Systemic Contact Dermatitis

Rajiv I. Nijhawan, MD[a], Matthew Molenda, MD[b], Matthew J. Zirwas, MD[b], Sharon E. Jacob, MD[c,*]

KEYWORDS

- Systemic contact dermatitis (SCD)
- Allergic contact dermatitis (ACD) • Allergen
- Nickel • Balsam of Peru • Metals • Patch testing

Systemic contact dermatitis (SCD) describes a cutaneous eruption in response to the systemic exposure of allergens.[1] It was first described in the literature by Jadassohn in 1895,[2] but has been referred to by many different names, such as systemic eczematous "contact-type" dermatitis medicamentosa,[3] mercury exanthema,[4] baboon syndrome,[5] and hematogenous contact eczema.[6] A recommendation has been made to use the phrase "systemic allergic dermatitis" because skin contact is not a requirement for the elicitation of a cutaneous response from a hapten; it can also occur hematogenously.[7] Regardless of name, sensitization to an allergen usually occurs first, as is seen in allergic contact dermatitis (ACD), which is a type of T-cell– mediated, delayed-type (type IV) hypersensitivity reaction.[8,9] Thereafter, varying degrees of exposure can elicit a broad spectrum of systemic symptoms. This review of SCD provides an overview of the disease with descriptions of common allergens and some insight into the possible mechanism of action seen in SCD.

WHEN TO SUSPECT SCD

There are multiple routes of exposure for the elicitation of SCD, such as transepidermal, subcutaneous, intravenous, intramuscular, inhalation, and oral ingestion.[10] Thus, SCD should be included in the differential of most eczematous eruptions. The most important factor to consider is the time course of exposure to possible allergens and development of symptoms, because SCD can have a latency period of a few hours to a few days from the systemic exposure.[7]

Clinically, SCD has a wide spectrum of presentation, from disseminated erythematous papules to deep-seated vesicles to erythema localized to the palms and fingers.[11] Additionally, SCD can present as dermatitis localized to the flexural aspects of the extremities[12] or diffuse erythema of the anogenital region, which is commonly referred to as baboon syndrome because of its distribution.[5] Erythematous axillae may also accompany the latter presentation,[5] and it has been referred to as SDRIFE or symmetric drug-related intertriginous and flexural exanthema.[13]

Often times, exposure to the allergen can cause a flare of the dermatitis in the same area where the initial episode of elicitation occurred. Memory T cells may remain at the same locations of the previous allergen contact, which likely explains the observation of re-test reactions and flares of previously exposed skin.[14] The reasons and mechanisms explaining T-cell retention have not been elucidated.

In cases of SCD, the reaction does not necessarily occur at sites of previous exposure and can occur anywhere, including a previous patch test site. Other individuals present with exfoliative erythroderma, and some patients may even experience systemic symptoms such as nausea, vomiting, diarrhea, fever, malaise, headaches, and arthralgia.[7,15]

PATHOGENESIS

ACD is commonly defined by 2 phases: a sensitization phase (also known as the afferent phase), in which the patient remains asymptomatic, and an elicitation phase, in which cutaneous inflammation

[a] 5 Darcy Drive, Branchburg, NJ 08876, USA
[b] Ohio State University, Columbus, Ohio, USA
[c] Rady Children's Hospital, 8010 Frost Street, Suite 602, San Diego, CA 92124, USA
* Corresponding author.
E-mail address: sjacob@contactderm.net (S.E. Jacob).

