



Patch testing: Uses, systems, risks/benefits, and its role in managing the patient with contact dermatitis

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Abstract Patch testing is the gold standard diagnostic tool for cell-mediated type IV hypersensitivity reactions like allergic contact dermatitis. Sensitized individuals have primed antigen-specific T lymphocytes that cause a reaction when antigens are applied to the skin owing to prior sensitization. Patch testing can be used in the adult and pediatric populations, but it is contraindicated in patients with a known history of severe allergic reactions to suspected allergens, generalized active dermatitis, or extensive eczema. Patch test systems can be a comprehensive panel (70–80 allergens), but they can also be targeted and limited to a more common allergen series (35 allergens). The decision for allergen selection should be based on an accurate patient history, physical examination, and availability of allergens. Measurement and interpretation of the test results requires training and experience, as well as consideration of relevance and clinical history. Patch testing is generally considered safe with just a few known complications: excited skin syndrome, active sensitization, and rarely anaphylaxis or other cutaneous complications. Appropriately pretesting patient education can help to mitigate some of these complications. Based on patch testing results, patients should be educated regarding proper allergen avoidance measures to resolve symptoms of allergic contact dermatitis.

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Allergic contact dermatitis and patch testing

Dermatitis can be classified into several types. These include, but are not limited to, allergic contact dermatitis (ACD), irritant contact dermatitis (ICD), atopic dermatitis (AD), nummular dermatitis, seborrheic dermatitis, and stasis dermatitis, to delineate a few presentations.^{1,2} Contact dermatitis (CD) may present with pruritus, erythema, vesicles, scaling, and lichenification.³ Differing in their pathogenesis, ICD comprise a much larger proportion of cases, accounting for approximately 80% of the patients, whereas ACD

may comprise 20% of the patients.^{3,4} ICD is defined as a localized, inflammatory reaction involving barrier dysfunction, whereas ACD represents a type IV hypersensitivity reaction as a result of contact sensitization to an allergen.^{3,5} ACD may be considered in patients with well-demarcated, pruritic, scaly eruptions that may be generalized or localized.³ ACD would be localized to the area of skin in contact with the allergen or disseminated as in systemic reactions. Additionally, attention to morphology is important when evaluating suspected ACD as contact allergens may be transferred from the hands to other parts of the body such as the face, particularly the eyelids.

The prevalence of ACD has increased, possibly due to increased exposure to sensitizers at younger ages as well as improved detection of ACD with patch testing.⁶ Com-

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mon sensitizers in North America include nickel, neomycin, cobalt, fragrances, balsam of Peru (*Myroxylon pereirae*), gold (positive patch tests may be common, but are not usually relevant), formaldehyde, lanolin/wood alcohols, and chromate.^{4,6}

Food handlers are the most prone to ICD, whereas ACD is seen more in cosmetologists, health care professionals, and construction workers.³ Morbidity associated with ACD has also been shown to have significant impact on quality of life.^{1,2} In a 2013 report, it was listed as the fifth most prevalent skin disease in the United States and had a total population medical cost of \$1.529 billion, eclipsing that of melanoma.¹

Patch testing plays a significant role in determining the offending agent, since its initiation by Josef Jadassohn (1863-1936) in 1895 and especially by Marion B. Sulzberger (1895-1983), who introduced it to American dermatologists in the 1930s.² Accurate diagnosis is essential to avoid the harmful effects of ACD. Patch testing has been the gold standard for diagnosis of ACD since its introduction (see above). It is also important to take a detailed history and to review home and occupational sources of contact allergens in addition to the patient's personal product profile.³ Accordingly, avoidance of the suspected allergens should be directed. Medical history alone, although important, is inadequate to diagnose ACD in most cases. Although avoidance may improve the dermatitis, identification of the specific allergen(s) by patch tests has shown to increase the patient's options, adherence, and improve outcomes.³ Patch testing has internationally defined guidelines, which are continuously reviewed and updated. Measurement and interpretation of the test results requires training and experience, as well as consideration of relevance and clinical history. Incorrect diagnosis or a delay in diagnosis can result in many patients continuing to suffer or using ineffective and even harmful therapies.¹

Patch testing is used for diagnosis of cell-mediated type IV hypersensitivity reactions like ACD because sensitized individuals have primed antigen-specific T lymphocytes that produce the reaction when antigens are applied to the skin.^{1,2} Histologic study of biopsy of specimens to determine whether contact dermatitis is irritant or allergic is often inconclusive because the two conditions may be indistinguishable, particularly in their late or chronic phases. There are no histologic features that have been shown to consistently support or differentiate one from the other.⁷ Patch tests are instead used to produce contact reaction by applying allergens in test doses to intact skin of suspected patients.

