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Contact urticaria and the environment

Abstract: The environment is defined by the aggregate of surrounding things, conditions, or influences. The biophysical environment includes the physical and biological factors, along with chemical interactions that affect an organism. Contact dermatitis includes any inflammatory skin reaction to direct or indirect contact with noxious agents in the environment. Although the main clinical expression of contact dermatitis is eczema, other expressions like urticaria, contact urticaria (CoU), or lichenoid eruptions are described. The main objective of this chapter is to review CoU, which is often misdiagnosed, as part of the CoU syndrome (CUS).

Keywords: contact dermatitis; contact urticaria; dermatitis; environment; urticaria.

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Introduction

The environment is defined by the aggregate of surrounding things, conditions, or influences. The biophysical environment includes the physical and biological factors, along with chemical interactions that affect an organism. Skin is one of the human target organs of environmental agents. Cutaneous tegument performs the main task of preserving our life. Mechanical barrier function, melanogenesis, immunological barrier function, thermoregulation, and environmental perception are the fifth functions for which a normal skin should be ready. Human skin is a vital organ, and if one loses his skin, he will be in danger. The epidermal and dermal binomiun is immunologically very active, and by itself, is a complex and complete organ in continuous turnover.

Contact dermatitis includes any inflammatory skin reaction to direct or indirect contact with noxious agents in the environment. Although the main clinical expression of contact dermatitis is eczema, other expressions

like urticaria, contact urticaria (CoU), or lichenoid eruptions are described. The main objective of this chapter is to review CoU, which is often is misdiagnosed, as part of the CoU syndrome (CUS). CoU is an immediate cutaneous reaction clinically expressed with pruritus and wheals, angioedema, or both. Contact induced wheals can manifest alone or in conjunction with immediate induced eczema.

CoU as a manifestation of CUS

CUS comprises a heterogeneous group of immediate contact inflammatory reactions that usually appear within minutes after contact with eliciting substances. Occasionally systemic involvement can be present. It was first defined as an entity in 1975 by Maibach and Johnson (1). To date, scientific knowledge of CUS remains limited. Thus, it is highly probable that people suffering active symptoms are not diagnosed properly and consequently remain untreated.

CoU refers to a wheal and flare reaction following external contact with a substance, usually appearing within 30 min and clearing completely within hours, without residual signs (2). The term was first introduced by Fisher, but this phenomenon has long been recognized (3). Urticarial lesions due to nettles and hairy caterpillars were reported in the 19th century and continue to be reported today (4). In a randomly design survey carried out in Spain, contact wheals and pruritus were observed in 52.1% and 100% of people induced by pine processionary, respectively (5). Throughout history, some naturally existing urticariogens were used therapeutically as rubefacients, counter-irritants, and vesicants (6).

Hjorth and Roed-Petersen defined protein contact dermatitis (PCD) as characterized by immediate dermatitis induced after contact with certain proteins (7–9). Food caterers suffering exacerbation of the itch immediately after contact with meat, fish and vegetables, followed by erythema and vesicles were described. Application of the relevant foods to the affected skin resulted in either urticaria or eczema (10). Atopy and PCD were associated in approximately 50% of affected patients (11).

Patients can develop CUS immediately after contact with the trigger substance, CoU and/or dermatitis/eczema. These immediate contact reactions can appear on

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normal or eczematous skin. Wheals are the characteristic symptoms of CoU, while eczema appears rapidly on the hands in PCD. Both cutaneous symptoms and entities can be induced by the same trigger factor and can be suffered by the same patient simultaneously or consecutively.

CUS, CoU, and PCD are conditions characterized by the immediate development of contact skin reactions (immediate contact skin reactions; ICSR) mainly consisting of pruritus, wheals, and/or eczema. This chapter focuses on CoU as a manifestation of the interaction between the environment and the skin.