Dermatol Clin 27 (2009) 355–364
doi:10.1016/j.det.2009.05.005
0733-8635/09/$ – see front matter © 2009 Elsevier Inc. All rights reserved.

occurs mediated by the immune system.[16] In the sensitization phase, which lasts 10 to 15 days, a hapten penetrates the lipophilic stratum corneum and binds to 1 of a wide array of extracellular and cell membrane–associated proteins, but it does not have dedicated cellular receptors.[17,18] These haptens have antigenic properties and are taken up by the skin dendritic cells, mainly Langerhans cells (LHCs), which are the major antigen presenting cells (APCs) of the skin. After taking up and processing the antigen, LHCs present it in association with a major histocompatibility complex type II (MHCII) on the cell surface. These APCs then migrate through the lymphatic system to the paracortical areas of regional lymph nodes where the antigen/MHC molecule complexes are presented to naïve T cells. When a naïve CD4+ T cell that has a complementary T-cell receptor encounters the MHC/antigen complex and has appropriate costimulatory signals, it undergoes clonal expansion, and these clones enter the systemic circulation as memory T cells. Additionally, this immune system priming and amplification requires the role of resident cells, such as keratinocytes, mast cells, endothelial cells, and natural killer cells.[19–21] The thresholds for sensitization vary among all individuals, and susceptibility factors play a role in the development of ACD, such as age, T-cell repertoire, and type and duration of allergen exposure.[22]

The elicitation phase (also known as the efferent phase) defines the second part of ACD, which occurs after reexposure to the antigen, taking approximately 24 to 72 hours to clinically manifest after exposure. In elicitation, the skin is exposed to an antigen to which sensitization has already occurred; the antigen is once again taken up by APCs and presented to the antigen-specific memory-effector T cells, which become activated. These activated T cells produce type 1 cytokines (interferon-γ), and the other cells in the skin react by releasing other cytokines and chemokines.[16] The inflammatory reaction resulting from this release resolves in a course of several days to a few weeks, likely secondary to down-regulatory mechanisms. It has also been suggested that a type III response is involved in SCD, with the deposition of antigen-antibody complexes in the skin that leads to inflammation clinically seen.[23] Hapten-antibody complexes have been identified in serum of patients with cutaneous symptoms.[24] Resolution and prevention of the ACD occur with sustained allergen avoidance.

PROTEIN CONTACT DERMATITIS

Hjorth and Roed-Petersen first described ''protein contact dermatitis'' in 1976 and postulated that type I (immediate IgE-mediated) and type IV (delayed-type hypersensitivity) reactions were involved in the pathogenesis.[25] The proteins involved in this subset of dermatitis are grouped into 4 subsets: (1) fruits, vegetables, spices, and plants; (2) animal proteins; (3) grains; and (4) enzymes.[26] Clinically, patients with protein contact dermatitis present similarly to ACD; however, they have negative patch test reactions but positive skin-prick and scratch test reactions and often also have positive atopy patch tests.[27] Although the pathogenesis is not completely understood, there is some thought that it may be caused by IgE-bearing LHCs similar to atopic dermatitis.[27]

THE ALLERGENS AND MANAGEMENT OF SCD

Various metals, medicaments, foods, botanicals, and chemicals have been implicated as the causative agents of SCD. Metals that are electrophilic have the ability to ionize and react with proteins, and these complexes can be recognized by dendritic cells that allow for sensitization to occur.[28] In general, the allergen type, duration, environment, and patient susceptibility are all factors in the development of SCD. The authors focus on 2 of the most common allergens that elicit SCD, nickel and balsam of Peru (BOP), while also briefly touching on some other causative agents.

Nickel

Nickel allergy is 1 of the most common causes of ACD, and its incidence is thought to be increasing. Sensitized individuals who are exposed to nickel on their skin or mucosal surfaces generally have a predictable localized response, including erythema, vesicles, scaling, and pruritus. However, systemic reactions such as flare-ups of a previous patch test site/contact dermatitis site, flare-ups of hand dermatitis, or generalized dermatitis can also occur with exposure to the nickel antigen.[29] Still, whether dietary nickel can induce localized or generalized eruptions continues to be a matter of debate. A review of the literature suggests that dietary nickel can cause cutaneous eruptions consistent with ACD.