Uses of patch testing

Patch testing is an essential tool in making the diagnosis of ACD in patients with dermatitis. The indications, contraindications, populations who can be patch tested, and precautions

are outlined below to ensure appropriate use of the test and patient safety.

Indications

Patch testing is indicated for any patient who is suspected to have contact allergy, regardless of the site.⁴ This can include regional dermatitis including hand dermatitis, localized leg and foot dermatitis, or involvement of the face and eyelids.⁸⁻¹⁰ Patch testing is also indicated for worsening of formerly stable dermatitis, resistant dermatitis, systemic contact dermatitis, photo or airborne distribution, and patients whose skin conditions may be exacerbated by CD (such as AD, seborrheic dermatitis, stasis, nummular dermatitis, psoriasis, and dyshidrosis).^{8,9,11,12} Patients with high-risk occupations for ACD, such as health care workers, dental assistants, cosmetologists, nail salon workers, machinists, and those in the rubber and plastic industry, should also be considered for patch testing.

Patients with eczematous dermatitis benefit most from patch testing.^{3,11} It is important to note that occupational hand dermatitis is one of the most common occupational diseases and is seen in a wide range of industries.² A positive patch test to at least one allergen has been reported in 65% of these patients.²

Use in different populations

ACD is just as common in children as it is in adults.¹³ Recent literature has supported the safety of patch testing in children and has rendered adjustments of chemical concentrations for the pediatric population unnecessary.^{6,14} Due to the patterns of exposure and physical size of a child's back, however, patch test screening panels to evaluate ACD in children may be different than that of adults.

Patch testing in patients with a history of AD has been another topic of debate. There has been recent agreement in the literature, however, that patch testing can still be considered in these individuals, including children with treatment-resistant AD.^{5,6} There are consensus studies and small series on patch testing patients, including AD patients, who are receiving immunosuppressive therapy.^{5,9,15-17} Postponing patch testing might be considered until the patient can be tapered off the medication; otherwise, testing can proceed with the proper precautions for personal products, such as rinse-off products that are susceptible to irritant reactions, and for other irritant reactions to metals, fragrances, formaldehyde, and lanolin.⁵

Pharmacologic therapy during patch testing

In patients with severe, widespread dermatitis, it may be necessary to use systemic therapies for symptom control.

These systemic agents may interfere with the elicitation of delayed-type hypersensitivity, and thus interfere with patch testing (causing false negative results); hence, attention to certain principals must be considered. Systemic corticosteroids should be avoided at least 1 week before patch testing.^{3,12} If prednisone must be used, <10 mg/d is acceptable, whereas a greater dose is typically contraindicated.^{3,12} Variable outcomes have been described for dupilumab on patch testing results, and the recommendation is to patch test patients before initiating dupilumab.⁹ Antihistamines are permitted and may be continued before and during patch testing because they have no effect on the delayed hypersensitivity.^{9,12}

Patients receiving systemic immunosuppressants can still produce a positive patch test, but the effects are still being studied.¹⁶ When impractical to discontinue immunosuppressant medication, the lowest dose of therapy should be used, and a possible retest should be performed after the medication has been discontinued.¹⁷ In these instances, false negative results may occur (especially to chemicals that elicit weak patch test reactions), but positive results have still been reported.^{14,18}

Uses of patch testing beyond the evaluation of CD

The use of patch testing in diagnosis of cutaneous drug eruptions is also a current area of study, although the evidence is limited. More than one diagnostic test may be required to confirm suspected drug allergies and adverse drug reactions. Drug provocation tests, or medication rechallenge, are considered the gold standard but can involve medical and legal risks.^{19,20} More serious reactions may even disallow the use of rechallenge, leaving patch testing as a first choice in suspected type IV allergic reactions to medications.²¹ Patch testing is a useful confirmatory test in many instances of T-cell mediated cutaneous adverse drug reactions (morbilliform drug eruptions, erythema multiforme, Toxic Epidermal Necrolysis (TEN), Acute Generalized Exanthematous Pustulosis (AGEP), and Drug-Related Eosinophilia and Systemic Symptoms (DRESS)) induced by certain classes of drugs (see below).

Patch testing may have a role in diagnosing common drug allergies. It can be used to exclude CD when patch testing with active drugs. Positive patch test results of many drugs have been reported, most commonly with anticonvulsants, antibiotics, corticosteroids, calcium channel blockers, and benzodiazepines.^{19,22} With regard to antibiotics, patch testing has shown to be more appropriate for non-immediate allergy to beta-lactams (mainly aminopenicillins), in addition to clindamycin, pristinamycin, and quinolones.²¹

Additionally, patch testing can be used to evaluate eruptions in patients who have metal-containing implanted devices, such as hip or knee implants, in whom there is concern that there may be an allergy to the metal implants. Ortho-

pedic, gynecologic, endovascular, neurosurgical, and dental implants all contain metal and can cause dermatitis.¹⁵ There is much controversy over the utility and validity of patch testing to diagnose adverse reactions to metal implants. Positive testing before the implant and after the implant may not be conclusive. Nonetheless, a patch test is the most appropriate tool to use for these patients.