CoU as occupational dermatosis

The global incidence of CUS is not known, although immediate contact reactions are common in dermatological consultations (9, 12–15). Nowadays, CoU has been classified as a separate occupational skin disease in many countries. With the exception of latex allergy showing prevalence of 5%–10%, for other triggers, isolated cases or short series of occurrences in patients have been described (11). The described prevalence of CUS tends to be wrong in most of the countries because of underreporting (16). When CoU is registered as a skin occupational diagnosis, it became the second most frequent occupational skin disease after eczema. In the “Finnish Register of Occupational Diseases” (1990–1994) CoU was described as the second most frequent cause of occupational dermatosis (29.5%) following contact allergic dermatitis (70.5%) (17, 18). The common trigger agents involved were cow dander (44.4%), natural rubber latex (23.7%) and flour, and grains or feed (11.3%) (18). An 8.3% CoU prevalence of occupational CoU was found in a retrospective study done in a tertiary level clinic specializing in occupational dermatology in Melbourne, Australia (19). Hands, arms, and face were the most frequent body areas involved, with atopy being a significant risk factor for natural rubber latex, foodstuffs or ammonium persulfate CoU. Health workers, food handlers, and hairdressers were the most common people suffering occupational CoU. Recently, a survey conducted in 335 restaurant, catering and fast-food employees in Singapore showed as the most common occupational dermatosis, irritant contact dermatitis (10%) being occupational CoU urticaria sporadically reported and caused by lobster and prawn in two patients (20).

Health care workers in Europe show a prevalence of occupational CoU from 5% to 10%, whereas in the general population it lies between 1% and 3%. Other occupations that show also a high risk to develop CoU are food handlers or workers involved in agriculture, farming, floriculture, and plastics, pharmaceutical and other laboratories,

as well as hunters, veterinarians, biologists or hairdressers. Atopy favors further sensitization where protein allergens are concerned (21).

The classification of occupational dermatosis in the 11th revision of the “International Code of Diseases (ICD)” includes contact dermatitis joint with CoU. The implementation of this new classification has been delayed until 2017. Occupational screening questionnaires that include specific questions searching for urticaria symptoms are very few. The development of a standardized set of criteria to define what is occupational or not has yet to be fully addressed in current literature.

Evolving knowledge about the mechanisms involved in CUS

The mechanisms underlying ICSR are partially understood. Each trigger substance has its own mechanism or mechanisms of action. Non-immunologic CoU (NICoU) is due to vasogenic mediators without the involvement of immunological processes. Urticariogens may act following different patterns. The most classic example concerns dimethyl sulfoxide (DMSO), which damages the blood vessels, making them leaky and leading to mast cell degranulation (22). Sharp hairs from animals or spines from plants penetrating the skin can deliver a cocktail of irritant chemicals or pro-inflammatory mediators causing NICoU (23). The pathogenesis of immunological CoU (ICoU) reflects a type I hypersensitivity reaction, mediated by allergen-specific immunoglobulin E (IgE) in a previously sensitized individual (24). Skin challenge involves allergen penetration through the epidermis, IgE binding on mast cells, its degranulation, and the subsequent release of histamine and other vasoactive substances like prostaglandins, leukotrienes, and kinins.

A combination of type I and type IV allergic skin reactions, the latter supported by positive delayed patch tests, has been suggested as PCD pathogenesis (25). PCD is considered an eczematous IgE-mediated reaction through proteins. PCD has been shown to have a similar reaction pattern to aeroallergen-induced atopic eczema or dermatitis (40).

Demonstrated responsible agents of CoU syndrome

Proteins (molecular weight 10,000 to several hundred thousands) and chemicals (molecular weights below

1000) can trigger CUS (22). Plant or animal proteins, chemicals like drugs and preservatives, or more diverse substances like metals and industrial chemicals can induce ICoU. Raw fruits and vegetables are common causes of ICoU in daily life. Natural rubber latex allergy raised global research interest at the end of the 20th century. Latex sensitization risk factors include atopy and prolonged exposure via the damaged epidermis (e.g., glove wearers with hand eczema). Low molecular weight molecules normally act as haptens, but for some of them, IgE antibodies have been also demonstrated (e.g., sensitized workers reactive to platinum and nickelsserum albumin complexes) (26–28).

NICoU is defined by stinging nettle wheals induced by *Urtica dioica*. Other responsible agents are preservatives, fragrances, and flavorings in cosmetics, toiletries, topical medications, or foodstuffs like benzoic and sorbic acid (29, 30). Household, industrial, insecticide and laboratory chemicals can also induce NICoU.

Few substances elicit mixed features of NICoU and ICoU through an unestablished mechanism. Other than these, IgE is involved in ammonium persulfate-induced CoU, wherein specific IgG and IgM activate the complement cascade through the classical pathway (31, 32). Immediate reactions to formaldehyde seem not to be mediated by IgE playing a prostaglandin role because of increased thromboxane B2 and prostaglandin PGF2 levels (33, 34).