Dietary nickel causes dermatitis

ACD flares caused by dietary nickel have been demonstrated. Jensen and colleagues[30] showed a dose-dependent relationship between ingestion and flare-up. Their study determined that 0.3, 1, and 4 mg of nickel sulfate hexahydrate produced cutaneous reactions in 40%, 40%, and 70% of nickel-sensitive participants, respectively. 10% of the placebo group had cutaneous reactions in sites of previous dermatitis. Of note, 60% of the

participants receiving 4 mg of nickel sulfate hexahydrate had widespread cutaneous reactions, whereas the rate in the placebo group was 0%. Although the study only had 10 patients in each dosage group, these data show that ingesting a single dose of 4 mg or more of nickel sulfate hexahydrate causes a cutaneous reaction in most nickel allergic patients.[30]

Although a study by Santucci and colleagues[31] provides additional evidence that sudden large doses of dietary nickel can elicit cutaneous flare-ups, it also asserts that nickel-allergic patients can adapt to gradual increases in dietary nickel. Out of 25 nickel-allergic patients, 22 had cutaneous reactions to a $NiSO_4$ 10 mg oral challenge at the beginning of the study. However, upon gradual increase in oral dose of $NiSO_4$ (3 mg for 1 month, 6 mg for 1 month, and 10 mg for 1 month), only 3 out of 25 patients had to withdraw from the study because of intense worsening of cutaneous symptoms. Out of the 25 patients, 14 had no associated flare-up at all with the gradually increasing doses.[31] This study suggests that a tolerance to increasing nickel in the diet may be achieved if exposure is gradually and consistently increased. However, because individuals often have varied diets, and it would be difficult to justify supplementing nickel in a long-term diet plan without additional studies, the initial challenge is the most important part of this study in the opinion of the investigators.

Specific studies on hand dermatitis in relation to ingested nickel have also been done. Menné and Thorboe[32] correlated flare-ups in dishydrotic eczema with increased levels of nickel in the urine. They postulated that increased urine levels were a result of dietary bursts of high nickel content. However, it should be noted that most dietary nickel is eliminated in the feces, and a measurable amount is also excreted in sweat. Renal, cardiac, and hepatic diseases have also been shown to increase urinary nickel.[33] Nielsen and colleagues[34] also demonstrated flares of hand eczema with high nickel intake in 10 out of 12 patients. In a complimentary study, Sharma used a nickel chelator (disulfuram) and a low-nickel diet that demonstrated complete healing of hand eczema in 10 out of 11 patients in the treatment group.[35]

Avoidance of dietary nickel has also been shown to improve SCD, which gives further support that nickel ingestion plays a role in its pathogenesis. That is, a low-nickel diet and nickel chelators have been shown to improve recalcitrant dermatitis (hand or otherwise) in nickel-sensitized individuals. Scattered case reports and studies have linked clinical improvement of eczema in nickel-sensitized individuals who adhere to a low-nickel diet.[36–38] Veien and colleagues[37] showed clinical improvement of dermatitis in 58 out of 90 nickel-sensitive patients in the short term (4 weeks) with a low-nickel diet. Follow-up questionnaires sent to the improved patients 1 to 2 years later demonstrated that 40 out of 55 respondents reported long-term improvement from the low-nickel diet. Disulfuram, a nickel chelator, has also been shown to be an effective initial adjunct to clearing persistent dermatitis and an effective monotherapy in placebo controlled trials.[35,39] In the monotherapy trial, it should be noted that 3 out of 11 patients who received disulfuram at gradually increasing doses from 50 to 200 mg showed signs of hepatic toxicity over the 6-week treatment period.[39] In the opinion of the investigators, this adverse potential drug effect is not acceptable because dietary modification can be considered as an alternative benign treatment.

Nickel ingestion has also been shown to cause detectable changes in the immune system. For example, individuals whose dermatitis flared after ingesting nickel were shown to have a decrease in CD8+ CD45RO+ CLA+ blood lymphocytes. This decrease correlates with migration of CD8+ memory T cells into tissues, which is consistent with contact dermatitis.Ingestion of nickel by nickel-sensitive patients has also been shown to increase serum levels of interleukin (IL)-5. Although contact dermatitis is classically thought of as a type IV hypersensitivity reaction with cytotoxic T cells (Th1 response), IL-5 is a Th2 cytokine. IL-5 enhances proliferation of eosinophils and may explain why eosinophils can be seen on biopsy of ACD.[40]

The elicitation studies, avoidance studies, and immunologic assays, above all, provide evidence to support the hypothesis that dietary nickel can induce SCD. Because dietary nickel avoidance in nickel-sensitized individuals has demonstrated improvement in patients with recalcitrant dermatitis, and because proper dietary modification should do no harm to patients, the investigators assert that counseling on ways to minimize nickel exposure should be given to patients with confirmed nickel sensitivity. Sources of dietary nickel and treatments are further discussed in the next section.