Contraindications

Patch testing is contraindicated in patients with a known history of severe allergic reactions to suspected allergens, generalized active dermatitis, or extensive eczema, especially if present on the back, which is typically the site where patch tests are applied.^{3,4,10} Such patients are at risk for developing angry back syndrome, in which multiple allergens appear to be reactive, but upon retesting, these results are not reproducible. The underlying dermatitis and symptoms need to be controlled before consideration of patch testing. The procedure should also be postponed if dermatitis is present on the upper part of the back or other sites, where the patch test may be applied. Patients should also avoid recent ultraviolet (UV) exposure to the test area from artificial and natural sources.⁹ In heavily tanned patients or those who have received a suntan, there should be a minimum period of 2 to 4 weeks before patch testing.^{3,9}

It is advised that patch testing be avoided in women who are pregnant or breastfeeding because immunologic changes that occur during pregnancy can interfere with the results.^{3,11,14} Additionally, there is little information about systemic absorption of the patch test materials and its effects on the developing fetus.

Patch test systems and allergen selection

Different patch tests are available based on allergen count and can be classified as targeted, limited, standard, and comprehensive.¹

Standard series and comprehensive patch tests

The various series of available patch tests are shown in Table 1.⁴ There are 33 series available, which primarily exist to address specific occupation exposures, personal care products, and other series for special circumstances.

Standard screening patch tests include the American Contact Dermatitis Society (ACDS) Core Series (80 allergens) and the North American Contact Dermatitis Group (NACDG) Series (70 allergens). These contain the most common sensitizers that cause ACD and are updated regularly. Other baseline or standard series exist, such as the European Baseline Series, and are recommended as the first battery for

Table 1 Patch test series

Series number	Series name
B-1000	Bakery Series
C-1000	Cosmetic Series
CAD-1000	Cutaneous Adverse Drug Reaction Series
CS-1000	Corticosteroid Series
DMP-1000	Dental Materials Patients
DMS-1000	Dental Materials Staff
DS-1000	Dental Screening
E-1000	Epoxy Series
EP-1000	European Photopatch Baseline Series
EPE-1000	European Photopatch Extended Series
F-1000	Fragrance Series
H-1000	Hairdressing Series
I-1000	Isocyanate Series
IS-1000	International Standard Series
LU-1000	Leg Ulcer Series
MA-1000	(Meth) Acrylate Series Adhesives, Dental & Other
ME-1000	Medicament Series
MET-1000	Metal Series
MN-1000	(Meth) Acrylate Series (Nails-Artificial)
MP-1000	(Meth) Acrylate Series Printing
NA-1000	North American Baseline Series
NAC-80	North American 80 Comprehensive Series
NAE-65	North American 65 Extended Series
NAP-1000	North American Photopatch Series
O-1000	Oil & Cooling Fluid Series
PG-1000	Plastics & Glues Series
PL-1000	Plant Series
R-1000	Rubber Additives Series
S-1000	European Baseline Series
SH-1000	Shoe Series
SU-1000	Sunscreen Series
TF-1000	Textile Colors & Finish
V-1000	Various Allergens

patients receiving patch testing.^{2,9} These series have been formulated by testing large numbers of patients, updating the series consistently, and optimizing the results to contain the fewest false negative and false positive results possible for a given allergen.² Certain institutions such as the Mayo Clinic have also compared patch test results of their standard series with those of the NACDG, which have yielded similar results with few modifications.²³

In a comprehensive patch test, patients are tested to a large number of allergens, typically between 65 and 200.¹ The standard series and the comprehensive series are more extensive options that typically require greater time (owing to manual loading of allergens into wells) as well as cost.⁷

Targeted and limited patch tests

Targeted patch testing is usually appropriate, when a patient's history involves only one or very few allergens.¹

An example of a screening series is the thin layer rapid use epicutaneous (TRUE) test, which is Food and Drug Administration approved and indicates those who are 6 years of age and older.² It is a commercially available test commonly used for patch testing and includes 35 allergens and one control. It is considered to be easier to apply, more convenient, and less labor intensive, and it has increased the number of patch tests performed since it was introduced in 1995.^{8,9,12}