Many kinds of compounds are responsible for occupational and non-occupational CUS including animal products, plants and plant derivatives, foods, fragrances, cosmetics, flavorings, medications, preservatives, disinfectants, enzymes, metals, and miscellanea of different substances (Table 1).

Table 1 Compounds responsible for occupational and non-occupational CUS.

Animal products
Plants and plant derivatives
Foods
Fragrances
Cosmetics
Flavorings
Medications
Preservatives
Disinfectants
Enzymes
Metals
Miscellanea of different substances

Symptoms of CUS-staging the severity (Tables 1–3)

The main manifestation of CoU is the wheal, angioedema, or both. Eczema can be the sole manifestation of the PCD. Pruritus is almost always present as it is the hallmark symptom (35, 36). Our clinical experience suggests that CoU and PCD can be acquired simultaneously by the same patient induced by the same trigger factor. CoU and PCD encompass CUS.

CUS has been classified in four stages. Stages 1 and 2 show cutaneous symptoms. Stage 1 includes flare reactions, wheals and eczema, as well as symptoms like itching, tingling, or a burning sensation. When CoU is present, it shows itchy wheals that are strictly limited to contact areas and disappear within a few hours without residual lesions. PCD typically affects the hands (especially the fingertips) and sometimes extends to the wrists and arms. Chronic paronychia, with redness and swelling of the proximal nail fold after handling food (37), and natural rubber latex (38) have also been observed in PCD.

Table 2 Definition of the cutaneous manifestations involved in Stage I of CUS.

CoU
Immediate Contact Dermatitis (chemicals, proteins, Protein Contact Dermatitis, PCD)
Itching, tingling or burning sensation
– CoU refers to a wheal and flare reaction following external contact with a substance; it usually appears within 30 min and clears completely within hours, without residual signs of irritation.
– Dermatitis refers to tiny vesicles that rapidly appear after external contact with a substance; in some cases it can be demonstrated only on slightly or previously affected skin and can be part of the mechanism responsible for chronic eczema.

Table 3 Stages of the CUS.

Stage 1	Localized urticaria (redness and swelling) Immediate Contact Dermatitis (eczema-protein contact dermatitis) Itching, tingling, or burning sensation
Stage 2	Generalized urticaria
Stage 3	Bronchial asthma (wheezing) Rhinitis, conjunctivitis (runny nose, watery eyes) Oro laryngeal symptoms (lip swelling, hoarseness, difficulty in swallowing) Gastrointestinal symptoms (nausea, vomiting, diarrhea, cramps)
Stage 4	Anaphylactic or anaphylactoid reaction (shock)

Stage 2 refers to the development of generalized urticaria after a local contact.

Meanwhile, Stages 3 and 4 include extracutaneous reactions or symptoms that may also occur as part of a more severe reaction. Stage 3 may include bronchial asthma, rhino-conjunctivitis, orolaryngeal symptoms, or gastrointestinal dysfunctions. Internal organs may be involved in CUS patients, depending on the allergen or preexisting conditions like atopic dermatitis (39, 40). By contact or in the case of a volatile allergen, rhino-conjunctivitis and asthma may accompany the skin manifestations, as in the case of bakers who are in continuous contact with flour. Abdominal pain, diarrhea, and oral allergy syndrome may develop when the allergen comes in contact with the oropharyngeal mucosa (41). The severity of this multi-systemic disease has been reported by Von Krogh and Maibach (22). Finally, in Stage 4, anaphylactic or anaphylactoid reactions may occur as the most severe type of CUS manifestation. CoU can be life threatening; in fact, certain substances like latex protein can induce anaphylaxis and even death.

Cutaneous lesions involved in CoU

CUS clinical symptoms are determined by the route, duration and extent of exposure; the inherent sensitizing properties of the allergen; and the genetic and/or acquired susceptibility of an individual.

If we talk about urticaria, the disease is defined by its primary lesion, which is called wheal or hive. This lesion is characterized by three major features, namely, a transient edema of the dermal tissue, a surrounding reflex erythema, and intense pruritus or itch at the same time (42). Clinically, these three typical features are as follows: central swelling of variable size, almost invariably surrounded by a reflex erythema, and itching or sometimes burning sensation. The wheal has a fleeting nature and the skin returns to its normal appearance usually within 1–24 h (43). Angioedema is characterized by a sudden, pronounced erythematous or skin colored swelling of the lower dermis and subcutis with frequent involvement below the mucous membranes. Sometimes, this is painful rather than itchy, and frequently occurs below the mucous membranes. Its resolution takes up to 72 h. According to the latest published consensus classification of chronic urticaria, CoU belongs to the group of inducible urticarias (58) (Table 4).