Dietary nickel

The normal daily intake of nickel has been estimated to be between 0.3 and 0.6 mg.[33] Although the normal dietary amount of nickel is lower than the ingested amounts producing the most convincing results in the studiesdiscussed earlier, individual diets may vary. For example, an individual might consume the following on 1 day: Breakfast, a bowl of oatmeal (0.22 mg), 1

banana (0.02 mg), 1 apple (0.005 mg); lunch, 2 slices of whole wheat bread (0.01 mg) with 2 slices of bacon (0.01 mg), a piece of lettuce (0.001 mg), a tomato slice (0.002 mg), and a chocolate (Hershey) bar (0.015 mg); dinner, a serving of broccoli (0.023 mg), a baked potato (0.015 mg), and a pork-chop (0.005 mg); snack, a half cup of peanuts (0.218 mg); drinks, 2 cups of coffee (0.003 mg).[41] Total nickel intake for the day would be 0.547 mg, which is well within the range of doses shown to cause flares. Additionally, one cannot assume that dietary nickel is insignificant at amounts as low as 0.3 mg because this dose was still shown to cause reactions in 40% of patients in an elicitation study.[40] Furthermore, the observation that chronic hand dermatitis responded to reduction of nickel intake and/or nickel chelators provides reasonable evidence that oral nickel may play a role in its pathogenesis. For these reasons, when a nickel-sensitized individual has chronic or frequently relapsing dermatitis that cannot be explained by contact exposure, the authors suggest counseling on how to minimize oral nickel intake.

Nickel can naturally occur in food or can be inadvertently added by processing, cooking, or storage. Foods that consistently contain relatively high amounts of nickel per serving include seafood (especially shellfish), chocolate, legumes, grains, and nuts.[33] There are technical difficulties in labeling other foods as "high-nickel." For example, plant foods may contain trace nickel or high nickel depending on the soil/region they are grown in. Another example is that processing foods with metal equipment (ie, flour mills) may emit nickel into the food.[41] Yet another example is nickel in tap water, especially hot water, which can leach nickel into the stagnant water within the plumbing pipes or faucet fixtures.[42] One additional source that can introduce nickel into the diet is stainless steel cookware or utensils, especially with high cooking temperatures and acidic foods.[43] The release of significant amounts of nickel from stainless steel cookware was refuted by a French study that cooked foods typical in a French diet.[44] However, the foods they tested with their cookware were admittedly nonacidic. These examples illustrate the complex sources that make it difficult to avoid ingested nickel. However, some practical recommendations in achieving a low-nickel diet can be made from the information available.

Treatment of SCD caused by nickel

Because the goal for physicians is first to do no harm, the authors feel that recommending a low-nickel diet and external nickel avoidance is the most appropriate first step in treating recalcitrant dermatitis in nickel-sensitive patients. This treatment has been shown to be effective, and there is no evidence of adverse effects occurring from these recommendations. Although supplementing nickel in gradually increased dosages may produce tolerance, long-term supplementation has not been studied and is therefore not advised.[31] Because of the potential for hepatotoxicity in patients taking disulfuram for its nickel chelating properties, this medication should be used cautiously, if at all. An alternative way to decrease dietary nickel absorption (and promote fecal excretion) is to recommend addition of iron-rich foods to the diet in clinically appropriate scenarios. Iron and nickel are absorbed by way of the same gastrointestinal transport system, but iron is the preferred cation. Less nickel is absorbed when competing with iron-rich foods.[41]

From a practical perspective, the low-nickel diet must be explained in a simple achievable way to maximize patient compliance.The low-nickel diet requires slightly more patient education than simply recommending avoidance of seafood (especially shellfish), chocolate, legumes, grains, and nuts. Although nickel content varies in foods and water due to the numerous reasons listed earlier, a nickel-sensitive patient may find improvement in their dermatitis if some basic principles are followed.

