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REVIEW ARTICLE

Allergic Contact Dermatitis in Pediatric Practice

Kam Lun Hon[1,*], Alexander K.C. Leung[2], James W.C.H. Cheng[3], David C.K. Luk[3], Agnes S.Y. Leung[4,5] and Mark J.A. Koh[6]

[1]Department of Paediatrics, CUHKMC, The Chinese University of Hong Kong, Hong Kong, China; [2]Department of Pediatrics, The University of Calgary, The Alberta Children's Hospital, Calgary, Alberta, Canada; [3]Department of Paediatrics and Adolescent Medicine, United Christian Hospital, Kwun Tong, Hong Kong, China; [4]Department of Paediatrics, Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin, Hong Kong, China; [5]Hong Kong Hub of Paediatric Excellence, The Chinese University of Hong Kong, Shatin, Hong Kong, China; [6]Department of Dermatology, KK Women's and Children's Hospital, Bukit Timah Road, Singapore

Abstract: ***Background*:** Allergic contact dermatitis (ACD) is prevalent among pediatric population, adolescent and young adults. Patients with ACD experience a lot of sociopsychological and quality-of-life (QoL) difficulties. Children and their caregivers alike are vulnerable to the burden of ACD.

***Objectives*:** We have, in this paper, provided an overview of ACD and discussed common and unusual causes of ACD.

***Methods*:** We performed an up-to-date literature review in the English language on "allergic contact dermatitis" *via* PubMed Clinical Queries, using the keywords "allergic contact dermatitis" in August 2022. The search included meta-analyses, randomized controlled trials, clinical trials, case-control studies, cohort studies, observational studies, clinical guidelines, case series, case reports, and reviews. The search was restricted to English literature and children.

***Results*:** ACD may be acute or chronic and it affects more than 20% of children and adults with significant quality-of-life impairments. ACD is manifested by varying degrees of cutaneous edema, vesiculation, and erythema. The hypersensitivity reaction is one of the most prevalent forms of immunotoxicity in humans. Localized acute ACD lesions can be managed with high-potency topical steroids; if ACD is severe or extensive, systemic corticosteroid therapy is often required to provide relief within 24 hours. In patients with more severe dermatitis, oral prednisone should be tapered over 2-3 weeks. Rapid discontinuation of corticosteroids can result in rebound dermatitis. Patch testing should be performed if treatment fails and the specific allergen or diagnosis remains unknown.

***Conclusion*:** ACD is common and can be a physically, psychologically, and economically burdensome disease. Diagnosis of ACD is primarily based on history (exposure to an allergen) and physical examination (morphology and location of the eruption). Skin patch test can help determine the causative allergen. Allergen avoidance is the cornerstone of management. Topical mid- or high-potency corticosteroids are the mainstay of treatment for lesions on less than 20% of the body area. Severe cases of ACD may require treatment with systemic corticosteroids.

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1. INTRODUCTION

Allergic skin diseases are very common in paediatric practice [1]. Some diseases are short-lived and only a temporary annoyance, whereas symptoms of more chronic diseases can have lasting effects and cause a significant impact on quality of life (QoL). One of the more common allergic skin diseases is allergic contact dermatitis (ACD) [1-7]. ACD is a form of allergic skin response caused by contact with a specific environmental allergen; the other type of contact dermatitis is irritant contact dermatitis (ICD), which is a non-immunologic process [8-10].

ACD may be acute or chronic with different effects on QoL [11]. ACD is manifested by varying degrees of cutaneous edema, vesiculation, and erythema. It is the most prevalent form of hypersensitive immunotoxicity in humans [6]. ACD is often underrecognized in pediatric patients [11, 12]. The condition should be considered in children with recurrent or chronic dermatitis, especially if the lesion is localized

*Address correspondence to this author at the Department of Paediatrics, CUHKMC, The Chinese University of Hong Kong, Hong Kong, China; Tel: (852) 35052982; Fax: (852) 2636 0020; E-mail: ehon@hotmail.com

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in exposed areas of the body and does not respond to standard topical treatment for dermatitis. Physicians should keep patient-specific factors and emerging trends in mind when managing suspected ACD in children, when they encounter atypical or chronic dermatitis, and consider patch testing in affected children [13, 14].