CoU is characterized by a local immediate and/or delayed urticarial reaction, with swelling and redness

Table 4 Classification of chronic urticaria subtypes.

Chronic urticaria Subtypes	
Chronic spontaneous urticaria (CSU)	Inducible Urticaria
Spontaneous appearance of wheals, angioedema or both ≥ 6 weeks due to known or unknown causes	Physical urticarias
	Symptomatic dermographism ^a
	Cold urticaria ^b
	Delayed pressure urticaria ^c
	Solar urticaria
	Heat urticaria ^d
	Vibratory angioedema
	Cholinergic urticaria
	CoU
	Aquagenic urticaria

^aAlso called urticaria facticia, dermographic urticaria, ^balso called cold CoU, ^calso called pressure urticaria, ^dalso called heat CoU.

Source: Zuberbier et al., The EAACI/GA2LEN/EDF/WAO Guideline for the definition, classification, diagnosis, and management of Urticaria, 2013 revision and update.

at sites of epidermal or transdermal contact with certain agents. Generalized cutaneous reactions, rhinitis, asthma, or anaphylactic reactions may be associated. Thus, CoU differs from other types of urticaria by the route of access of the antigen or the noxious agent to the body. It penetrates transepidermally, whereas the more common mode of absorption of urticarial substances is transmucosal, which occurs via the respiratory or gastrointestinal tract. CoU is the oldest form of urticaria recorded. In fact, the association of nettles and urticaria was discussed in the Greek literature more than 2000 years ago (44).

The basic clinical appearance of the primary lesion of CoU does not differ from that of other types of urticaria. Depending on the type of contact, the wheal can show different aspects. Linearly arranged wheals are habitually caused by nettles of plants, while punctate wheals arise exactly at the site where the stinging hairs penetrated the skin. The shape of the wheals can also change with time, and intense reactions induce confluent lesions. Wheals can start in a follicular pattern if the contactant penetrates through the hair follicles. The associated local symptoms are tingling, itching, and sometimes burning at the sites of the wheal. Burning of the lips can also occur when patients react to food.

The wheals start with redness at the site of contact, followed by whealing at the same site within 10–30 min after contact. The maximal size is reached 45 min afterwards, and within 2 h, the swelling disappears. Generally, redness can persist even up to 6 h and may remain for more than 24 h in some rare cases. CoU can reappear

after 4–5 h; this dual response has been demonstrated experimentally in the ears of BALB/mice and in humans (45). Delayed onset of CoU after repeated applications of the trigger substance has also been reported (46). The time course and intensity of CoU lesions differ depending on the nature of the eliciting agent. This variability may also be due to differences in the reactivity of the cells, which secrete the vasoactive amines or the sensitivity of the target tissue to the mediators or chemicals released.

Useful tools to diagnose the etiology of CoU

Diagnosis of CUS is based on full medical history and skin testing with suspected substances. In vitro techniques are available for only a few allergens, including latex. The measurements of specific IgE in serum are useful for some proteins. The basophil activation test is based on the demonstration of CD63 expression following exposure to allergens by flow cytometry. It can be interesting when rare allergens are studied when specific IgE antibodies are not available. This method has been found to be useful in examining chicken meat in a previous study (47).

The simplest cutaneous provocation test for ICoU, the NiCoU, is the “open test”. The suspected substance is applied and gently rubbed on slightly affected skin or on a normal-looking 3×3 cm area of the skin, either on the upper back or the extensor side of the upper arm. Often, it is desirable to apply contact urticants to skin sites suggested by the patient’s history. A positive result is an edema and/or erythema typical of CoU. An immunological and non-immunological contact reaction usually appears within 15–20 min, with the non-immunological one lasting within 45–60 min. ICoU can also show delayed onset, although this is rare. Open testing is generally negative unless the substance is applied on damaged or eczematous skin, where it may cause a vesicular reaction.