In 2007, Sharma[45] proposed 9 points important in achieving a low-nickel diet. Using Sharma's points and the available literature as a guide, the authors of this review agree with the following simplified recommendations:[41] (1) avoid or moderate high-nickel foods (listed earlier), canned foods, leafy green vegetables, vitamin supplements/drinks with nickel, and margarine; (2) eat animal meats (other than shellfish), eggs, dairy, polished rice/refined wheat/corn cereal, nongreen vegetables, citrus fruits, high vitamin C- and high iron-containing foods; (3) run tap water for a few seconds before washing, drinking, or cooking to flush out nickel that may have leaked from pipes or fixtures; (4) avoid stainless steel cookware and utensils, especially with acidic foods. Glass or ceramic cookware are good alternatives.

Motivated patients may request additional information on a nickel diet and a more comprehensive list of nickel content in foods.[46] *Managing Food Allergy & Intolerance: A Practical Guide* has a list of nickel levels in common foods.[41] Before directing a patient to additional resources, however, it is important to emphasize the variability of nickel content in foods grown in different soils.

In summary, there is significant evidence that dietary nickel can cause SCD. The most conservative and safe treatment, dietary modification, has been shown to be effective, but it requires significant patient education and compliance.

Balsam of Peru and Related Chemicals

Contact allergy to (BOP) or *Myroxilon pereirae* is commonly evidenced with positive patch test reactions.[47] Coreactivity to fragrance mix, cinnamic aldehyde, and balsam of tolu is also commonly seen.[48] After first being described by Bonnevie in 1939,[49] Hjorth[50] recognized the association of allergy to BOP to allergy to spices and flavorings, such as cinnamon, vanilla, and cloves. This relationship presents the possibility of the occurrence of SCD to orally ingested agents that contain substances related to or contained in BOP. Cross reactions are also seen with cinnamon, cinnamic aldehyde, clove, orange peel, and eugenol.[51]

BOP is a fairly specific marker for an allergy to spice, although it is not very sensitive.[52] It is also believed that topical products containing BOP, including cosmetics, sensitize patients predisposing them to SCD with oral ingestion.[53] Studies have evidenced the clinical improvement of balsal allergic patients who avoid foods that are balsam related,[48,54–56] demonstrating the importance of educating these patients regarding dietary avoidance.[48] Oral challenge with BOP has not proven to be a predictor of which patients might benefit from these diet restrictions.[57,58] A study also showed that 41% of patients with a positive patch test reaction to BOP also reacted to spices.[59] For patients with BOP allergy, the authors recommend a strict avoidance of BOP products and foods and BOP-related products, such as flavorings and spices.

Other Common Metal Allergens

Cobalt

Cobalt is a metal that is more commonly reported to cause SCD, and its prevalence is clinically relevant because it is the main component of vitamin B12 (**Box 1**).[28] Fisher[60] described a patient who had a recall reaction at the site of a previous vitamin B12 injection after oral ingestion of cobalt. An allergy to either cobalt or nickel can increase one's sensitivity to the other metal. In 1987, Veien and colleagues[61] described 7 out of 13 patients who were sensitive to cobalt but not to nickel, as having a flare of their dermatitis with oral challenge of 1 mg cobalt sulfate. In another study, Veien and colleagues[62] reported that out of 9 patients who had positive patch test reactions to cobalt and not nickel, 6 experienced flares of their dermatitis after a placebo-controlled oral challenge of 1 mg of cobalt. When dietary restriction of cobalt was initiated, 4 of these 6 patients had an improvement of their dermatitis. Cross-sensitization has been seen in cobalt allergic patients with nickel and palladium.[63] Palladium is seen increasingly in dental appliances, jewelry, and electrical appliances,[28] and avoidance can be imperative for the management of these patients.