Although the TRUE test may be more convenient and less costly, it has a lower sensitivity than larger baseline series such as the NACDG series.^{2,7,9} This test has been reported to have a conservative hypothetical allergen detection rate of 66% at most, and this calculation is based on the 78% of patients who had clinically relevant results in the NACDG series.^{1,2} Reportedly, up to 50% of allergens causing occupational dermatitis can be or have been missed using the TRUE test.^{2,7} Because some common allergens are missing from this series, supplemental testing should be implemented as well if possible. Additionally, new contact allergens are described in the literature every year that could be missed by limited patch testing. ACDS and NACDG have published a core group of allergens similar to the TRUE test with trays for expanded testing, and many international trays are available as well.¹⁶

More extensive and comprehensive patch tests have a higher probability for diagnosis of specific allergies and cures.¹

Modifications

It should be noted that a strip patch test also exists, which is a form of patch testing used for allergens with poor percutaneous penetration. It involves a modification whereby the penetration is improved by affixation and removal of adhesive tape strips to the skin before applying the allergens.²⁴ Literature on its use is limited, but studies have suggested it is a valid and reliable tool for diagnosing ACD sensitization, particularly if false negative reactions are suspected in a conventional patch test.^{24,25}

A patch test series may be modified for use in children as well. Many abridged series have become common in the pediatric population.⁶ The technique remains the same, but factors such as a reduced test area on the back and greater mobility of children have led to smaller test series and use of stronger adhesive tape.¹⁴ When testing a smaller number of substances than the standard series due to reduced space, certain allergens must be omitted. These can include those found in more occupational settings, whereas those that children may be more exposed to are selectively included.¹⁴

Selection of allergens

The selection of allergens for patch testing is dependent on a proper patient history, physical exam, and availability

of the allergens themselves. Most patients benefit by starting with standard screening patch tests such as the NACDG Standard Series, European Baseline Series, or ACDS Core Allergen Series.² In children, especially those less than 6 years old, targeted patch testing may be more helpful.⁵

Nickel is one of the most common allergens tested, with a high rate of sensitivity due to widespread practices of ear and body piercings.⁷ Nickel has been associated with elicitation of follicular contact dermatitis.²⁶ Many other patch tested metals, such as chromium, cobalt, copper, and fluoride, have been associated with follicular contact dermatitis as well.²⁶

Fragrance components are also commonly patch tested and typically tested via fragrance mix I, which can detect most perfume allergies.^{3,7} Fragrance mix II may be added to increase the sensitivity. Balsam of Peru (*M pereira*) is also a naturally occurring, commonly tested fragrance, and is the second most common allergen identified by the NACDG.^{3,7}

Paraphenylenediamine (PPD) is a commonly tested allergen as it is a cause of ACD to black and brown hair dyes, tattoos, and henna.³ In children, PPD should be excluded unless allergy to it is highly suspected because there is risk of active sensitization.⁵

Preservatives are also used in patch tests, with methylisothiazolinone and methylchloroisothiazolinone as common causes of CD.³ Typically, the two have been patch tested together as a mixture, but recently it has been recommended to patch test the mixture as well as methylisothiazolinone alone.⁸ Formaldehyde is a widely used preservative and has been reported to be relevant in 89% of patients allergic to it.⁷

Although gold has concerns regarding its relevance and persistent positive reactions, it is still important to consider patch testing for it, particularly in eyelid dermatitis and gold dental restorations.²

There are many other commonly tested allergens, and selection may vary. It is important to note that of the most common allergens in the NACDG panel, some are not included in the TRUE test and can be commonly missed. These include bacitracin, methylidibromoglutaronitrile, 2-bromo-2-nitropropane-1,3-diol, cinnamic aldehyde, propylene glycol, dimethylol dimethyl hydantoin, iodopropynyl butyl carbamate, ethylene urea melamine formaldehyde, and disperse blue 106 dye.²⁷

Importantly, unknown chemicals should never be tested without reviewing the list of ingredients. For patient's personal products, testing the individual components separately should be performed if feasible.¹⁴

Risks and benefits

The benefit of patch testing is that it allows for the proper diagnosis and identification of ACD, which can then be managed by avoiding the responsible allergens. It has shown to

result in a greater reduction in the disease severity index from pre-diagnosis to post-diagnosis than in cases that were managed without patch testing.¹ Use of patch testing has shown to have a range of indications and has improved the quality of life of patients with dermatitis.^{1,28} It is also a cost-effective procedure that can reduce the economic impact of this chronic skin disease.¹ Although patch testing is generally safe with rare complications, there are some risks to be aware of.