We have, herein, provided an overview of ACD and discussed common and unusual causes of ACD. We performed a literature review in the English language on "allergic contact dermatitis" *via* PubMed Clinical Queries, using the keywords "allergic contact dermatitis" in August 2022. The search included meta-analyses, randomized controlled trials, clinical trials, cohort studies, case-control studies, observational studies, clinical guidelines, case series, case reports, and reviews. The search was restricted to pediatrics and English literature. The information retrieved from the search was used in the compilation of the present article.

2. EPIDEMIOLOGY

ACD accounts for 20% of contact dermatosis and affects up to twenty percent of individuals in the general population [7, 15, 16]. Its prevalence is rising worldwide [17-20]. In Europe, about twenty percent of the general population has been reported to suffer from ACD on exposure to one or more contact allergens [21].

In a retrospective data analysis of the NACDG (North American Contact Dermatitis Group), 14.6% of patients had positive allergic patch test reactions to one or more topical medication sources [22]. Compared to those without allergic reactions to medications, patients with allergic reactions to medications were found more likely to be older than 40 years and/or have primary sites of dermatitis on the anal/genital region, legs, or trunk. The most common allergens were neomycin (29.4%), bacitracin (29.1%), followed by propylene glycol 100% (10.6%), tixocortol-17-pivalate (10.0%), lidocaine (7.9%), budesonide (4.9%), and dibucaine (4.4%). Propylene glycol (100%) was found to be the most common inactive ingredient (10.6%). Positive patch test reactions associated with mostly clinically relevant topical medications were present in 14.6% of patients. A total of 6.5% of the patients with medication allergy would have had ≥1 positive patch test reactions missed if only tested with the NACDG screening series. Patients with topical medication allergy were two times as likely to have anogenital involvement. Active medication ingredients, especially bacitracin, neomycin, and tixocortol-17-pivalate were frequent culprits.

A Danish study found cobalt in 72.0% and chromium in 54.6% of earrings [23]. The cobalt spot test was positive for one component, but all chromium spot tests were negative. Earrings for piercing release cobalt and chromium, and may be a source of cobalt and chromium allergy [23]. An Israeli study identified nickel sulphate as the commonest contact allergen, especially in atopic individuals, and it was found to be present in 13.4% of the patch tests [24].

A 15-year-period systematic review showed the most common allergens to be nickel, cobalt, thimerosal, fragrance, lanolin, neomycin, and fragrance in children, and nickel, cobalt, thimerosal, potassium dichromate, fragrance, and *Myroxylon pereirae* in adolescents [25].

A 4-year experience of patch testing with the Japanese baseline series reported patch test results of 5,865 patients registered from over 60 facilities [17]. The five contact allergens with the highest positivity were gold sodium thiosulfate (25.7%), nickel sulfate (24.5%), urushiol (9.1%), p-phenylenediamine (8.9%), and cobalt chloride (8.4%). The five contact allergens with the lowest rates were mercaptobenzothiazole (0.8%), formaldehyde (0.9%), paraben mix (1.1%), mercapto mix (1.1%), and p-phenylenediamine black rubber mix (1.4%). Gold sodium thiosulfate and nickel sulfate were reported to have the highest positivity rates.

In patients from the Russian Federation, the frequency of ACD incidence was 26.2%, while that in patients representing the population of the People's Republic of China was 22.2% [26]. Positive patch reactions to allergens were most often observed for thiomersal (29.8%), nickel sulfate (25.2%), and a mixture of carbamates (20.7%) in the Russian group, and for nickel sulfate (30.7%), thiomersal (26.4%), and a mixture of carbamates (23.8%) in the Chinese group. The investigators concluded ACD to be in about a quarter of patients with allergic dermatoses in groups from both Russian and China regions. The investigators also found that increased expressions of defensin and interferon-gamma (IFN-γ) genes can be considered a marker of inflammation in patients with ACD [26].

In a New Zealand series, the 10 most frequent positive allergens were nickel sulfate (22%), fragrance mix I (8.6%), cobalt chloride (7.3%), *Myroxylon pereirae* (5.6%), colophonium (5.1%), p-phenylenediamine (4.9%), methylisothiazolinone/methylchloroisothiazolinone (4.1%), fragrance mix II (3.9%), potassium dichromate (3.5%), and methylisothiazolinone (3.4%) [27].