When the open test result is negative, “prick testing” of suspected allergens is often the method of choice for immediate contact reactions. The skin prick test with fresh material or commercial reagents is the gold standard. The principle of the prick test relies on bringing a small volume of allergen (~5–10 nL) into contact with mast cells by puncturing the skin with a lancet. When a prick by prick is done with the same lancet, the fresh material is pricked, after which the skin is immediately punctured (Figure 1). A positive reaction is assessed after 15–20 min. The diameter of the classical wheal and flare reaction of

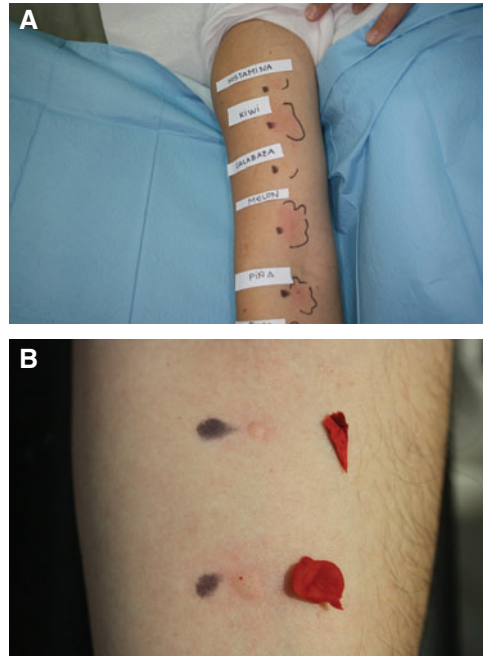


Figure 1 Prick test in two CoU patients: (A) positive prick by prick test by different fruits in a patient with CoU and systemic involvement showing occupational relevance as she worked as fruit vendor (B) positive prick by prick induced by color plasticine in a patient who suffered from hand wheals consequence of the plasticine manipulation.

the skin is measured. The released mediators, mainly histamine, are only present in the wheal.

Sometimes a “rubbing test” (i.e., gentle rubbing with the material on intact or lesional skin) might be required if an open test result is negative. The “scratch test” and “chamber scratch test” (contact with a small aluminum chamber for 15 min) are less standardized than the prick test, but are useful when a non-standard allergen must be studied. However, the former carries a higher risk of false-positive reactions and lacks sensitivity compared with the prick test.

For the prick, prick by prick, rubbing and scratch tests, histamine hydrochloride serves as the positive control and aqueous sodium hydroxide serves as the negative reference. A proposed scheduled protocol with consecutive tests has been proposed to study immediate contact skin reactions (Figure 2).

When other than cutaneous organs are involved, it is important to begin ICoU testing with much diluted allergen concentrations and to use serial dilutions to minimize allergen exposure. When testing with poorly or non-standardized substances, control tests should be assessed on at least 20 people to avoid false-positive interpretations. Non-steroidal anti-inflammatory drugs and antihistamines should also be avoided because of the

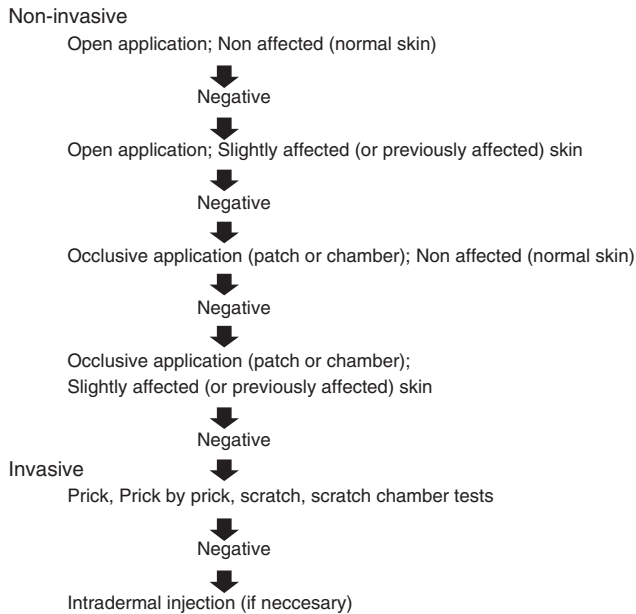


Figure 2 Diagnostic algorithm proposed to assess CoU etiology.

risk of false negative results. Following the recommended protocol is also important for minimizing the occurrence of hazardous extra-cutaneous reactions. Life-threatening reactions have been documented during skin tests; therefore, caution is advised, especially when testing certain occupational substances. Likewise, skin tests should be performed only if resuscitation equipment and trained personnel are readily available (48–50).