Excited skin syndrome (angry back)

Excited skin syndrome occurs when two or more strong positive reactions cause a series of multiple false positive patch test reactions.^{2,9} It is a generalized, erythematous reaction on the back that is hypothesized to occur for a few reasons. It may occur in patients who have current dermatitis at the test site and can also occur in some individuals who have active dermatitis in areas distant from the test site.^{9,11} Some patients with dermatitis at these distant sites or those who produce strong patch test reactions in general may develop hyperreactivity of the skin, which can also contribute to the "angry back."¹¹ Excited skin syndrome may also occur if substances that are cosensitizers have similar chemical affinities or tend to have cross reactions are placed in close proximity to each other.^{2,9,11} This may induce the false positive results seen and is why similar test substances should be split up among patch test panels. These patients should be retested with the positive allergens separately.⁹ Figure 1 illustrates an example of excited skin syndrome.

Active sensitization

Patch testing can rarely involve risk of active sensitization, which will present as a late reaction 10 to 20 days after the patch test. Allergens reported to carry some risk of active sensitization include PPD, p-tert-butylcatechol, high concentrations of acrylates, chloroacetamide, primula extracts, isothiazolinones, and beryllium.^{5,7,9,14,29} The risk of active sensitization is very low and to confirm its diagnosis, patients should return for repeat patch testing.²⁹

Anaphylaxis

Very rarely, certain substances may cause anaphylactic reactions when patch tested, particularly in patients with strong immediate-type hypersensitivity.¹⁴ Bacitracin, neomycin, and patients with contact urticaria have been reported to carry this risk.^{6,7,9}



Fig. 1 Angry back syndrome. This patient was being evaluated for hand dermatitis with a history of atopic dermatitis. This is the 48-hour reading, 30 minutes after removing the patches with multiple positive patch tests, rim reactions at the edges of the chambers, and diffuse erythema over multiple patch test sites. This adverse reaction to patch testing was not life-threatening. The results of the patch testing were considered uninterpretable, and repeat patch testing was necessary.



Fig. 2 Reactivation of contact dermatitis (“generalized Id reaction”). This man was being patch tested to evaluate a patchy dermatitis over his trunk and extremities, and his skin was clear at the time of patch testing. At the 96-hour reading, he exhibited a 2+ reaction to fragrance mix and 2+ reaction to balsam of Peru, and he experienced a rapid recurrence of his dermatitis during the patch testing. This complication was not life-threatening but required the administration of systemic corticosteroids. After 3 months of allergen avoidance, his dermatitis did not recur, indicating the fragrance and balsam of Peru strong positive patch tests were relevant to his dermatitis.

Other cutaneous complications

There are many other low-risk complications that can occur during patch testing:

- 1 Irritant dermatitis reactions under the adhesive portion of the patches or irritation from the patch tested material itself (ie, benzalkonium chloride, cobalt, or manganese).^{5,9}
- 2 Sarcoid reactions, more commonly described with metals such as palladium.⁹
- 3 Bacterial and viral infections with plant substances.^{9,11}
- 4 Pressure effect, an imprint caused by chamber pressure when testing a solid substance.⁹
- 5 Persistence of a positive reaction, more commonly seen with gold and palladium tetrachloride.^{9,14} This can sometimes last up to several weeks.⁹
- 6 Koebner phenomenon in patients with active psoriasis and lichen planus,⁹ in patients with psoriasis and sus-

pected ACD, or in patients with suspected lichenoid ACD.

- 7 Depigmentation or hyperpigmentation, especially after sun exposure, and in patients with skin of color who experience strong (2-3+) patch test reactions (see #11 below).^{11,12,14}
- 8 Flare of previous or existing dermatitis as a result of percutaneous absorption of the allergen or a strong positive reaction.^{12,14} An example of this is shown in [Figure 2](#).
- 9 Granulomas associated with beryllium, zirconium, and rarely gold salts.¹²
- 10 Necrosis, scars, and keloids are extremely rare but can occur when testing unknown toxic substances.^{9,11,12}
- 11 Postinflammatory hyperpigmentation after strong patch test reactions, particularly in patients with skin of color, as seen in [Figure 3](#).



Fig. 3 Extreme patch test reaction (blistering, 3+) to para-phenylenediamine hair dye (patch #4), with cross-elicitation to disperse orange (blistering, 3+) (patch #25) at 48-hour patch test reading. The patient experienced severe itching, was uncomfortable, and required systemic corticosteroids (intramuscular triamcinolone acetate 40 mg) and potent topical corticosteroids to alleviate her itching at the final read at 96 hours. Although this is not a life-threatening complication, the patient was uncomfortable, and these two patch test sites did heal with postinflammatory hyperpigmentation.

Patient safety and instruction

It is important to communicate the objectives, schedule, and time required for patch testing to the patient. The test typically requires three office visits over the course of a week, with the final visit involving thorough review of results and clinical relevance.¹ Patients should also be asked to bring with them personal care products or other substances that might be causing or worsening their symptoms.⁶ Before patch testing, the underlying dermatitis, symptoms, or any flares must be controlled, and all indications and contraindications should be properly considered. Patients should be informed of what not to do before and during the patch test period. They should not wet their backs or predispose their backs to sweating throughout the entire patch test period.^{2,11} They should not expose themselves to UV radiation for 2 to 3 weeks before testing as well as during the entire duration of the patch test.^{2,7,11} Patients should also be educated about symptoms such as itching or possible late reactions.^{9,14} Pro-

viding written information about the procedure may be helpful.