In Singapore, a recent study found the most frequent reactions to occur in response to nickel sulfate (49%) and fragrance mix (19%) [28]. It was also noted that patients with atopic eczema were more likely to be sensitized to disperse blue dye and less likely to fragrances instead.

2.1. Pediatrics

The efficacy and safety of the TRUE (Thin-layer Rapid Use Epicutaneous) test panels were evaluated in Turkish adolescents and children in an open-label prospective study reported in 2011 that analysed 102 consecutive patients aged six to eighteen years referred for suspected ACD [29]. Positive reactions were found in over 10% of the children to nickel sulfate (29.7%), p-tert-butylphenol formaldehyde resin (16.8%), wool alcohols (15.8%), fragrance mix (12.9%), and cobalt dichloride (12.9%). 76% of the 101 subjects tested positive to ≥ allergens.

In a 2020 report, the most frequently determined allergens by the TRUE test were methylchloroisothiazolinone (16.3%), disperse blue (11.6%), and bacitracin (11.6%). Preservatives, such as formaldehyde, methylchloroisothiazolinone, and formaldehyde releasers are the most frequent al-

lergens in children with ACD. Increased utilization of these compounds in personal hygiene products for children attributes to this finding [30].

A recent 2021 Turkish study in children and adolescents reported a contact sensitization rate of 46.1% [31]. ACD was diagnosed in 30.9% of individuals, comprising occupational (15.3%) and non-occupational (84.7%) ACD. In almost every age group, nickel was the leading allergen. The investigators suggested additional patch testing with mercury/mercury(II) amidochloride, ammonium persulfate, toluenesulfonamide formaldehyde resin, and polyethylene glycol (as a marker for allergy to nitrofurazone) in appropriate Turkish children and adolescents [31].

3. COMMON ALLERGENS

Common allergens associated with ACD are tabulated in alphabetical order in Table **1** [21]. Current prevalence estimates of positive reactions range from 14 to 70% of children patch tested [32, 33]. Globally, the most common allergens are nickel, fragrances, and preservatives [24]. Allergic reactions to p-phenylenediamine (PPD) and chromate are less common, but these often occur in occupationally exposed individuals [34].

Nickel and cobalt are common allergens found in metallic coatings for jewellery, utensils, paper clips, zippers, paints, coins, and many products in common use. Both nickel and cobalt are the most common contact allergens responsible for ACD, with the European Union establishing the "Nickel Directive" to limit sensitisation to the metal. Cobalt is often used in nickel-plated objects and causes ACD as cobalt is commonly found in nickel-sensitised patients. However, the patients' contact history is important to obtain, including their hobbies. Locally, we identified two cases of hand dermatitis by using patch tests, one due to colophony as a lubricant for the musical instrument of Erhu (Fig. **1**), and another one due to nickel and cobalt in pastel paints (Fig. **2**). These cases illustrate the importance of the careful history of recreation exposure together with patch testing in reaching a definite diagnosis for ACD. Co-reactions to metals may occur and should not be misdiagnosed as cross-reactions.

Of note, topical medications, such as local anaesthetics and steroids, can cause ACD [35]. Benzyl alcohol is a widely used solvent, fragrance, and preservative material, and a rare sensitizer in humans. Sensitization to benzyl alcohol occurs primarily in patients with stasis dermatitis. Hence, benzyl alcohol is usually not regarded as a significant contact allergen [36].

Consumer products as well as topical medications contain allergens that can cause ACD [37]. Furthermore, contact allergy to corticosteroid compounds (such as triamcinolone acetonide, tixocortol-21-pivalate, budesonide, hydrocortisone-17-butyrate, and clobetasol-17-propionate) can cross-react. Testosterone and estrogen transdermal patches, local anesthetics (lidocaine, benzocaine, dyclonine, and pramoxine), antihistamines (ethanolamine, piperazine, propylamine, piperidine, phenothiazine, and pyrrolidine), topical antibiotics (spectinomycin, bacitracin, neomycin, and mupirocin),

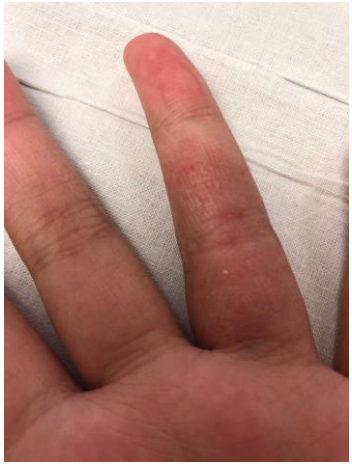

Fig. (1). ACD in a child due to colophony used as a lubricant for the bow of an Erhu. (*A higher resolution / colour version of this figure is available in the electronic copy of the article*).

