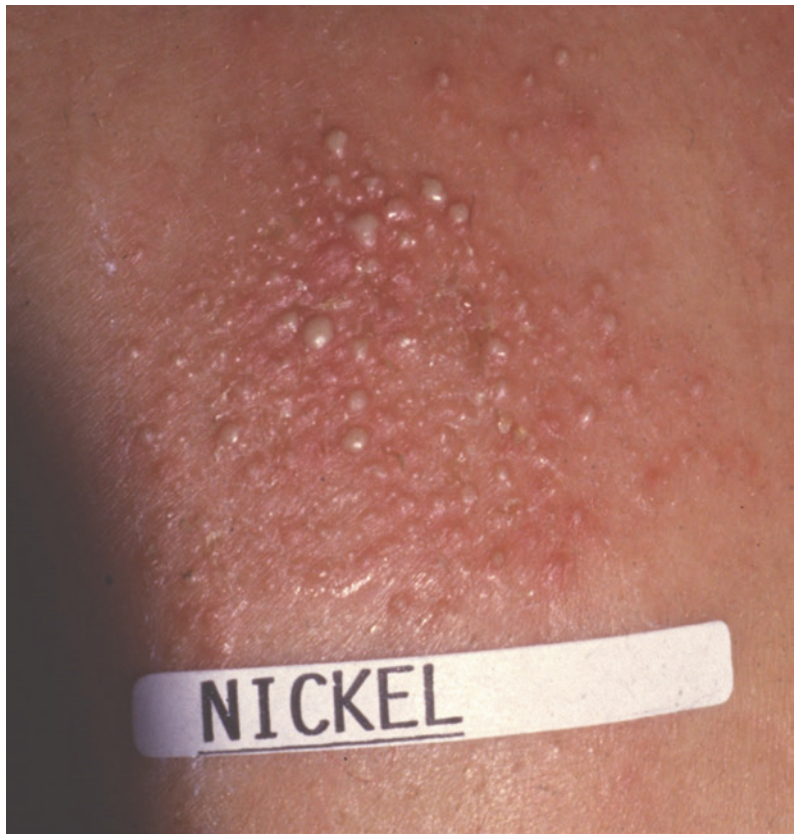

Fig. 23.4 Irritant pustular patch test reaction to nickel

standardized doses on the market. Other frequent test materials are topical medicaments, cosmetics, and rubber and leather products.

The execution of tests with the patient's own materials requiries proper experience and a highly trained staff. Above all it is important to know all about the products to be tested, relying on safety data sheets, lists of ingredients on the packages (INCI lists) products information leaflets, and the internet. Much of this information needs to be provided directly by the manufacturers, although producers are often not aware of contaminants or materials present under a different nomenclature.

The concentration of a substance that must be patch tested is vitally important. It may be too low in a product and so give rise to false-negative reactions. Many products need to be diluted in view of their irritant potential (shampoos, toothpastes), and this can also give rise to false-negative reactions. On the other hand, when a product is not sufficiently diluted it can elicit false-positive reactions or induce sensitization. It is therefore important to know the ingredients of a product in order to be able to test them singly. In this regard, some cosmetic companies provide the separate ingredients of a product at adeguate concentrations for patch testing, while others tend to supply the ingredients in dilutions as used in the products, that may be too low and therefore give rise to false-negative reactions. Dermatological centers with experience in non-standard test materials prefer to decide for themselves about the concentration, provided they have access to the pure substance and have a detailed knowledge of the chemical toxicity.

In any case, it is wise not to test completely unknown substances because of the possible

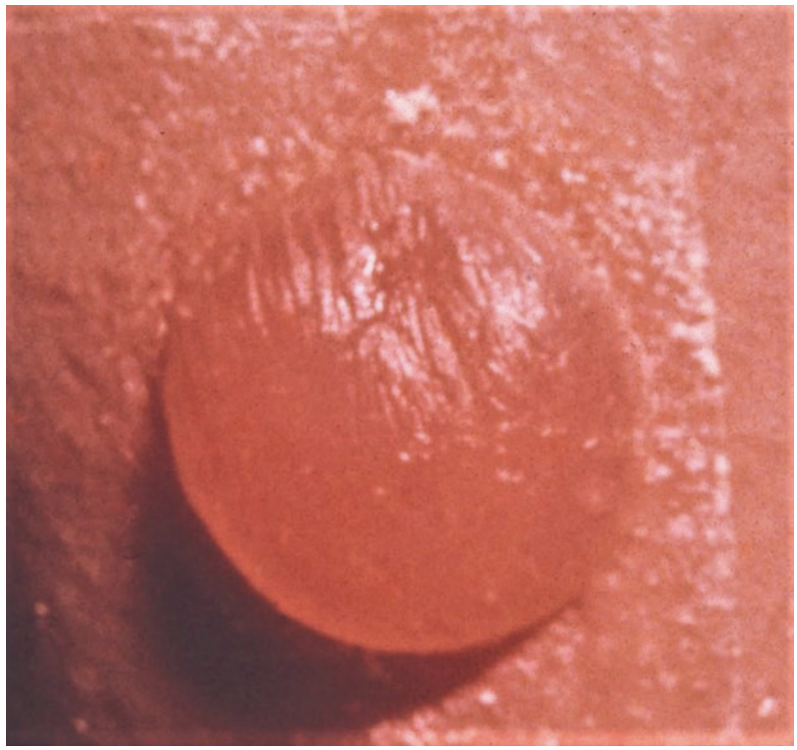

Fig. 23.5 Irritant bullous patch test reaction: an artefact in conscious simulator

local (necrosis, scarring, pigmentation/depigmentation) and systemic side effects they could induce. For the same reason, one should not test extremely hazardous substances, like strong acids and alkalis, and poisonous chemicals.