Allergen placement is typically on the upper part of the back, because it provides sufficient space, but the outer surface of arms and thighs may be used if more space is needed or if the upper part of the back is not appropriate.² The midline and scapula should be avoided, and patch test units should not be placed under a brassiere shoulder band, as this can cause dislocation of the units.⁴

Factors such as hair, oily skin, perspiration, humidity, and heat can affect tape adherence. The area should ideally be free of hair, oiliness, or any moisturizers before patch testing.³ If needed, hair can be removed or trimmed, but the possible complication of folliculitis should be considered.^{3,4,8,9} For oily skin, the skin can be mildly and gently cleansed with ethanol or other solvents to improve adhesion.^{4,11} Afterwards, the sites of patch testing can be marked with an appropriate marker to indicate the test sites.⁹

Proper storage of all standardized allergens is very important before patch testing. Most allergens should be stored at a temperature between 36°F (2°C) and 46°F (8°C) and protected from light.¹¹ This may differ for more unstable allergens, such as isocyanates and acrylates, which should be stored in the freezer at -0.4°F (-18°C). These are general guidelines, and special characteristics of patch test allergens should be considered as well.

All allergens being tested in an aqueous vehicle should be prepared close to the time of placement or at the time they are placed.^{2,3} Early preparation of allergens could lead to false negative results. Some allergens on petrolatum base, however, can be prepared 24 to 48 hours before application.³ Petrolatum is the most used vehicle and has many benefits, but different allergens may require other suitable vehicles such as water, solvents, and hydrophilic gel.¹¹ It is very important to ensure that unknown substances never be tested. Testing without a review of ingredients and safety data sheets could lead to cutaneous or systemic harm to the patient.^{2,12}

There are certain materials the clinician must have for patch testing. For the allergen to remain in direct contact with the skin for the appropriate length of time, a patch test unit composed of sets of chambers is needed.⁴ Hypoallergenic tape is needed, to which the chambers are applied. Other supplies include a refrigerator for storage of allergens, markers, possibly anatomic locator diagrams and digital photography for identifying location of patches, fluorescent markers to outline the units, and a Wood lamp to uncover invisible markings.⁸

Procedure

The procedure involves placing 20 to 25 μ L of commercially available hapten in the patch test chambers, which are usually supplied in strips of 10.⁴ Petrolatum-based allergens can be placed directly in the chamber whereas liquid-based allergens are first placed on filter paper inside of the cham-



Fig. 4 Placement of patch tests. Day 0, placement of NACDG 80 patch test series. The medical assistant dispensed the chemicals into the chambers, affixed them to the patient's back, and labeled the 80 allergens. Two days later, the patches will be removed and the results will be scored. On the final reading (day 4 or 7), the positive scores will be recorded, the patient will be given an allergen avoidance handout indicating the chemical name(s) of their allergens and where they are found, as well as a safe shopping list for personal care products (Contact Allergen Management Program database, see text). NACDG, North American Contact Dermatitis Group.

ber.⁸ The use of a micropipette is recommended for the latter.¹⁴ It is important to ensure proper labeling of the tape side versus the chamber side as they mirror each other.¹² When the patch test unit is applied, it should be held by its protective cover and the clinician should place his or her palm on the tape for 5 seconds to ensure proper adhesion.⁴ After all the patch tests are applied, the top-liners should be gently removed, the chambers should be marked, and the location sites should be registered in a patch testing record form.⁴

Day 0 is considered the day of patch test application, day 2 is removal and optional reading, days 3 or 4 are when the main reading is done, and day 7 is when a delayed response reading should be performed for allergens that may show delayed reactions.^{2,4} Figure 4 shows an example of patch test placement on day 0. A preliminary reading can be taken on day 2 to assess any difficulties, errors, or poor adherence. This read should be done at least 15 to 30 minutes after removal, but it is important to note that this read is only preliminary and final readings should still be done during days 3

Table 2 Patch test reading criteria

Grade	Presentation	Assessment
—	No reaction	Negative
±	Faint, macular, homogenous erythema	Doubtful
+	Erythema, induration, infiltration, possible plaques	Weak positive
++	Erythema, induration, infiltration, papules, possible vesicles	Strong positive
+++	Intense erythema, induration, infiltration, coalescing vesicles, possible bullous or ulcerative reaction	Extreme positive
IR	Mixed morphologies	Irritant

to 7.² Reportedly, additional readings after day 7 are considered most useful for identifying reactions to neomycin; certain metals such as gold, cobalt, beryllium, and palladium; or to specific preservatives such as dodecyl gallate and propolis.^{2,3,9,29}