Fig. (2). ACD involving the hands of a child due to paints, confirmed by patch test. (*A higher resolution / colour version of this figure is available in the electronic copy of the article*).

sunscreen, formaldehyde releasers (diazolidinyl urea, quaternium-15, 2-bromo-2-nitropropane-1,3 diol, imidazolidinyl urea, dimethyloldimethyl hydantoin), the non-formaldehyde releasers (parabens, isothiazolinones, methyldibromo glutaronitrile, thiomerosal, and iodopropynyl butylcarbamate), *Myroxylon pereirae* (balsam of Peru), and fragrance mixes can also cross-react and cause ACD.

3.1. Pediatrics

ACD occurs twice more often in females than in males and often starts at a young age, with a prevalence of 15% in 12 to 16-year-old females [7, 34, 38]. Individuals sensitive to

Table 1. Selected common antigens and medicaments associated with ACD.

Antigens	Remarks and References
Anesthetics	The treatment of ACD involves prolonged use of topical anesthetics, such as diphenhydramine or pramoxine [35, 37, 71-73].
Bacitracin	It is a common topical antibiotic [22, 30, 37].
Colophony	Colophony (Rosin) is sawdust or sap from fir trees and pine trees or sprue, and is often used in adhesives, musical instruments, paints, waxes, lipsticks, topical medications, and many other household and industrial products [74, 75]. The common allergens that share sensitisation with colophony include Balsam of Peru and fragrances. Depilatory wax has been incriminated [74, 76, 77]. ACD may affect the hands (Fig. **1**). The face can also be involved [78].
Myroxylon pereirae (Balsam of Peru)	It is derived from tree resin. It is used in drinks and food, toiletries and perfumes, pharmaceutical items, and medicine. It may be a component of artificial vanilla and/or cinnamon flavorings. The allergenic ingredients of *Myroxylon pereirae* include eugenol, isoeugenol, and cinnamyl alcohol. Two patients presented with perioral dermatitis and cheilitis [79-81].
Chromium	It is used in leather tanning. Also, it is a component of uncured cement/mortar, some bar soaps, and facial cosmetics [23, 27, 82, 83].
Cobalt chloride	It is found in medical products; antiperspirant; hair dye; metal-plated objects, such as buttons, tools or snaps; and in cobalt blue pigment [23, 27, 84].
Formaldehyde	It is a preservative found in paints, paper products, medications, household cleaners, cosmetic products, and fabric finishes. It is often released into products by formaldehyde releasers [30, 37, 85].
Fragrance mix	It is a group of the eight most common fragrance allergens found in cosmetic products, foods, antiseptics, insecticides, perfumes, soaps, and dental products [9, 38]. It is important to consider contact sensitivity to citrus in individuals who have positive reactions to fragrance mix I and II, and are occupationally exposed to citrus fruits [81, 86].
Gold	Gold sodium thiosulfate is a precious compound and metal often found in jewellery and dental materials [87, 88].
Isothiazolinones	These are preservatives used in many household, personal care, and commercial products [27, 37, 89].
Mercaptobenzothiazole	It is used in rubber products, shoes, gloves, and car tires [27, 75, 83, 90, 91].
Neomycin	It is a topical antibiotic common in first aid ointments and creams, deodorants, cosmetics, pet food, and soap. It is found by itself, or in neosporin or triple antibiotics (neomycin, bacitracin, and polymyxin) [22].
Nickel	Nickel sulfate hexahydrate has been recognized as a significant cause of allergy [27, 87, 92, 93]. This is frequently found in stainless steel cookware, jewellery, and clasps or buttons on clothing [87, 92]. Current estimates are that roughly 2.5 million US adults and 250,000 children suffer from nickel allergy [93]. Nickel allergy is preventable [26, 87, 91].
p-Phenylenediamine (PPD)	Para-phenylenediamine (PPD) is an amine mainly used as an ingredient in hair dyes and henna tattoos. Its sensitization if occurs, becomes lifelong. One can develop active sensitization to various products, including different inks, black clothing, dyed fur, dyed leather, hair dye, and certain photographic products [94-96]. Photographic developers, especially those containing metol, also cause ACD [90].
Quaternium-15	Preservatives in cosmetic products (shampoo, self-tanners, sunscreen, and nail polish) and in industrial products (paints, polishes, and waxes) also cause ACD [85, 97-99].
Platinosis	Soluble salts of platinum (Pt-salts) are important allergens in the catalyst industry. Clinical manifestations involve both the skin and the respiratory system [100-102].
Steroid	Paradoxically, topical steroids are used in various types of dermatitis, but these could sensitize the skin and induce contact dermatitis [22, 35, 37].
Thiomersal	Mercury compounds are used in vaccines and in local antiseptics [14, 26, 103].
Urushiol	It is an oily coating from plants of the Toxicodendron genus poison ivy, poison sumac, and poison oak. It is also found in mango skin, mango plants, cashews, and smoke from burning urushiol-containing plants, which can cause skin and severe lung irritation [90, 104].

