Systemic Contact Dermatitis: Sometimes It *Is* the Food

Margo Reeder, MD; Amber Reck Atwater, MD

PRACTICE **POINTS**

- Although most cases of allergic contact dermatitis are from direct skin contact, systemic contact dermatitis (SCD) can occur from ingesting certain allergens.
- Systemic contact dermatitis tends to present as a symmetric pruritic eruption, which may involve the flexural or intertriginous surfaces, eyelids, hands, or genital skin.
- Allergens known to cause SCD include certain plants, fragrances, metals, preservatives, and medications.

Systemic contact dermatitis (SCD) represents a unique pattern of allergic contact dermatitis that may cause a symmetric eruption involving intertriginous skin, genitals, eyelids, and/or hands. Common culprits known to elicit SCD for some patients include preservatives, metals, and fragrances. Certain medications including steroids and antihistamines can cause SCD. For patients who do not improve with skin allergen avoidance alone and who have a pattern of dermatitis suggestive of SCD, counseling on allergen avoidance through oral, parenteral, and inhaled routes is indicated.

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One of the perils of patch testing is fielding questions about which type of allergens will be used. Patients often ask if the patch test includes milk, foods, dander, mold, pets, and grass. Most patch testers spend a substantial amount of time explaining that the purpose of patch testing is to detect applied chemical allergens: It's not what you eat; rather, it's what touches your skin. However, the big caveat is that some oral, parenteral, inhaled, and even cutaneous allergens can produce systemic contact dermatitis (SCD), which represents a unique clinical scenario that we will review in this month's Final Interpretation column.

There are many patterns of SCD. Familiarity with potential clinical presentations can aid in diagnosis and counseling. Systemic contact dermatitis tends to be symmetrical. Dyshidrotic hand dermatitis is a reported pattern for systemic metal allergy, most commonly nickel. Refractory eyelid or genital dermatitis can reflect a systemic exposure, particularly if the dermatitis is in areas not caused by direct skin contact with the allergen. Systemic drug-related intertriginous and flexural exanthema is, as the name describes, an eruption involving axillae, genital skin, and flexural sites. It usually is a type of drug reaction, but the culprit can be an ingested allergen. So-called baboon syndrome SCD can cause persistent genital and intertriginous dermatitis. Other clues to SCD include dermatitis flare at the patch test site and erythema multiforme. Some patients also describe systemic symptoms, including headache, fatigue, and malaise.

Rhus Dermatitis

Poison ivy is the most common cause of acute contact dermatitis but also can be a cause of SCD. From the family Anacardiaceae, this sneaky plant is common in many parts of the United States; most allergic patients are familiar with their allergy from prior exposure.

In 1982, 54 Little League baseball attendees developed diffuse vesicular dermatitis involving the flexures after ingesting packaged cashews contaminated with cashew shells.[1] In the same family as poison ivy, the cashew nut tree (*Anacardium occidentale*) produces a cashew apple containing the cashew nut. The cashew shell is the site that contains the allergenic oils. Typically, cashews are processed to remove the shell and oil prior

Dr. Reeder is from the Department of Dermatology, University of Wisconsin School of Medicine and Public Health, Madison. Dr. Atwater is from the Department of Dermatology, Duke University School of Medicine, Durham, North Carolina.

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Correspondence: Amber Reck Atwater, MD, 5324 McFarland Rd #210, Durham, NC 27707 (amber.atwater@duke.edu).

to consumption. Ingestion of raw cashews is more likely to lead to SCD than roasted cashews because the heat in the roasting process can break down any allergenic oil.[2]

Metals

Systemic exposures to nickel usually are dietary. Clinically, SCD from nickel most commonly presents as refractory dyshidrotic hand eczema or papular elbow dermatitis.[3] Nickel is commonly found in vitamins and supplements as well as certain whole grains, vegetables, beans, coffee, chocolate, and tea.[4] Sometimes, cookware also can be a source of nickel exposure, particularly with steel cookware, from which nickel can leach into food.