Other than patch and photopatch tests, additional methods can also be employed, such as open and semi-open or semiocclusive tests, use tests, repeated open application tests (ROATs), and prick tests (in cases of protein contact dermatitis or immediate skin reactions). Patch tests are done with products lacking any irritant substances (cosmetics, lotions, topical medicaments), while open and semi-open tests are useful if the products contain irritant ingredients (shampoos, liquid soaps, nail varnishes, medicaments containing benzoyl peroxide, tretinoin, capsaicine, quaternary ammonium compounds, industrial products such as glues, paints, inks, varnishes). The material is appliesd on the skin with a cotton swab (about 15 μl) on a small area (2×2 cm) and left to dry; then it is covered with acrylic tape [71].

The choice of vehicle depends on the product characteristics, solubility and pH. When testing water-soluble chemicals, it is necessary to check the pH before testing. Neutral products (pH 4–9) can be diluted in distillled water (at this pH range few irritant type reactions occur). For more alkaline or acidic substances, the use of buffer solutions is recommended to reduce skin irritability: acid buffer (pH 4.7) is used for alkaline products ($pH > 9$) and alkaline buffer (pH 9.9) for acid products ($pH < 4$) [72]. Substances with a pH of less than 3 or more than 10, that are normallly used in closed systems, should not be tested. Water-insoluble chemicals are usually diluted in petrolatum or, alternatively, acetone, ethanol, olive oil.

Solid materials can be used as is, placing scrapings or fragments in the test chamber or directly on acrylic tape. Pieces of material

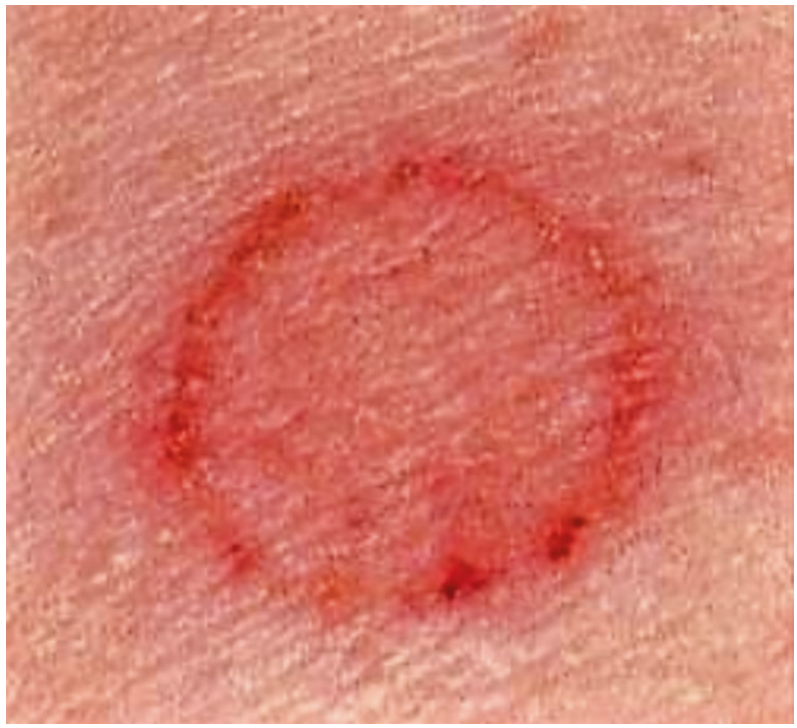

Fig. 23.6 Irritant patch test reaction ("edge effect") (Reproduced with permission by Nettis and Angelini) [8])

Table 23.9 Most common causes of false-positive reactions

High concentration of the hapten
Irritant vehicle (in particular solvents)
Impurities or contamination products in the test substance
Eczematous lesions on or near the site of application of the test
Execution of patch tests in the active disease stage
Highly irritable skin
Intense reaction to the patch
Substance in crystals form not uniformly distributed in the vehicle
Mechanical irritation due to solid material compressed in the support
Excited skin syndrome
Finn Chamber® (following immunotherapy with intradermic allergenic extracts for allergy to pollens, some patients develop sensitization to aluminium. Moreover, some substances with a mercury base can react with aluminium)

(textiles, gloves, shoes) (2×2 cm moistened with saline solution) or scrapings of plastic materials are placed in occlusion for 48 hours. In these conditions, however, the possibility of false-negative (sensitizer concentration too low, sensitizer not released) or false-positive reactions (pressure effect of sharp particles) should be taken into account. The sensitizer can be extracted with water or solvents, depending on the characteristics of the material to be studied. Alternatively, for solid materials ultrasonic bath extracts can be used (small pieces of the material, in water or organic solvents, extracted in an ultrasonic cleaner device and finally filtered) [73]. Another method is to perform patch tests with thin layer chromatograms of textiles, gloves, rubber, and any other materials [74].

Table 23.10 Most common causes of false-negative reactions

Low concentration of the hapten
Insufficient quantity of hapten applied
Substance not released by vehicle
Insufficient occlusion
Too short a duration of the contact due to detachment of the test apparatus
Test not applied at the recommended sites
Topical treatment with corticosteroids or UV irradiation at the test sites
Reading of tests not prolonged over time: some substances can give 'delayed' reactions
Allergen in non active form, because insufficiently oxidated (turpentine) or degraded
High patient sensitization threshold
Systemic treatment with corticosteroids or immunosuppressants

Table 23.11 Testing of some patients' products

Product	Concentration	Comment
Eye makeup	As is	Semi-open test first (mascara, cleansers)
Facial makeup	As is	Photopatch for sunscreens in lipsticks
Moisturizers	As is	Photopatch for sunscreens
		ROAT or use test to confirm positive patch test reaction with lotions
Sunscreens	As is	Photopatch tests
Self-tanning creams	As is	
Perfume products	As is	Photopatch for chronic actinic dermatitis
Deodorants	As is	
Shaving products (creams, soaps)	1% (w)	Semi-open test
Cleaning products	1% (w)	Semi-open test
Hairdressing products		
Spray, gels	As is	Semi-open test first
Dyes	2% (w)	Active sensitization possible; semi-open test
Nail cosmetics		
Lacquers	As is	Semi-open test only
Lacquer removers		Do not test (highly irritant)
Glue for artificial nails	0.01–1%	Semi-open test first
Paints, lacquers	0.1–5% (pet.)	Detailed information on chemical composition first
Organic solvents	0.1–10% (pet.)	
Greases, oils		
Lubrificant greases	As is and 20% (pet.)	Semi-open test first
Lubrificant oils	As is, 50%,10% (oo)	
Hydraulic oils	1% (oo)	
Metal working fluids		
Water-based	5% (w)	
Oil-based	50% (oo)	
Adesive tapes	As is	
Glues	1–10% (pet.)	Semi-open test only; strong irritants

w = water, pet = petrolatum, oo = olive oil

Table 23.11 reports details on how to test some patients products [71]. Leave-on cosmetics and topical medicaments can be tested as is but a negative result does not exclude a contact allergy (possible low concentration in the product). Rinse-off cosmetics can be tested at concentrations of 1–10% in aq., depending on the formulation.