one allergen are at a higher risk of sensitization to other allergens [7]. Furthermore, family members of patients with ACD are at increased risk of developing ACD [7].

4. PATHOPHYSIOLOGY

ACD occurs in two stages: an induction phase that primes and sensitizes the immune system for an allergic response, and an elicitation phase that triggers a response [6, 7, 39, 40]. ACD involves a type IV, T cell-mediated delayed hypersensitivity reaction elicited by the contact of the skin with an environmental allergen. Contact allergens are soluble haptens (chemical molecules with molecular weight less than 500 daltons) that penetrate the stratum corneum of the skin. Haptens are not immunogenic by themselves. They can only be recognized by the body's immune system after binding to an epidermal protein (protein-reactive) forming a hapten-

protein conjugate. In the induction phase of ACD, the hapten penetrates the stratum corneum and binds to an epidermal protein.

The hapten-protein conjugate is regarded as a foreign body by the Langerhans cells (LCs) and dendritic cells (DCs), which then engulf and process the hapten-protein complex, transport it to the regional lymph nodes *via* lymphatic vessels, and present the antigen to T-lymphocytes. This process is controlled by cytokines and chemokines, including tumor necrosis factor-alpha (TNF-α) and interleukins (IL) (such as IL-1, 13, and 18) that promote or inhibit the mobilization and migration of these LCs [6, 7]. The LCs at the regional lymph nodes differentiate and transform into immunostimulatory DCs, which present the allergenic epitope associated with the allergen to T-lymphocytes. These T-cells then divide and differentiate, and may respond more quickly and aggressively if the allergen is experienced again [41].

During the elicitation phase, re-exposure to the sensitized allergen triggers a reaction in the original site of sensitization as a memory response possibly due to local skin memory T-cells. Also, cytotoxic T-lymphocytes play an important role in controlling the reactivation of allergens in ACD [42]. Memory response usually takes two to three days after contact with the allergen and may persist for two to four weeks. Generally, the intensity of the inflammatory reaction is dependent on the concentration and the sensitizing ability of the allergen [16].

Keratinocytes are critical in the initiation of early type IV hypersensitivity responses. Keratin 17 (K17) is a cytoskeletal inducible protein that regulates multiple cellular processes and drives allergen-induced skin inflammation [43].

Some authors suggest that atopy may have a role to play in ACD [44-47]. A 2017 meta-analysis of 74 studies, however, did not find a significant association between contact sensitization and atopic dermatitis (random effects model odds ratio = 0.89; 95% confidence interval = 0.77 to 1.03) [48]. The investigators found contact sensitization to be increased in individuals with atopic eczema in the general population.

