

Contact Dermatitis Practice Gaps and Challenges



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KEYWORDS

• Allergic contact dermatitis • Patch testing • Allergens • Screening allergen series

KEY POINTS

- Patch testing remains the criterion standard for diagnosing allergic contact dermatitis.
- Assessing patients for allergic contact dermatitis requires a detailed exposure history, expanded patch testing, 2 patch test readings, and thorough patient education.
- New chemicals are continually being added to the consumer's environment, and as such, physicians must be aware of the possibility of new allergens and test appropriately.
- Patch test screening series need to be updated to identify new allergens that are introduced into the consumer environment.

Patch testing has been the criterion standard for diagnosing allergic contact dermatitis (ACD) since the 1800s. The procedure itself has not changed significantly since it was first introduced. Allergens are placed on the upper back, left in place for 48 hours, removed, read, and reread 72 hours to 1 week later. Although the procedure itself might seem straightforward, patch testing performs best in the hands of those who are most familiar with the process and can maximize its usefulness. The actual application of the testing materials is only part of the procedure; allergen selection, interpretation, and the education of allergen avoidance are all significant components of the patch test procedure and are paramount to the successful management of the patient.

Practice gaps are unfortunately evident in the clinical practice of evaluating the patient suspected of ACD. Some of these practice gaps include the selection of allergens (which is in part dependent on allergen availability), how the testing procedure is performed, and what information is provided to the patient on completion of the test (**Box 1**). In addition, new chemicals are continuously being introduced into the marketplace and workplace, resulting in ongoing consumer exposure of potential new allergens presenting yet

Box 1

Patch testing practice gaps

Allergen selection
Patch test procedure
Patient education
Evolution of allergens

another set of challenges. A more recent issue has become the concern over potentially allergenic materials in metal implantable devices and how best to manage these situations. Appropriately evaluating these patients and providing useful information to the patient and referring surgeons is a daunting task.

The assessment of a patient suspected of ACD begins with a detailed and thorough patient history. The information obtained after this in-depth inquiry leads to allergen selection. Allergen selection presents a practice gap. Dermatologists across the country test to many different baseline screening series as well as to other expanded specialty series (**Box 2**). The decision of which screening series to use can be dependent on several factors, including allergen availability,

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Box 2**Allergen screening series**

ACDS core allergen series

European baseline series

International baseline series

North American series

TRUE test

Specialty or supplemental series ie, flower, shoe etc

cost, and patient history. Studies have shown that the introduction of the US Food and Drug Administration (FDA) -approved preimpregnated allergen system, the thin-layer rapid use epicutaneous test (TRUE) test, has increased the use of patch testing among dermatologists, presumably due to increased ease of use.¹ The number of allergens in the FDA-approved testing series has increased over the years and now has 35 allergens and one control. Although a very good starting point, it can still miss up to 26.7% of allergens because of the limited number of allergens tested.² Even expanded series can miss relevant allergens, underscoring the need for a detailed and thorough history of exposures at home and in the workplace, including any potential consort exposures because this history may point to the need for a specialty tray of allergens (ie, dental tray, nail tray).² The continual introduction of new chemicals requires that the dermatologist remain vigilant and aware of new potential allergens in the patient's environment and test when appropriate. Not all dermatologists can maintain these expanded series. The practice gap of breadth and depth of allergen testing can be overcome through the understanding that negative testing to 35 allergens does not rule out ACD as a diagnosis and referral to centers with expertise in patch testing, and access to more allergens should be considered.

The influx of novel chemicals in the consumer environment results in the introduction of potential new allergens. This introduction of potential new allergens can lead to another potential practice gap. Not only must we test these new allergens in order to detect them, but also we must first be able to identify these allergens. One recent example was the successful identification of dimethyl fumarate as an allergen in multiple cases of "sofa dermatitis."³ Several astute dermatologists were able to piece together the puzzle and identify the allergen as dimethyl fumarate, an antifungal, present in small sachets in the furniture.³ The identification of this allergen closed the knowledge gap that existed and led to a change

in usage of this allergen, and as a result, this problem has largely been eliminated.

Another example of industry changes that led to the emergence of new allergens is seen in product preservation. In an ongoing effort to find the best preservative systems available (low cost, low toxicity, long shelf-life, and broad biocidal activity), industries introduce new chemicals into the marketplace. These new preservatives are potential new allergens. One can look to preservative usage databases to see this by the numbers. For example, formaldehyde and quaternium-15 have been widely used preservatives and over time have been found to be significant causes of ACD. As a result, these allergens have become less frequently used in personal care products, and new preservative systems have begun to replace them, demonstrated by corresponding increased usage numbers of these new chemicals.⁴ Examples of some of these newer preservative allergens include methylisothiazolinone (MI), the allergen of the year 2013, and iodopropynyl butylcarbamate (IPBC). MI has traditionally been tested to as part of a mix, but in 2005 this chemical was approved as a stand-alone preservative. As a result, we are seeing more allergy to this chemical.⁵ MI is not on the TRUE test and therefore can be missed if expanded testing is not performed to the chemical itself. IPBC was previously used as an industrial fungicide but was approved for use in cosmetics in the 1990s. This newer preservative system has been shown to cause ACD from usage in cosmetics.⁶ These new chemicals have demonstrated their own ability to sensitize and cause ACD. Neither is on the FDA-approved screening series and would be missed unless they were tested for with expanded trays, highlighting the need for vigilance and awareness of the changing trends in allergen usage over time and the need to periodically update screening series so they remain current and useful in the ability to detect allergens and diagnose ACD.