Metal-working fluids are often diluted before use at the work place. The allergens they contain are biocides, rust preventives, emulsifiers, and tall oil derivatives. It is best to take the products to be used directly off the machine because they may contain important impurities, like metals, preservatives and perfumes added as odour masks in the circulatory system. Fresh water-based products are tested at a concentration of 5% in aq.; used products have generally been diluted at 4–8% and so can be tested as is, while otherwise the concentration must be adjusted to 5%. Oil-based metalworking fluids, fresh or used, are tested at a 50% concentration in olive oil.

Powdery materials (ground dust, scrapings or small cut pieces) should first be moistened with water or organic solvents and then tested in chambers. Larger pieces (textiles, gloves) can be tested semi-open, covered with surgical test tape, without a chamber.

As regards plants, fresh or dried material can be tested as is provided that the botanical identity is known. The different parts of the plant are tested in duplicate, with a drop of saline and ethanol, since some components are water-soluble and others ethanol-soluble. Tropical woods may be strong irritants or sensitizers.

Naturally, any center that intends to test the patient's own products must be equipped with the proper laboratory equipment (containers, syringes, stirrers, spatulas, mortars, pipettes, etc.).

23.7 Potential Adverse Effects

According to the various authors, the greatest hazard is the omission of patch testing procedures in the management of patients with contact dermatoses [7, 75], as this omission could cause the dermatitis to become chronic and gradually worsen, seriously affecting the patient's work and quality of life.

Table 23.12 Adverse effects of patch testing

Irritant reactions
Active sensitization
Koebner phenomenon
Persistence of positive reactions
Necrosis, scarring, and keloids
Flare-up and/or worsening of dermatitis
Hyper- and hypopigmentation at the sites of positive reactions
Anaphylactoid reactions
Adhesive tape and patch test material reactions
Bacterial and viral infections

Like all in vivo diagnostic methods, patch tests can have adverse effects, albeit rarely and in most cases of a mild degree (Table 23.12). The occurrence of adverse effects is directly proportional to the dermatologist's experience and to any failure to observe the correct norms for the performance of the tests and recommendations reported in the guidelines. In any case, adverse effects must be regarded as "complications" not "risks" of patch tests, and therefore should not exclude their use.

Irritant Reactions. Skin irritation can be observed when testing non standardized products or substances, despite appropriate dilutions. Irritant and allergic reactions to patch test materials and to adhesive tapes have been greatly minimized since the introduction of modern acrylate adhesives and aluminium patches (Finn Chamber ®) (Figs. 23.7, 23.8, 23.9, and 23.10) [76–86].

Active Sensitization. This is an important complication of patch testing, even if rare. It consists of a positive patch test reaction that generally develops after two weeks from an initial negative response on the same site. It can sometimes be difficult to differentiate active sensitization due to patch testing from a delayed patch test elicitation reaction [87]. To confirm the diagnosis of active sensitization, the patch tests need to be repeated: a positive elicitation response appearing after a normal latency of

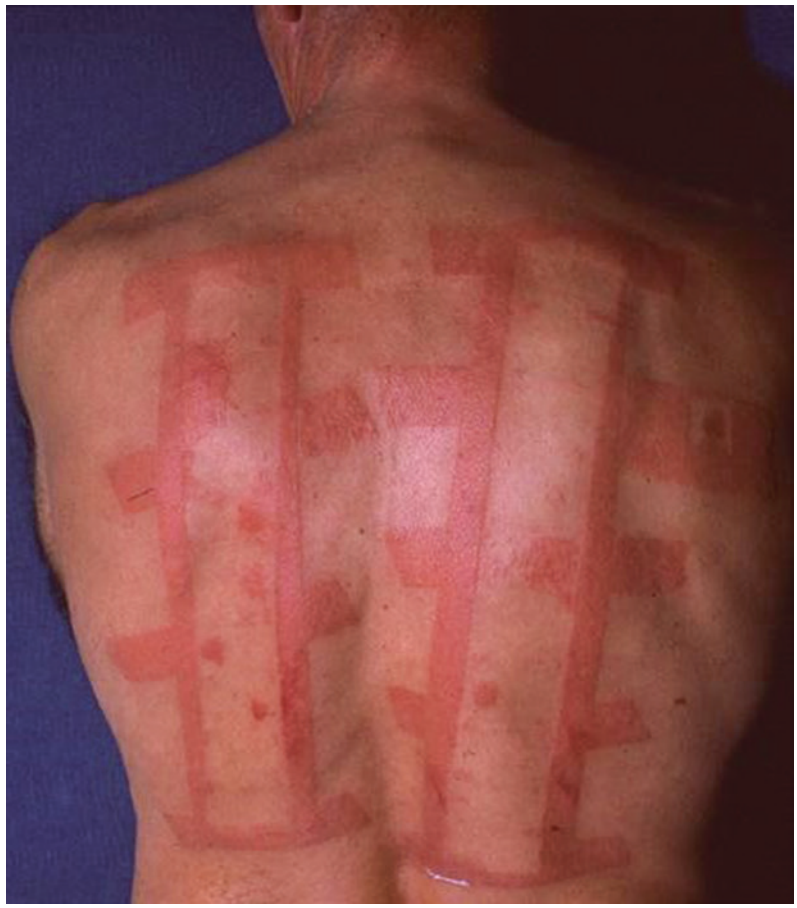

Fig. 23.7 Allergic reaction to adhesive tape from colophony

1–4 days supports the suspicion of active sensitization, especially in cases when the substance has been diluted 10–100 times [88]. However, in some cases it is likely that the tests may have the effect of boosting a preexisting weak sensitization.