In general, a diet lower than 150 µg/d is needed to prevent flares.[5] A point-based diet is available for nickel-allergic patients.[5] Patients should ingest a restricted amount of nickel (15 points daily); those who are extremely allergic might need to limit nickel ingestion to less than 5 points daily. Because of the challenges associated with maintaining a low-nickel diet, chelation therapy has been recommended to prevent nickel absorption. Disulfiram[3] and ascorbic acid[5] have been recommended, but larger studies are lacking.

Cobalt and chromium are other metals that, when ingested, can lead to SCD; both can be found in multivitamins. Other sources of dietary chromium include vegetables, coffee, beans, certain meats, and seafood.[4] For cobalt, the dietary exposures are similar with the addition of nuts, apricots, and whole-grain flour. A point-based cobalt avoidance diet has been published. This diet recommends less than 12 µg of cobalt daily; patients can ingest up to 12 cobalt points daily.[6]

Likewise, gold has been reported to cause SCD, with one case attributed to gold in a homeopathic cardiac medication.[7] Gold SCD also should be considered in the setting of ingested gold-containing alcoholic beverages and historically has been associated with intramuscular gold sodium thiomalate for the treatment of rheumatoid arthritis.[8]

Metal implants, including prosthetic joints, stents, and other devices, have been implicated in SCD. (More to come on this topic soon; yes, dear reader, that *is* a teaser!)

Fragrances

Balsam of Peru—Secreted by the tree *Myroxylon balsamum* var *pereirae*, balsam of Peru (BOP) contains several potential allergens, including cinnamon oils (eg, eugenol, vanillin, cinnamates), coniferin derivatives, and benzoic acid derivatives.[9] Foods and beverages associated with BOP include citrus, pickled vegetables, chocolate, ice cream, chili, pizza, tomatoes, wine, beer, gin, vermouth, flavored tea, and soft drinks.[10] Flavoring agents, spices (eg, cloves, curry, vanilla, cinnamon, allspice, ginger, anise), and condiments (eg, ketchup, barbeque sauce) are potential sources, as are cough medicines, lozenges, and flavored tobacco.

Salam and Fowler[10] described BOP-allergic patients whose condition improved with dietary restriction of BOP. Avoidance of tomatoes, citrus, spices, and cola most commonly contributed to improvement.[10] Scheman et al[9] proposed BOP subgroups, including the eugenol, vanillin, cinnamate, benzoate, ferulic acid, and coniferin groups. Targeted patch testing can identify relevant subgroups, and patients can focus dietary restrictions by subgroup.

Plants—Systemic contact dermatitis has been reported in association with a number of plants and herbals, including chamomile in tea,[11] goldenrod in a medicated extract,[12] *Hosta plantaginea* roots,[13] and garlic extract for hyperlipidemia.[14] Many more have been described.

Propolis—Also known as bee glue, propolis comprises a mixture of balsams, resins, waxes, essential oils, pollen, cinnamic alcohol, and vitamins. It can be found in many cosmetic products, foods, and chewing gum.[15] Propolis has been reported to be the source of SCD from ingestion of propolis capsules, which have been used to promote immune stimulation,[15] and propolis solution as a natural tonic.[16]

Propylene Glycol

Propylene glycol (PG) can be found in (believe it or not) foods and medications. In foods, it typically is used for its softening, humectant, and preservative properties.[17] Common food sources of PG include sauces, desserts, snack foods, and salad dressings.

Many topical prescription medications, including corticosteroids and newer nonsteroidal anti-inflammatory topicals, might contain PG; providers must specifically request PG-free products for PG-allergic patients. A detailed PG-avoidance diet lists products to avoid and products that are PG free.[18]

Preservatives

Sulfites—These compounds are preservatives found in cosmetics, hair dyes, and certain foods. Systemic contact dermatitis caused by sulfites in food has been described in numerous patients. One unfortunate vacationer developed axillary and groin dermatitis after ingesting large amounts of grapes, wine, shrimp, and french fries while vacationing in Italy.[19] Among dietary sources, beer and wine contain higher levels of sulfites. Sulfites also can be found in some pickled foods; bottled citrus juice; dried fruits; and commercial prepared foods, such as powdered potatoes and gravy mixes. Other reports of SCD from sulfites include an enema preparation[20] and anesthetics[21] as the source of the allergen.