Common environmental causes of CoU – some key messages

In the general population, it is estimated that the prevalence of latex allergy is <1%. Currently, there are 13 allergens of latex that have been well identified and characterized; these are labeled by Hev b1-13. The current diagnostic algorithm for allergy to latex includes a thorough anamnesis, in vivo skin tests, the request for latex-specific IgE and, if necessary, a provocation test with a latex glove. It is also important to identify susceptible individuals who may be allergic to latex. The prevention of latex allergy is based on primary prevention and may require the substitution of latex.

Enzymes are complex proteins or glycoproteins produced by living organisms for the purpose of accelerating biochemical reactions and metabolic processes. Nowadays, protein engineering can modify or create enzymes with increased stability or with activity on new substrates.

Cutaneous contact with enzymes may give rise to irritant reactions as well. For example, inhalation of large amounts of proteases can damage the airway and lead to the development of emphysema. Commonly, enzymes behave as allergens and are mostly responsible for immediate reactions mediated by specific IgE antibodies causing CoU and protein contact dermatitis; the respiratory tracts are also often involved. Its occupational relevance should always be assessed and primary preventive measures must be developed.

Plants in the environment like as weeds, woods or ornamentals, cause CUS. IgE-mediated urticaria is predominantly found in cultivated plants, whereas toxic or non-immunological urticaria is most commonly seen in wild plants. Several species of plants have been reported to cause urticaria, by unknown/unclassified mechanisms. The common diagnostic tools are the prick-prick test, histamine release test, or use test. All tests should be controlled using 10–20 non-allergic volunteers in order to determine whether the reaction is immunological.

Agriculture has high rates of occupational skin diseases reported. Delayed contact allergy commonly occurs from pesticides; however, a scarcity of reports describe pesticide-induced CoU. Our present knowledge of CoU due to agricultural chemicals, pesticides in particular, remains deficient. According to the opinion of some experts, if the testing methodology to determine the potential causes of CoU becomes standardized, along with improved accuracy of physician's diagnoses, then reports of pesticide-induced CoU will undoubtedly increase.

Direct or indirect skin contact with animals and animal-derived products occurs in numerous occupations, in everyday life, and while one is engaged in hobbies. Proteins in animal epithelia, excretions, and organs can cause both immunologic and non-immunologic immediate skin reactions. Contact reactions from food items can also be caused by contaminants, parasites, or added substances. Individually tailored skin tests for both immediate allergy and specific IgE in blood are needed for diagnosing immediate allergy to animals or animal products. Commercial test materials can give false negative results; thus, the skin tests should be made, if possible, with the same materials and in the same format as when they caused the skin problems being diagnosed.

Foods responsible for CoU syndrome include fruits, vegetables, spice, plants, animal proteins, grains, and enzymes. Food proteins are the most frequent causative proteins involved in CUS. Diagnosis of CoU/protein contact dermatitis is based on a full clinical history and on skin tests. Food additives responsible for CoU syndrome include flavoring, fragrances, taste enhancers,

conservative and preservatives agents, and coloring agents and dyes. If food additives are involved, diagnostic tests must be defined and standardized.

Seminal plasma hypersensitivity is increasingly being recognized as a cause of anaphylaxis and/or intermittent episodic vulvovaginitis. Localized seminal plasma hypersensitivity presents with immediate post-coital vulvovaginal burning, pain, and swelling rarely associated with vesicles can occasionally be present with systemic involvement. It is believed that this condition is more common than recognized. Seminal plasma hypersensitivity can be demonstrated with a positive prick test reaction, radio allergo immuno assay (RAST), and specific RAST inhibition in addition to neutralization of passive transfer antibodies. The most effective treatment approach for women with IgE-mediated seminal plasma hypersensitivity is immunotherapy.

Topical drugs or, occasionally, systemic drugs that come in contact with the skin or mucosae, may induce CoU, which is certainly very often overlooked. Moreover, as they all are transient, they are seldom present at the time of consultation or at the time of testing. Complementary tests (skin tests with immediate readings and, eventually, *in vitro* tests) are mandatory in certain situations, as a precise diagnosis of the culprit drug, and a suggestion of alternative safe drugs, can be lifesaving. Any drug can induce an immediate reaction, but most cases have been described with betalactam antibiotics, topical anesthetics, and more recently, with antiseptics like chlorhexidine. Published reports of CUS induced by other drugs represent relatively exceptional cases.