Box 1
Metals that cause SCD

Metals
Aluminum
Chromium
Cobalt
Copper
Gold
Mercury
Nickel
Zinc

Mercury

Mercury is 1 of the earlier recognized metals to cause SCD, usually as a result of inhalation of mercury vapors from a broken thermometer, commonly after previous sensitization to other mercury compounds, such as thimerosal, merbromin (Mercurochrome), topical disinfectants,[64] ophthalmologic preparations,[65] and antiparasitic powders.[66] SCD from mercury can also be caused by amalgam dental restorations.[67,68] Mercury has also been reported to induce acute generalized exanthematous pustulosis.[64] Although systemically absorbed mercury may lead to lymphocytic proliferation, its excretion through sweat may also attract and concentrate T cells in the flexural areas, which may explain the common clinical presentation of mercury-related SCD.[64,69]

Gold

Gold, which has commonly been used as a restoration material in dentistry and as an intramuscular injection as an antiinflammatory for the treatment of rheumatoid arthritis, has emerged as a significant metal allergen.[70] Diagnosing gold allergy traditionally through patch testing has proven to be challenging if late leads are not performed 7 days or later, and thus it is recommended to follow up patients with suspected gold allergy for 3 weeks, in case a late reaction presents.[70] Intramuscular injection with gold sodium thiosulfate has shown to flare patients' previous dermatitis

and/or patch test reaction in addition to increasing these patients' body temperature.[71]

Copper

Although copper has been less commonly reported to induce SCD, it is an allergen to consider. Copper has been used in dental devices, with evidence of delayed-type stomatitis.[72] Copper-sensitive women have also experienced SCD from intrauterine contraceptive devices that happened to contain copper.[73,74]

Medications

SCD from medications has been reported from a broad spectrum of drugs (**Box 2**). It is suspected that SCD from drugs is different from other drug eruptions because sensitization is required and the mechanism is likely different.[7] It is believed that a patient's intrinsic sensitivity to the drug and the size of drug dosage is related to the severity of the cutaneous inflammation.[75]

Box 2
Medications that cause SCD

- 5-Fluorouracil
- Allopurinol
- Aminopenicillins
- Ampicillin
- Bacitracin
- Benzocaine
- Cinchocaine
- Clobazam
- Corticosteroids (inhaled)
- Corticosteroids (systemic)
- Erythromycin
- Ethylenediamine
- Gentamycin
- Hydroxyzine
- Intravenous immune globulin (0.4 g/kg)
- Mesalazine (5-aminosalicylic acid or 5-ASA)
- Methyl salicylate
- Miconazole
- Mitomycin C
- Naproxen
- Neomycin
- Oxycodone
- Penicillin
- Psuedoephedrine
- Streptomycin
- Suxamethonium
- Terbinafine
- Tetracaine

Oral drugs

Some of the most convincing evidence of the existence of SCD is due to the cutaneous reactions seen with a well-observed temporal relationship in medications that are available for topical and oral use.[10] Reports of SCD to the following have been evidenced in the literature: miconazole,[76] gentamycin,[77,78] methyl salicylate,[12] erythromycin,[79] corticosteroids,[80] such as prednisone[81] and dexamethasone,[82] mesalazine (5-aminosalicylic acid or 5-ASA),[83] ethylenediamine,[84] and clobazam.[85] A delayed-type reaction with a cutaneous eruption similar to toxic epidermal necrolysis has also been reported to ampicillin.[86] Many of these drugs are important for the management of patients' other medical conditions, thus alternative drug classes or chemical structures may be substituted, such as switching dexamethasone for prednisone or vice versa.[82]

Botanicals/Foods

There is significant evidence that foods and botanic products can also cause allergic reactions that present as SCD (**Box 3**). An increasing number of people are using herbal remedies and alternative therapies, which often contain plant extracts. Additionally, these items have also been introduced in cosmetics, providing multiple ways for sensitization.