Another example of industry change that effects consumer allergen exposure is evident in the fragrance arena. In 1977, fragrance mix I was introduced as a screening allergy to identify those allergic to fragrance.⁷ This mix underwent its own evolution in order to be most helpful in detecting allergy to fragrance. However, over time, it has become less effective in detecting the newer fragrance chemicals that have entered the marketplace. As a result, fragrance mix II was developed in 2005 to screen for the newer fragrance chemicals.⁸ Almost certainly, as more novel fragrances make their way into the marketplace, we will need to appropriately adjust and modify our screening allergens. Already newer fragrance

allergens, such as linalool and limonene, are being reported.⁹

ACD to botanicals continues to be a challenge and a practice gap. Botanicals are increasingly being used in the personal care product market as consumers look for “natural” products. Screening for these chemicals is difficult because there are many botanicals and most are not adequately screened for by a single allergen. As a result, individual products and individual botanical allergens need to be used for patch testing in order to reliably detect allergy to a specific botanical. The patient exposure history becomes a critical part of the evaluation in order to identify any potential botanical allergens.

It is apparent that the introduction of new allergens in the marketplace will be a recurring event, and as a result, screening series must be adjusted and updated to reflect current usage patterns. The FDA-approved series has improved detection rates with the addition of key allergens. However, one must question how this screening series will hold up with its current composition as new allergens are introduced and seemingly problematic ones are phased out.

Education in the field has not changed dramatically. A recently conducted study did show that more faculty members designated as ACD experts are now members of the American Contact Dermatitis Society (ACDS), and ACD lectures are more routinely given in residency programs. Indications are also pointing to more expanded testing series being used by graduating residents, although this did not reach statistical significance.¹⁰ The increase in ACD experts as members of the ACDS is likely due in large part to the robust database created by the society that is a valuable resource in patient education. The Contact Allergen Management System (CAMP) database is available on the ACDS Web site, www.contact-derm.org, and allows clinicians to enter a patient's known allergen(s) into a database that then screens products within the database, providing a list of products that are free of the patient's known allergens as well as any potential cross-reactors. This database streamlines the education process and makes compliance easier for the patient because it provides a “safe” list for them to shop with in addition to giving them the names of their identified allergens.

Although the patch test procedure itself has remained essentially the same over the years, in addition to allergen selection, there are several other practice gaps and challenges in the field. The patch test procedure involves application of the allergens to the upper back with occlusion for 48 hours during which time the allergens

must be kept dry. At 48 hours, the patches should be removed in the office to insure that proper adherence of the patches occurred and to perform the first reading. The patient should then have a second patch test reading at 72 hours to 1 week later. Unfortunately, some gaps in care exist because this procedure is not always followed. Some patients are instructed on how to remove the patches at home, presumably to make fewer visits for the patient. However, this effort to increase patient convenience compromises the procedure. It does not allow for proper inspection of the patches to make sure that they remained in place and occluded, thereby insuring the integrity of the procedure. The second reading is also important because it helps discern between irritant and ACD and helps identify any late reactors. Unfortunately, this is another practice gap because second readings are not always conducted, most likely due to patient and/or provider convenience, and as many as 30% of allergens could be missed.¹ There are several potential late responders that will not be seen at the 48-hour reading, which means those not conducting a second patch test read may be missing these allergens and providing an incomplete assessment of the patient's allergy (**Box 3**). This gap in proper patch test procedure is likely due to convenience for patient and providers but needs to be adjusted in order for the patch test procedure to be properly performed and provide the most complete information.

The ongoing practice gap and knowledge gap of the reliability of patch testing performed while a patient is on immunosuppressive agents such as systemic steroids have been further complicated with the increased use of other immunosuppressive drugs and the new class of biologics. Although most physicians performing patch testing prefer a patient to be off prednisone for at least 1 week, many providers will test, when necessary, at the lowest dose possible, but preferably less than 10 mg per day.^{11–13} The use of other immunosuppressive agents, such as mycophenolate mofetil, methotrexate, azathioprine, cyclosporine, and tumor necrosis factor- α inhibitors,

Box 3

Some allergens with possible delayed reactions

Bacitracin
Disperse blue dyes
Cocamidopropyl betaine
Corticosteroids
P-Phenylenediamine

does not appear to be an absolute contraindication to patch testing.^{13–15} Testing at the lowest possible dose is recommended and 2+ and 3+ reactions are most reliable. When patch testing patients on these medications, one must consider the possibility of suppressed, or weak but relevant reactions.