Cosmetic components can cause CoU with or without systemic symptoms, and may sometimes be life-threatening. CUS induced by components included in cosmetics is grossly under-diagnosed and under-reported because patients lack awareness. Hair-dye chemicals and bleaches, hair glue, antimicrobial agents and preservatives, fragrance components, toothpaste flavors, botanically-derived cosmetic ingredients, permanent makeup and tattoos, and even alcohol could trigger CUS.

Preservatives and disinfectants are well documented causes of allergic contact dermatitis; CUS due to preservatives and disinfectants is less commonly studied. It is widely accepted that sodium benzoate, benzoic acid, benzyl alcohol and sorbic acid cause non-immunologic CoU and formaldehyde, parabens, povidone-iodine, chloramine and chlorhexidine can cause immunologic CoU. Preservatives and disinfectants may also cause generalized urticarial, bronchial asthma, rhinitis, conjunctivitis, otolaryngeal and gastrointestinal symptoms and even anaphylaxis. The mechanism through most of the

actually described preservatives responsible for immediate cutaneous reaction is unknown (e.g., isothiazolinones or formaldehyde releasers).

Reactive dyes (usually an azo, anthraquinone or phthalocyanine derivative) show different reactive functional groups to which carrier proteins bind to induce immune responses. Reactive dyes can be responsible for CUS in all stages (Stages 1–4). Patch testing, prick testing, bronchial challenge tests, and detection of specific IgE to RD-human serum albumin conjugates in serum are used to assess responsible agents for the reaction although these still need standardization. This means that it is still difficult to establish the relevance between the reactive dyes responsible for the CUS and the textile composition involved.

Prevalence of CoU from hairdressing products is not fully documented, and only case reports and case series have been published. Hair shampoos, hair conditioners, hair dyes and bleaches, permanent wave preparations, fragrance, and other styling products like sprays, gels, waxes, mousses, lotions, and pomades have been described as responsible for CUS symptoms. Hairdressers who are exposed daily to hair dyes and bleaches join those from other occupations with a well demonstrated cutaneous disease. Proper handling of such trigger substances requires special education and knowledge of specific preventive measures.

In spite of the frequent exposure to metals, few cases of CoU caused by metals have been reported. The metals involved in CoU are all members of the group called transitional metals in the periodic table of elements. Metals are mainly allergenic as salts and not as the metallic form. The mechanism behind CoU caused by metals is unclear, but an IgE-mediated mechanism as indicated in most cases is supported by a positive SPT to the metal.

Epoxy resin is commonly used in occupational and non-occupational setting. The epoxy-resin system includes epoxy resins and other components like curing agents, reactive diluents, modifiers, and additives. Contact dermatitis caused by epoxy resin is often described in the literature although CoU from epoxy compounds has infrequently been reported and often represents occupational cases. Skin prick test with the “own” epoxy resins helps in diagnosis, that is, when provoked, a positive wheal can be observed. However, further studies to standardize the diagnostic method are required.

Organic acid anhydrides used in the chemical industry are cyclic and mostly highly reactive with low-molecular weight. They have the ability to cause respiratory immunoglobulin E-mediated sensitization, and occupational rhinoconjunctivitis and asthma. The adverse health

effects occur in the use of the compounds as curing agents for epoxy resins. Workers may be exposed to organic acid anhydrides in powder or liquid form during various manufacturing processes (e.g., during organic acid anhydrides synthesis or when epoxy resins are hardened, polyester paints are cured, alkyd or polyester painted metal surfaces are welded, or when paints are burned from surfaces). Although the symptoms of CoU are often mild and transient, it is important to diagnose immediate sensitization and investigate possible respiratory symptoms.

Treatment and prevention of environmental CoU

The treatment of CoU requires the identification of the eliciting trigger and knowing how to avoid it. Primary and secondary prevention are highly recommended when CoU shows occupational relevance, along with necessary common guidelines, to prevent well known occupational risks like latex allergy, to name a few (51).

Considering their good safety profile, second generation antihistamines must be considered as the preferred first-line symptomatic treatment for most cases of CoU. Before considering alternative treatment, higher doses of antihistamines should first be used. Severe cases of CUS require a short course of oral steroids or even treatment in an emergency unit.

Conclusion

Surrounding things, conditions, or influences in the environment can be responsible for cutaneous impairment resulting in skin diseases. CoU is one of these diseases. The objective of this paper is to contribute to the general knowledge of this disease in helping the dermatologist with its diagnosis, thus encouraging them to recognize, study, and report the new isolates or series of cases worldwide.

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