In terms of foods, although allergic and irritant contact dermatitis is a common cause of hand

Box 3
Plants that cause SCD

- Arnica
- Balsam of Peru
- Chamomile
- Cinnamon oil
- Compositae (daisy family)
- Echinacea
- Feverfew
- Marigold
- Mugwort
- *Parthenium*
- Ragweed
- Vanilla oil

dermatitis in food handlers,[87] there have been a few published reports on SCD from diet other than the nickel- and BOP-related foods, but this entity may be underreported and underdiagnosed.[88,89]

Compositae (Asteraceae)

Botanicals from the family Compositae (Asteraceae), commonly referred to as the 'daisy family', are increasingly being used for alternative remedies.[90] This broad family also includes flowers, herbs, vegetables, and weeds (eg, ragweed, chamomile, *Tanacetum vulgare*, *Arnica montana*, parthenolide, *Achillea millefolium*, marigold, mugwort, and *Echinacea*).[28,87] Additionally, extracts from this family are found in many different cosmetics and personal hygiene products. The main allergens in these plants are sesquiterpene lactones, which are the main inducers of both ACD and SCD. Wintzen and colleagues[91] reported recalcitrant atopic dermatitis in Compositae-sensitive patients, secondary to their food intake. Chamomile, commonly found in tea, has also been evidenced to cause severe SCD with just minimal amounts of sesquiterpene lactones.[90]

Parthenium hysterophorus ("parthenium weed")

Parthenium hysterophorus, a common weed allergen in India,[92] has been shown to sensitize 56% of those occupationally exposed to it.[93] Other than a cutaneous eruption occurring from airborne exposure, it is suspected that an eczematous reaction may also occur by inhalation or ingestion.[92] To determine whether a patient had SCD to parthenium from inhalation or cutaneous exposure, Mahajan and colleagues asked the patient to inhale from a polythene bag containing parthenium without any direct or airborne contact with the weed. About 8 to 10 hours later, the patient's dermatitis flared.[92] When researchers tried to hyposensitize patients with parthenium sensitivity, 30% had flares of their dermatitis.[94]

Garlic and onions

Garlic and onions are 2 food items commonly recognized as inducers of allergy.[95] A case report details the development of hand dermatitis after the ingestion of garlic tablets.[96] Allergens seen in garlic include diallyl disulfide, allyl-propyl sulfur, and allicine.[97,98]

Other Common Chemicals

Propylene glycol

Propylene glycol, used for many purposes, including as a solvent, emulsifier, vehicle, antifreeze, and humectants,[87] has been implicated to cause systemic reactions in previously sensitized individuals. Its properties also allow for its use as a thickening agent in many foods, including cake mixes, salad dressings, popcorn, and soda drinks.[87] It is also found in topical corticosteroids and other medicaments, cosmetics, and fragrances.[99] Experimentally, researchers have shown that the ingestion of propylene glycol flares patients sensitive to this chemical.[100] Fisher[101] also reported a case in which a patient developed SCD after being administered intravenous valium, in which propylene glycol was used as a solvent.[101]

Formaldehyde

Formaldehyde has been implicated in systemic reactions that include migraine headaches, asthma, and generalized eczema.[102] Aspartame, a synthetic sweetener commonly found in children's chewable vitamins, diet drinks, and low-calorie food-items, is metabolized to methanol and later into formic acid, and it can be associated with SCD in formaldehyde-sensitive patients.[103] For sensitized individuals, avoidance of products and foods that contain formaldehyde, aspartame, or other formaldehyde releasers is recommended.

SUMMARY

SCD describes a cutaneous eruption in response to systemic exposure to an allergen. The exact pathologic mechanism remains uncertain. The broad spectrum of presentations that are often nonspecific can make it difficult for the clinician to suspect this disease, but it is an important diagnosis to consider in cases of recalcitrant, widespread, or recurrent dermatitis, in which patch testing reveals allergy to nickel or BOP. Diagnosis and appropriate management can be life-altering for affected patients.

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