Once allergens are identified, education is key to the management of the patient. Simply providing the names of the allergens to a patient compromises the usefulness of the patch test procedure. Patient education varies widely and is another practice gap issue. Dermatologists must educate and explain the allergens to the patient including any synonyms, where the allergen is likely to be found as well as possible cross-reacting chemicals that may need to be avoided. Providing a narrative sheet with this information is very helpful. Narrative sheets can be found in English and Spanish on the ACDS Web site. Another extremely valuable tool is the previously mentioned CAMP database available to members on the same Web site. This database provides patients with a list of “safe” products free of their known allergens and any cross-reactors. This database makes it much easier for patients to comply with avoidance. Follow-up visits to reinforce allergen avoidance and review progress are essential in the management of these patients.

A more recent and increasingly common question is the application and usefulness of patch testing in the evaluation and management of patients with metal devices. Dermatologists are increasingly being asked to patch test patients before the implantation of a metal device. This request sometimes comes from the concerned patient but is now more frequently coming from a referring surgeon who requires the testing before surgery. The controversy over patch testing and metal devices and how best to assist these patients and their surgeons remains a topic of debate. This topic of debate is seen in cardiology, in dental practices, and in thoracic surgery but is most apparent in orthopedics. With the rising number of joints being replaced in this country each year, it is perhaps not surprising that metal allergy has become a hot issue. The question of how patch testing in its current form can best assist these patients remains to be determined. Other tests, such as the lymphocyte transformation assay, may be useful to help answer these questions; however, these studies are costly, not widely available, and often not covered by insurance.

Knowing how best to manage these patients, and when to use patch testing in this situation, remains a practice gap without significant evidence-based data to guide clinicians. The dermatologist

must set realistic expectations and educate the surgeon and the patient on the limitations of this procedure. Patch testing is a cutaneous test that does not re-create the environment of the metal device, may not provide information relative to the implanted device, and is therefore limited in the information it can provide. It is also not predictive of future allergy and only provides information about the patient’s current state of sensitivity.

The question of preimplant testing for those with a history of metal allergy appears the most straightforward but still raises several concerns and questions. If a patient has a history of metal allergy, testing them to metals and reporting any allergens to the surgeon in order for these allergens to be avoided if possible seems reasonable. There are, however, reports of nickel-allergic patients with implants that contain nickel that are problem free.¹⁶ One must ask if a history of metal allergy or positive preimplantation testing is directing the surgeon to choose more expensive devices, or less durable device, even though no clear correlation between allergy and complication exists; this should be a concern given the significant number of joints replaced yearly and the resultant cost to society. Prospective studies evaluating the outcomes of those individuals with and without preimplant testing, impact of joint selection, and surgical outcomes are needed to help guide clinicians but are not yet available.^{17–20}

Postimplant testing is even more complicated. Patients who are suffering from joint failure, joint pain or loosening, dermatitis over the implant, or more diffuse dermatitis are sometimes referred for patch testing to assess for possible ACD to the metal device. If patch testing detects a metal allergen, it is not possible to determine if the metal allergy caused the problem, or if the problem, such as loosening of a joint, resulted in sensitization. When an allergy is found in a patient with a static metal device, such as a plate, cause and effect seems more apparent, and removal of the metal can result in resolution.²⁰ It is much more difficult to determine causation in the other situations. Decisions to remove or replace metal devices must be made with the surgeon and patient taking into consideration all the risks of another procedure with no guarantee of improvement. Clearly more evidence-based data are needed, and in the meantime, consensus expert opinion recommendations are being developed to help guide clinicians.

Patch testing has been an in-office procedure since the 1800s, and although the actual procedure has not changed considerably during that time, several challenges remain. Throughout the environment, we are exposed to hundreds of

Table 1
Patch testing best practices

Best Practice	Best Practice Strategies	Barriers to Best Practice
Expanded screening series	Obtain expanded series Referral centers	Cost, availability of allergens
Two patch test reads	Schedule 2 patch test reads	Time/convenience
Patch test off immunosuppressives	Patch test off immunosuppressives	Inability to wean off medicines

allergens daily, and new allergens will continually be introduced into our personal care products and our workplace. Our ability to detect relevant allergens necessitates that we routinely update and change our screening series in order to keep current with new allergens. Furthermore, as medicine continues to make advances, our bodies will be exposed to new and different chemicals and devices. We need to better identify the role of patch testing in these settings in order to best serve the needs of our patients (Table 1).

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