There are different subtypes of tests that can be performed as it pertains to the application of allergens. Closed patch testing is the most common and involves application of allergens under occlusion to the skin for 2 days.^{8,9} An open patch test is for haptens that can potentially irritate the skin such as paints, oils, cleansing agents, and glues.⁹ This technique involves keeping the area open, gently removing the materials after 30 minutes, and performing the readings in a delayed manner as would be done for a closed patch test.⁹ A semi-open test is indicated for certain irritant products such as pharmaceutical products, cosmetics, and other patient-supplied products.⁹ In this test, a smaller amount of the product is applied on the skin. After it completely dries, it is evaluated for contact urticaria and then covered with tape.¹⁴ Readings are made similarly to closed patch testing. Photopatch testing is indicated for photoallergic contact dermatitis, dermatitis on photo-exposed areas, or photosensitivity resulting from systemic drug use.¹¹ In this test, a duplicate set of allergens is applied on two sites of the back and UVA radiation is used. After 2 days of occlusion, one set is irradiated with 5 to 15 J/cm².^{11,14} Readings should be performed before irradiation, immediately after, and again at least 2 days later.¹⁴ The reader is referred to the references for detailed information related to photopatch testing.^{11,14}

Reading and interpreting patch test results

There remains a lack of complete agreement on grading patch test readings, but derivations of the criteria from the International Contact Dermatitis Research Group are generally followed. These are summarized in Table 2.^{2,4,7} Visual examples of the specific gradings can be seen in Figure 5. For

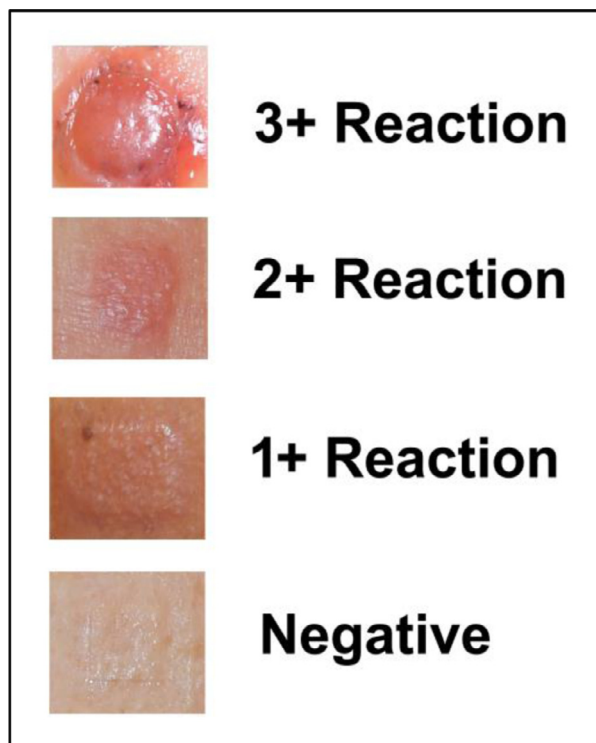


Fig. 5 Negative and positive reaction gradings.

photopatch testing, grading follows the same rules of patch test readings, and the reactions of the irradiated and nonirradiated sites are compared as well. A positive result occurs when there is no reaction at the nonirradiated site and a positive reaction at the irradiated site.¹⁴ If both sites have positive reactions, this indicates contact allergy.¹⁴ It should be noted that although immunosuppressants are not contraindicated in patch testing, the lowest dose should be used and grades of “++” or “+++” are the most reliable.¹⁵ It should also be noted that in these cases, weak reactions could represent stronger reactions that were suppressed.

For atopic dermatitis patients, irritant reactions are common and may be incorrectly graded as true positives.⁵ Irritant and true positives may also be more challenging to distinguish in these patients, and positive tests might also be weaker in patients with more severe atopic dermatitis.⁵ As it pertains to patch testing at the time of a flare, there are limited data on how long after a flare patch testing should be performed.