The allergens most prone to give rise to active sensitization are paraphenylenediamine, para-tertiary-butylcatechol, acrylates tested at higher concentrations, compositae mix, primula extracts, isothiazolinones, and chloracetamide [87–92].

To study the risk of patch tests sensitizing, Meneghini and Coll [93] repeated patch testing of 181 patients who had contact dermatitis and 100 patients with various dermatoses: new positive patch tests were observed in 31 patients with eczema and 4 from the other group. The authors concluded that the new reactions had been due to further environmental exposure rather than to patch test active sensitization. In a follow-up study, Meneghini and Angelini [94] followed a further group of 461 patients who were retested one or more times over a period of 3 years (Table 23.13); in 25% of the cases of allergic contact dermatitis, new positive reactions were observed. Nevertheless, the clinical history and follow-up of these patients highlighted the specific role of further contacts, especially of occupational type or with topical medicaments. Moreover, in a further 25% of the cases, despite the persistence of the harmful contact, the previous allergic reactivity disappeared, most likely due to the development of immune tolerance.

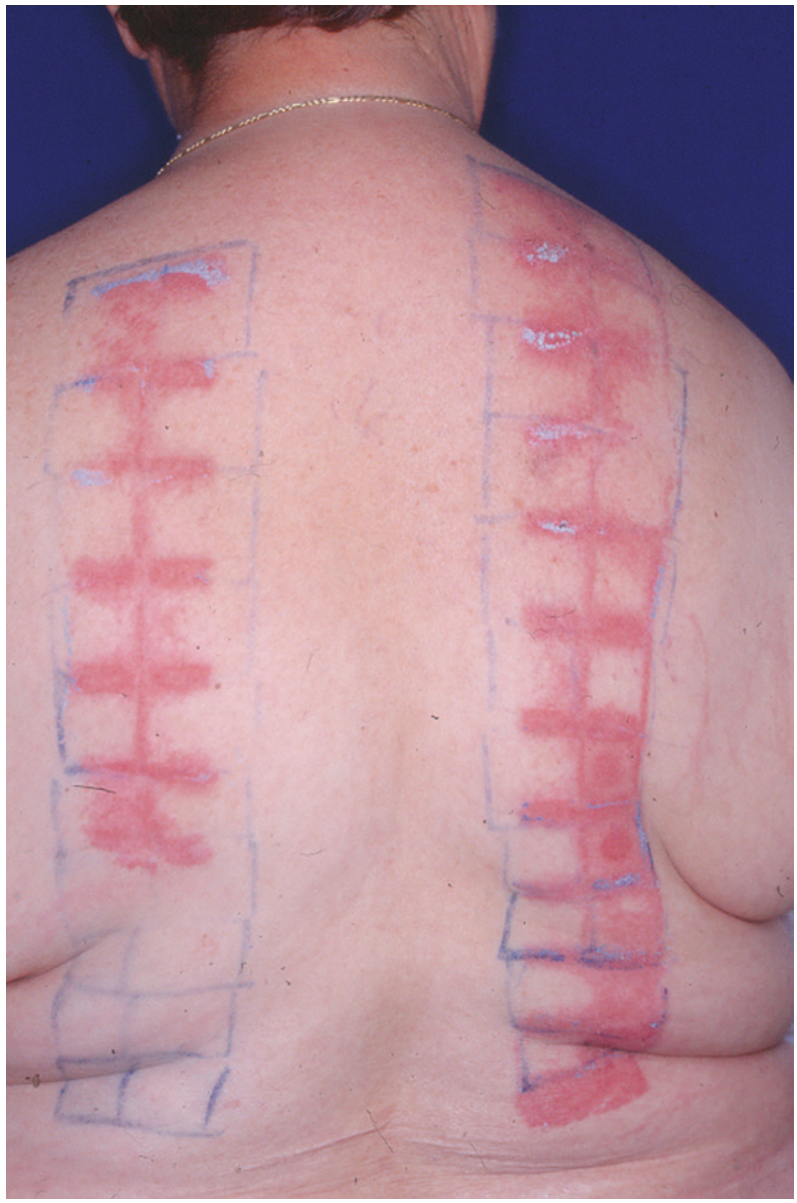

Fig. 23.8 Irritant reaction to acrylate-based adhesive tape

This phenomenon has been demonstrated in both experimental and clinical studies.

In addition, the same authors conducted daily observation for 20–30 days of 351 hospitalized patients affected by contact dermatitis and patch tested. They did not observe any cases of active sensitization (unpublished data). On the basis of this finding, the authors emphasized that patch testing does not cause new sensitizations provided that proper techniques are employed.

Flare-up of Contact Dermatitis. Sometimes, a strong positive patch test reaction may be accompanied by a specific flare of an existing or previous contact dermatitis. These flare-up reactions confirm the specific causal role of the allergen in inducing the contact dermatitis; they