Formaldehyde—Formaldehyde can cause SCD after ingestion of aspartame, which is hydrolyzed to phenylalanine, aspartic acid, and aspartic acid methyl ester in the intestine.[22] The methyl ester is converted to methyl alcohol, which is transported to the liver and oxidized to formaldehyde, which is then converted to formic acid. Hill and Belsito[22] reported a case of SCD presenting as eyelid dermatitis after ingestion of an aspartame-based artificial sweetener. A similar case of eyelid, neck, and leg dermatitis was reported after ingestion of drinks and candy sweetened with aspartame.[23]

Parabens—Although parabens are rare contact sensitizers, there are a few reports of paraben SCD. Cases include a predominantly flexural pattern from ingestion of a mucolytic-containing methylparaben,[24] a generalized eczematous eruption after intramuscular injection of ampicillin preserved with methylparaben and propylparaben,[25] and diffuse dermatitis from methylparaben in a local anesthetic.[26]

Sorbic Acid—Sorbic acid is utilized as a preservative in foods and occurs naturally in red fruit, such as strawberries and cranberries.[27] It is a rare allergen, but several cases of sorbic acid SCD have been reported, including perianal and buttock dermatitis,[27] hand dermatitis in an infant,[28] and hand-and-foot dermatitis in a storekeeper.[29]

Carmine

Carmine, or cochineal extract, is a red dye derived from dried pulverized scale insects of the family Coccidae. This chemical can be used in a multitude of foods and medications, including candies, yogurt, red velvet items, popsicles, food coloring, frozen meat and fish, ice cream, syrups, ketchup, sausage, donuts, cake pops, applesauce, canned fruits, soups, and drinks.[30] Machler and Jacob[31] described a child with recurrent episodes of erythroderma and periorbital edema in whom patch testing revealed a reaction to carmine. The patient's mother connected the flares with ingestion of red velvet cupcakes.[31] Ferris et al[32] reported a likely case of SCD attributed to carmine in a multivitamin.

Steroids

Ingested and injected corticosteroids have been associated with SCD, which is illustrated by a case of a generalized cutaneous eruption several days after joint injection with triamcinolone acetonide.[33] In another report, a patient developed an eruption in the body folds, later generalized, after topical application of a corticosteroid, first in ear drops and later in nasal spray.[34] Traditional corticosteroid classification systems might be less reliable in predicting relevant allergens in corticosteroid SCD; comprehensive testing, including oral challenge, might be necessary to identify alternatives.[33]

Ethylenediamine

Ethylenediamine is an uncommon allergen in patch test populations. It is present in aminophylline[35] and is utilized in the production of hydroxyzine[36] and other piperazine-derived medications, such as cetirizine, levocetirizine, meclizine, and olanzapine. Several cases of SCD caused by aminophylline,[35] cetirizine,[36] and hydroxyzine[37] have been reported, all in the setting of a positive patch test reaction to ethylenediamine.

When to Counsel About Systemic Exposures

In general, we usually do not counsel on systemic exposures to allergens at the final patch test reading unless the pattern of dermatitis or clinical history strongly suggests systemic exposure. In most cases, we find that counseling on topical allergen avoidance alone is sufficient to treat allergic contact dermatitis. Because of the restrictive nature of allergen-avoidance diets, counseling all patients on the potential for SCD might cause undue stress without much benefit. However, if a patient experiences persistent dermatitis on follow-up with topical avoidance alone, we often will delve into systemic exposures and counsel on further avoidance strategies, including medication and diet.

Final Interpretation

A multitude of chemicals have been reported as the source of SCD; these exposures can occur through ingestion, injection, and inhaled and cutaneous routes. Chemicals present in foods, medications, and beverages have been implicated. Systemic contact dermatitis is rare and should be considered when traditional avoidance of contact allergens is unsuccessful and the clinical pattern is consistent with SCD.

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