It is important to also consider possible sources of false negative and false positive results. False negative results can occur owing to failure to test the proper antigen, low concentration, inactive allergen, poor penetration of allergen, poor technique, lack of delayed reading, disregard of proper contraindications and prohibitions, a compound allergy, or failure to test for photo allergy.^{2,12} False positive results can occur owing to an irritating vehicle, reaction to the adhesive, pressure from solid materials or underwear, contamination

of test preparation, improper dilution of antigen in vehicle, excited skin syndrome, proximal cross reaction or cosensitization, and current or recent dermatosis at or even far from the test site.¹ Positive results in the presence of tight clothing, shoes, or bandages should also be considered as false positive owing to possible retention of allergens.³⁰ If false negative or false positive results are suspected, retesting should take place in at least 30 days.¹

It is important to be aware of the edge effect, especially as it pertains to patch testing with corticosteroids. Patch testing high concentrations of corticosteroids may lead to a negative result at first, or may present with the edge effect. This is described as a positive reaction outside the border of the patch test site with a negative reaction on the inside and is graded as a negative result.³ This result, however, may be positive on day 6 or 7 as a late reaction.³

A positive patch test result indicates that sensitization to the tested allergen has occurred, but it does not equate to a diagnosis of ACD.² Diagnosis of ACD can be made upon presence of dermatitis that can be explained by characteristics such as exposure and type of allergen. Information from the history, exposures, and physical exam must be combined with the results to determine if the positive reactions are clinically relevant. Relevance is definite when the patch test result with the suspected allergen is positive, when the dermatitis corresponds with the site of contact, and if the patient improves with allergen avoidance or if the allergy recurs with rechallenge.³ Probable relevance is if the allergen is present as an ingredient or component of the contactant and the presentation is associated with the exposure.^{2,3} Possible relevance is if the patient has had exposure to materials that contain the allergen and past relevance is when the result is positive, but the exposure occurred in the past.^{2,3,8}

To help confirm the clinical relevance of exposure to an allergen identified via patch testing, particularly a doubtful positive result, the repeat open application test (ROAT) may be useful. In this test, patients are typically asked to apply 0.1 mL of the product in question to a designated area (usually the upper arm) twice daily for 2 to 4 weeks or until an eczematous reaction occurs.^{5,9} It may also be helpful to include a control on the contralateral arm.¹⁴ Some literature states that ROAT should be done at three different sites because of variable reactivity on distinct areas of the skin.⁸ An appropriate application of ROAT may be when a patient has reacted to a cosmetic product without identification of a relevant allergen.⁵

Regardless of the classifications of relevance or the use of ROAT, true clinical relevance can only be determined after some months of proper allergen avoidance and subsequent clearance of dermatitis.

Patient management and considerations

Proper patient education and instructions on allergen avoidance is essential after patch testing. Adequate time

should be spent discussing a specific management plan for patch test positive patients. This involves reviewing the ingredient lists of the patient's personal care products and workplace exposures. Written information or handouts should also be provided and include the allergen name(s), synonyms, sources of exposure, potential cross reactions, strategies of avoidance, and list of safe alternative products.^{1,3,7,12}

To assist with identification of safe alternative products, tools such as the Contact Allergen Management Program and SkinSAFE can be used by the provider supervising the patch testing.^{2,12} The provider enters the allergens noted on patch testing during the final reading. Then, with the guidance of the patient, categories of personal care products are selected that exclude the troublesome allergens. This is called a "Safe Shopping List." This list is used to guide the patient in using only personal care products that exclude their allergens. After 3 months of allergen avoidance, the patients return for their evaluation to determine whether allergen avoidance resulted in improvement, complete resolution, or no change in the patient's dermatitis. This is how relevance of a positive patch test is determined. The handouts are available in English and Spanish and can also generate a list of products devoid of the allergen(s) and cross-reacting substances.

Bathing and handwashing habits may also be discussed, and patients should be advised to use gentle skin care products and appropriate moisturization.² Additionally, adjunct medical treatment can be prescribed. Topical emollients, anti-itch agents, and corticosteroids are some examples.^{2,3} Topical calcineurin inhibitors are not Food and Drug Administration indicated for treatment of ACD but can be used as an alternative to corticosteroids.³

The patient's employment should also be taken into consideration. When applicable and safe, patients should be advised to wear dry, intact gloves for wet work, along with any other appropriate protective equipment and skin preparations.³ A letter to the patient's employer may also be written to advocate for the patient to avoid certain exposures at work.¹⁰

A barrier to the effective treatment can be patient recall. Some studies have reported that patients do not properly remember their results or the information they received a few months after the final visit.^{14,31} Although avoidance is key in patient management, it is crucial the patients remember the instructions and education. Recall has generally been shown to decrease with increasing age and increasing time since patch testing.^{14,31} New retention strategies such as apps are being considered but may not be helpful to older patient populations.³¹ It may be useful to schedule a followup appointment to repeat or review the information with the patient a few months after the patch test period.¹⁴ There is limited data on factors that may impact patient recall and adherence, and this could be an area of future study.

Essential references

For the most up-to-date and comprehensive information on patch testing and contact dermatitis, clinicians should reference:

- 1 Fowler and Zirwas³²
- 2 Uter et al.³³
- 3 Cruz³⁴

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