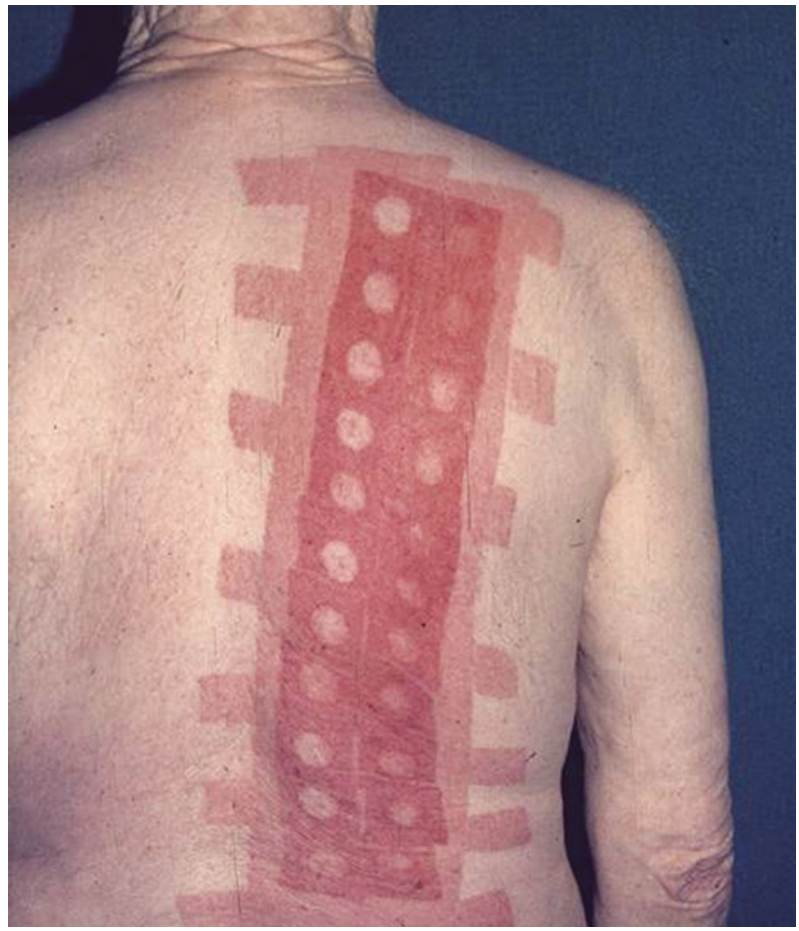

Fig. 23.9 Allergic reaction to common (colophony) and acrylate-based adhesive tapes (Reproduced with permission by Nettis and Angelini [8])

Table 23.13 Results of repeated patch tests done once or several times over a period of 3 years in 461 patients with contact dermatitis

A. 208 patients with allergic contact dermatitis
1. In 50% persistence of sensitization
2. In 25% disappearance of positive reactions
3. In 25% appearance of new positive reactions
B. 253 patients with irritant contact dermatitis No appearance of sensitization

seem to be more frequent in cases of polysensitized patients [95].

The Koebner Phenomenon. A positive patch test reaction in a patient with active psoriasis or lichen planus may reproduce these dermatoses at the patch test sites. This localized effect will resolve rapidly with the use of a topical corticosteroid product.

Persistent Reaction. A positive patch test reaction can sometimes persist for up to several weeks. The case of a persistent reaction to paraphenylenediamine lasting more than one month has been reported [96]. Notoriously, gold chloride 0.5% aq. causes persistent reactions, even when the allergic subject has not been reexposed to gold for a long time. Palladium tetrachloride has also been reported to cause persistent granulomatous reactions [97, 98]. Intralesional injections of a corticosteroid will rapidly resolve the problem.

Pigmentation Alterations. Hyperpigmentation from patch testing rarely occurs; it is more

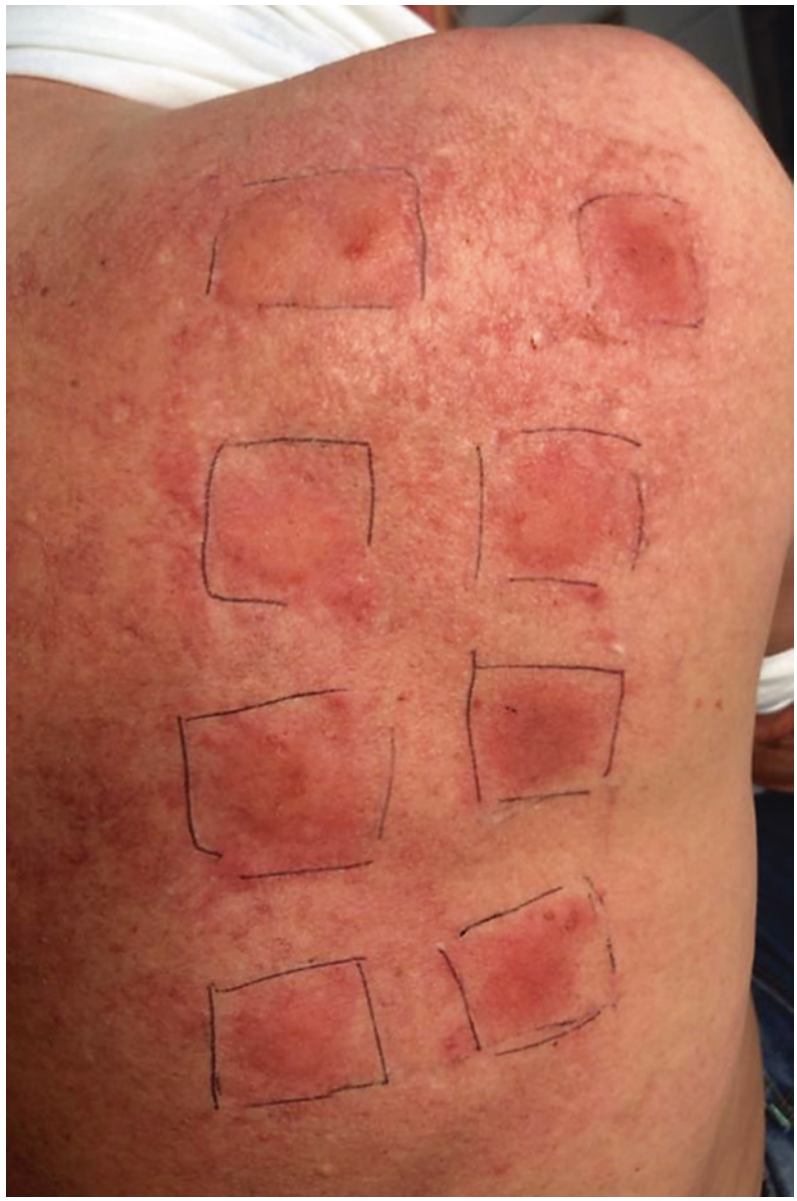

Fig. 23.10 Allergic reactions to modified colophony present in adhesive tape used to fix the filter papers patches

common in dark pigmented subjects. Such a change may last for several weeks. Exposure to the sun immediately after the removal of patch tests for fragrances can induce hyperpigmentation. Hydroquinone and various other depigmenting substances cause depigmentation (see Chap. 17). These pigmentary changes are not a serious problem because patch tests are normally performed on the back, and so such reactions are covered by clothing. Preparations like Covermark ® can hide the marks until they resolve.

Necrosis, Scarrings, and Keloids. These extremely rare adverse effects may occur after patch tests with strong acids and alkalis or chemicals of unknown composition, in particular if the patient keeps scratching or a superimposed infection develops.

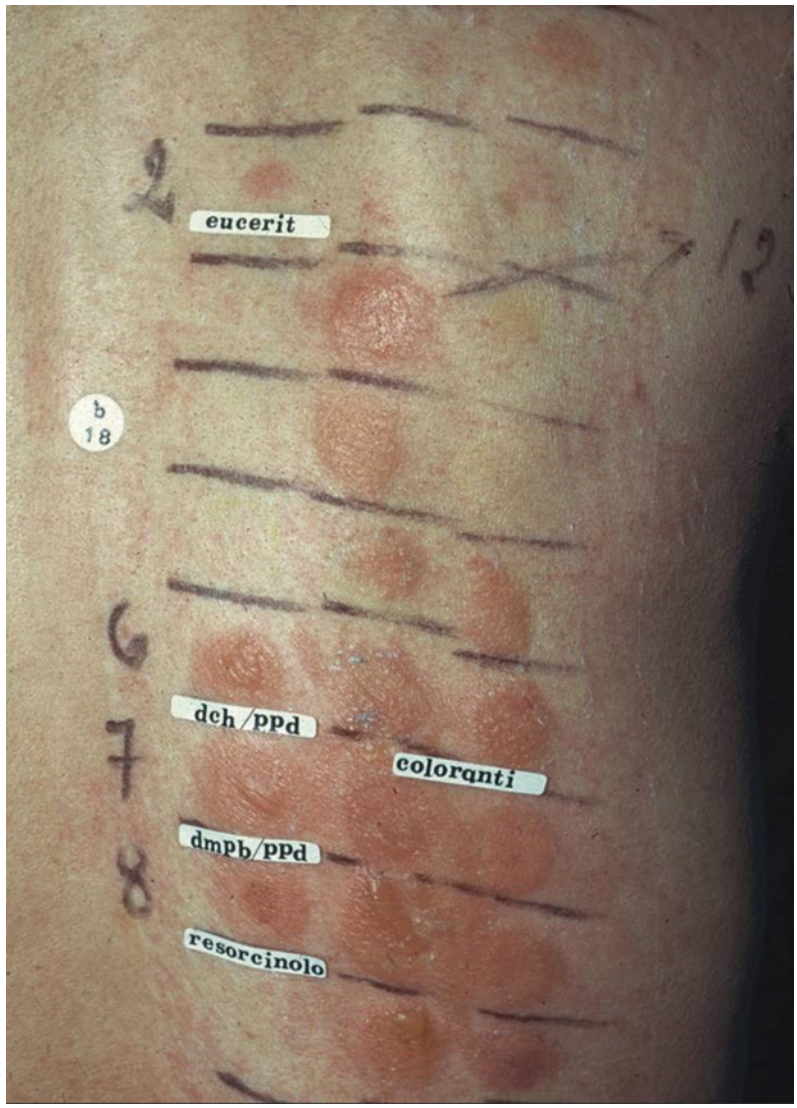

Fig. 23.11 Multiple positive patch test reactions (excited skin syndrome)

Anaphylactoid Reactions. In rare cases, these have been observed 30 minutes after performing patch tests with penicillin, neomycin, gentamycin, or bacitracin. Ammonium persulfate, used to bleach hair, can in rare cases produce a non specific idiosyncratic release of histamine and consequently an anaphylactoid reaction, and should not therefore be used for routine patch testing.

23.8 The Excited Skin Syndrome

The term "angry back" is used to describe a regional phenomenon caused by a strongly positive reaction whereby, due to a state of skin hyperreactivity, various other nearby patch test sites become reactive (Fig. 23.11) [99–101]. Repeating patch tests with the substances that gave these concomitant "positive" reactions, it

was found that 42% of them were negative, suggesting that false-positive reactions had occurred [101]. The approximately 40% incidence of excited skin syndrome has been confirmed by other authors [102]. In such circumstances each substance needs to be retested singly.

The allergens that most often induce strongly positive reactions, and hence non specific reactions in adjacent patch tests sites, are nickel sulfate and potassium dichromate. Therefore, when a patient's history strongly suggests causality of one of the two allergens, it can be tested in another skin site in order to minimize the phenomenon, also known as "status eczematicus" [103]. Since patch tests can be performed elsewhere besides the back, the term "angry back" was later changed to "excited skin syndrome" [104, 105]. In subjects with excited skin syndrome on the shoulders, patch tests repeated on the arms give comparable results, some of which are reproducible and others non reproducible; a strong reaction on an arm can produce a unspecific response on the other arm, so the phenomenon is not necessarily localized.

This phenomenon, not convalidated by other studies [58], has raised the problem of reactions that can be lost when retesting patients. It is, of course, true that over time new reactions can develop. This was demonstrated by Meneghini and Angelini [94] who patch tested 309 patients with contact dermatitis and found that 208 of them had one or more positive tests. Retesting the same patients with the same series of 31 allergens after 1–36 months from the first patch testing, a new situation emerged, featuring 52 cases of "loss" (25%) but 52 new cases (25%) (Table 23.13). Also other authors, retesting 174 patients with the same allergens five years after the original testing, found 18% of 'lost' cases, 29% with new reactions and 53% with the same positive reactions [106].

The principles to be followed in cases of excited skin syndrome are summarized in Table 23.14. If several positive responses to patch tests are obtained it is important to probe more deeply into the clinical history; this may be sufficient to resolve the problem, inasmuch as all the reactions could be found relevant. It is not necessary to retest singly those haptens that have elicited positive reactions if contact with them is easily avoided (e.g. neomycin), or when the clinical history decidedly denies any relevance. By contrast, it is clearly important to retest ubiquitous substances or those that are difficult to avoid, or otherwise when a medicolegal judgment is involved, or a job change for the worker under observation.

The pathogenic mechanism underlying the excited skin syndrome is not known. The phenomenon does not seem to be linked, in the absolute sense, to a state of delayed generalized hypersensitivity. In fact, it has been shown in albino mice [107] and guinea pigs [108] that it can also be provoked by an irritant mechanism.

23.9 Clinical Relevance

In order to establish the diagnosis of allergic contact dermatitis, at least two important steps should be considered: the accurate recording of positive patch test reactions as true allergic reactions or false-positives, and the assessment of their clinical relevance. This second point is extremely important in order to be able to offer the patient useful prevention norms.

Few works in literature have dealt specifically with the problem of the clinical relevance of positive reactions [109–115], and in one of these studies complaints were made about the lack or insufficient consideration of the relevance in most clinical studies of allergic contact dermatitis [112]. In practice, the question of relevance is not easily solvable and one cannot but agree with Ian Wahlberg when he said that "evaluating the relevance of a reaction is the most difficult and intricate part of the patch test procedure, and is a challenge to both dermatologist and patient. The dermatologist's skill, experience and curiosity are crucial factors" [114].

Table 23.14 Behavior strategy in patients with excited skin syndrome

1. If several positive reactions appear, concentrate on eliciting a more detailed clinical history
2. It is not necessary to retest substances singly if:
A. the substance can easily be avoided
B. the clinical history decisively denies any relevance
3. It is important to retest single substances if:
A. the substance is ubiquitous
B. the substance is not easy to avoid
C. the patient has the possibility of a job change
D. a medico-legal assessment is involved

Table 23.15 Assessment of clinical relevance of positive patch test reactions

1. Probe the present and past clinical history more deeply
2. Reconsider occupational and non occupational exposure
3. Important clinical aids a. Correspondence between the site of the dermatitis and site of exposure b. Peculiar clinical pictures due to specific allergens
4. Consider recurrence or worsening of the dermatitis following patch tests
5. Carefully consider all possible contact modes (direct, airborne, ectopic)
6. Consult detailed lists of ubiquitousness of allergens
7. Consider a visit to inspect the work place
8. Analyze the environmental conditions at the work place
9. Gather information about chemical products from the producers
10. Resort to additional tests

Table 23.16 Additional tests to make a more precise assessment of relevant reactions

Use test
Roat
Patch tests with scaled dilutions of the allergen
Chemical analysis of the incriminated product
Search for impurities in the incriminated product
Spot tests

Relevance is the capability of a diagnostic system—in this case, patch testing—to select and highlight data appropriate to a patient's needs [111]. In this regard, positive test reactions can be classified in three categories based on the medical history [1, 113, 116].

Current Clinical Relevance. "Current" or "present" relevance is applicable when exposure to the allergen eliciting positive results can be demonstrated, and this exposure can fully or partly explain the localization and the course of the current dermatitis that led the patient to seek a dermatological visit, and the resulting execution of patch tests. The dermatitis therefore dates back some weeks or even months.

Past Clinical Relevance. This refers to clinical events in the past, explainable by the allergen but not directly correlated to the current clinical problems. Among previous clinical events and the current situation there is therefore an interim period of some time.

The possible coexistence of *past* and *current clinical relevance* also needs to be taken into account. Between present and past relevance it is not always easy to make a clear distinction: in fact, the dermatologist is often faced with the same harmful contact repeated over time, even if discontinuously, that started in the past and is still present today.

Unknown Clinical Relevance. All the possible events that do not fit into the above three points can be summarized in this last point. The positive reaction to a patch test in this case may be a sign of manifestation of a latency due to a past sensitization to an allergen (mostly of ubiquitous type), without there having been any objective clinical signs (or perhaps the patient does not remember them because they were too long ago).

Other reasons for unknown relevance include:

1. Insufficient information provided by the patient, also perhaps due to the clinician's inability to ask the appropriate questions.

2. The problem of the substance being ubiquitous in the environment and so the significance of the contact not being clarified by the clinical history.
3. The patient may be sensitized but has never developed dermatitis because of lack of exposure to sufficient allergen quantities after the sensitization.
4. Contact occurred only with cross reacting substances that were used for completely different purposes.

The term of "unknown" relevance should in any case be used only with extreme caution and after having exhaustively excluded all the above-said points through proper clinical history taking and investigations.

The assessment of the clinical relevance of a positive patch test reaction is, as stated above, a complicated process with many pitfalls. The essential points for making as accurate an assessment as possible are reported in Table 23.15. In each case, depending on the results of the patch tests, the present and past clinical history need to be further probed, as well as any specific exposure in an occupational or non occupational setting. The various types of contact (direct, airborne, systemic, ectopic) must be carefully considered. An examination of the detailed lists available about the ubiquitousness of allergens, a visit to the work place and study of the environmental conditions, as well as questioning the producers about the chemical products used, can be measures offering practical aid.

A precise assessment will demand further tests (Table 23.16), that need to be resorted to in the circumstances listed below.

Positive Patch Test to Substances in Common Use Products. In cases of positive patch tests to a substance contained in a product (e.g. a cosmetic) in common use by the patient, can it be stated that the reaction is relevant only because the culprit hapten is present in the product in use? In fact, this cannot be stated with any certainty for two reasons. The first is that the allergen that resulted positive is contained in the incriminated product, but may be present in such low quantities that it cannot elicit a reaction and so induce the dermatitis in course (it should not be forgotten that in normal conditions of use patch tests are made to elicit a high level of skin stress). If in doubt, the use test or ROAT can be made: of 10 patients with positive reactions to patch tests with Kathon CG 100 ppm, only 5 responded to the ROAT with the incriminated product [117]. Otherwise scalar dilutions of the substances resulting positive can be made, to establish the minimal elicitation threshold and compare it with the quantity of substance contained in the incriminated product. In this way, the problem of stressing the patient with preventive norms that may then be found useless can be avoided. It is pointless to ban the use of cosmetics in nickel-sensitive patients because although it is true that these products contain nickel, they generally contain such low quantities (<0.5 ppm) as to be unable to elicit a positive reaction.

The second reason is that the substance that elicited the positive response is contained in the incriminated product, but may not be released because it may be in some way complexed or kelated to carriers, preventing its release. In this case, too, the use test with the product can resolve the doubt.

Chemical analyses of products must be made when the aim is to reveal any impurities not reported in the ingredients but that may result positive because they are present in the patch test standard series.

Evaluation of Patient's Own Products. Also in cases of positive reactions to products in the patient's own use, when correctly tested, if necessary chemical analysis of these or the use test should be made.

Evaluation of a Negative Patch Test Result. A negative patch test to a product does not necessarily exclude its current clinical relevance. If a specific product is strongly suspected to have contributed to the dermatitis, but gives negative patch test results, a use test must be performed. In fact, the dose required to elicit a positive patch test reaction is up to 28-fold greater than the dose needed at open application to elicit a reaction in 14 days [118].

A use test is therefore useful to establish the clinical relevance. However, it has some limits, being valid in particular for products destined for repeated use on the skin, such as creams and topical medicaments, or products that regularly come in contact with the skin, such as cutting fluids at the use concentration, for instance [1].

Further Recommendations. In cases of positive reactions to nickel, cobalt, chronium, and formaldehyde the spot test is recommended, to identify sources of exposure at the workplace or at home.

In cases of cross reactions, it should be remembered that the sensitization could be due to another, chemically similar substance, perhaps after air oxidation or metabolic activation. This possibility should be taken into account when the substance that caused the positive patch test is not present in the environment.

In cases of a doubtful reaction, further investigations need to be made. The patch tests concentration may have been too low and should be increased. A weak patch test reaction can also be attributable to cross-reactivity to another substance, that is actually the primary sensitizer.

Finally, if negative patch test results are obtained but there is a strong suspicion of true sensitization in course, the patch tests should be repeated, widening the range of test substances as far as possible and also reconsidering various 'individual factors' that could affect the response.

Final Diagnosis. In cases of a current clinical relevance in a sensitized subject, the diagnosis of allergic contact dermatitis is made. In cases of unknown relevance, the subject is clearly sensitized and so has a contact allergy, but the criteria for a diagnosis of allergic contact dermatitis are lacking. Nevertheless, since the subject is at risk, allergy must in any case be mentioned in the diagnosis and prevention norms should be suggested to the patient. In some cases exposure to an allergen may not fully explain the dermatitis; constitutional factors and exposure to irritants must therefore be considered.

Assessment of the Clinical Relevance. When is it necessary to make a specific assessment of the relevance of an allergic reaction? This should, of course, be done in all cases so as to be able to provide the patient with targeted prevention norms. Such an assessment is in any case mandatory in all cases involving a medico-legal judgment, change of work activity, pre-employment medical test.

23.10 Patch Testing in Children

Children, whether atopic or not, can be sensitized to various environmental substances, such as topical medicaments, cosmetic products, topical products used by their care-givers (dermatitis by proxy), or to any other chemicals that come in contact with the skin [17, 18, 119–122]. The contact allergens spectrum in children is similar to that in adults. Patch testing in children is considered to be safe, and so is recommended in cases of suspected allergic contact dermatitis or to exclude the disease.

The patch testing technique is the same as in adults. However, in children, and especially very young children, some technical problems need to be considered [123]. Because of the smaller test area on the back, it may be impossible to test the whole baseline series and so selection must be made of the allergens, that should include the products the child is actually exposed to, such as topical products, antiseptics, and toys (patient's own materials) with their potential ingredients, while contact allergens used for occupational settings can be omitted.

In cases of contact dermatitis following the use of temporary black henna tattoos, paraphenylenediamine at a concentration of less than 1% pet. for a shorter exposure time [64], or else open testing, to avoid strong patch test reactions, can be done [93].

Due to the greater mobility of younger children, a stronger adhesive tape should be used.

23.11 Patch Testing in Occupational Contact Dermatitis

In cases of work-related contact dermatitis, the dermatologist needs to have a certain experience of the various work activities, the respective substances the worker will be exposed to, and

the work cycles. In such cases, a medico-legal judgment is often required.

When taking the patient history, the specific work activity must be taken into account, and the specific environment where it is performed; analysis of the latter can be done in collaboration with the occupational healthcare staff, including an occupational hygiene specialist.

The products and materials the patient comes in contact with should be collected, and information on each of their ingredients acquired. Spot tests can be helpful to screen the environment for the presence of some allergens. For airborne allergens it is necessary to collect samples of air and dust for chemical analysis. Patch tests must also be made with materials at the work station, according to the norms reported for patients' own materials.

Assessment of the clinical relevance of the patch test results may be needed for medico-legal, prognostic and preventive purposes. Sometimes, the incriminated allergen can be present in both the occupational and a non occupational context, and it may be difficult to estimate the relative contribution of the two forms of exposure.

23.12 Patient Education

Patients should be properly informed about all clinical, etiological and environmental aspects, occupational or not, of their dermatitis. Sufficient time needs to be devoted to preventive measures, bearing in mind the obvious difficulties in managing the problem that patients may encounter. Information communicated orally must be supported by written information (prevention cards) to ensure that the patient gains the best understanding of their complex problem.

In addition, patients should be informed about possible concomitant causes that can complicate the dermatitis or cause it to become chronic: constitutional factors, personal hygiene, irritant contact at home or at work, and the possibility of cross reactions and secondary allergies.

Spot tests can be done by the patients themselves to identify metal objects containing nickel, for example, both at home and at work.

Another fundamental part of prevention is that Allergology Centers should arrange meetings with patients suffering from allergies, in order to reinforce the prophylactic criteria and to update their knowledge of practical allergological aspects.

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