5. CLINICAL MANIFESTATIONS

The symptoms of ACD are very similar to those of ICD [7]. Pruritus is a prominent symptom. Other symptoms include stinging, burning, and pain. The first sign of ACD is an eruption at the site of exposure, usually appearing 24 to 72 hours after exposure to the allergen [7]. In contrast, the eruption of ICD appears immediately after contact with the trigger [7]. Typically, ACD presents as a pruritic, well-demarcated, erythematous, eczematous, indurated, scaly plaque localized to the skin in contact with the allergen [15]. Depending on the type of allergen and the severity of ACD, the skin lesion may take the form of papules, vesicles, bullae, and blisters on an erythematous base [15]. The lesion can ooze, drain, or crust. Swelling/edema may be prominent in areas where the skin is thin, such as the lips and eyelids; the affected area may be tender or warmer. The skin lesion can occur anywhere on the body. In the general population, the skin lesion is common on the hands (22% of cases), across the body (18%), or on the face (17%) [7]. In the pediatric age group, the face, hands, legs, and feet are more frequently affected [11, 15]. ACD lesions may persist for weeks after the exposure of the offending chemical stops.

Once an individual has developed ACD to a certain allergen, the condition will persist life-long and the symptoms will reappear when re-exposure to the allergen. Continued or repeated exposure to the allergen may result in chronic ACD. In chronic ACD, the affected skin may become dry, scaly, hyperpigmented, leathery, and lichenified [11]. In addition to the lichenified pruritic plaque, excoriation, cracks, fissures, and impetiginization may develop.

Some products cause ACD only when the skin is exposed to sunlight (photosensitivity). In such cases, the eruption is limited to photo-exposed areas of the body. These products include sunscreen, shaving lotions, sulfa ointments, perfumes, topical nonsteroidal anti-inflammatory drugs, coal tar products, and a few airborne allergens.

6. DIAGNOSIS

Diagnosis of ACD is primarily based on history (exposure to an allergen) and physical examination (morphology and location of the eruption) [49]. The location of the skin lesion may provide clues to specific allergens. For example, ACD around the wrist may suggest an allergic response to a bracelet. ACD on the hands is often due to contact with hand soaps, detergents, slime, moisturizers, fragrances, preservatives, rubber, metals, or topical antibiotics [7]. ACD on the shin may result from shin guards that contain allergens, such as neoprene rubbers or glues [50]. ACD on the face is often due to makeup, spray-on fragrances, moisturizers, wrinkle creams, electronic devices that contain nickel, and topical medication [7]. ACD is often caused by shampoo and conditioner dripping down from the hair along the eyelids and the sides of the head and neck [7]. Inflammation involving one side of the face suggests the transfer of an allergen from either the hands or the face of a partner [7]. ACD secondary to poison ivy often presents as linear streaks of acute dermatitis where the poison ivy comes into contact with the skin. Lack of recurrence along with avoidance of the suspected allergen supports the diagnosis of ACD.

7. PATCH TESTING

A patch test is a contact-delayed hypersensitivity test commonly used to determine the exact external chemical/allergen causing the ACD [51-53]. Patch testing is the gold standard for the identification of contact allergens in patients with chronic and/or recurrent rashes that are not readily explained by the history and physical examination [24, 51, 52, 54]. Sensitized patients have primed antigen-specific T-lymphocytes that trigger a reaction when antigens are applied to the skin as a result of prior sensitization. Small quantities of potential allergens are applied to small patches and placed onto the skin, preferably on the patient's upper back, followed by the thighs [15, 50]. Hypoallergic adhesive

tape is applied over the patches to avoid dislodging. The patches are removed after 2 days. A raised bump will be noticeable underneath the patch if a skin reaction has occurred to one of the substances applied. The tests are read at 72 or 96 hours again. Patch testing is contraindicated in patients with a known history of severe allergic reactions to suspected allergens, or extensive or generalized active eczema. Patch test systems can be a comprehensive panel of 70 to 80 allergens. They can also be limited to a more targeted allergen series. The TRUE test panels contain 35 allergens. The decision for allergen selection is based on an accurate history and physical examination. On the other hand, false negative reactions may occur from inadequate allergens used, improper placement or dislodgement of chambers, immunosuppression (including the use of topical corticosteroid on the test area), or exposure to ultraviolet light in the setting of phototherapy or sun tanning [50]. Patch testing is generally considered safe and well-tolerated. Complications of patch testing are common and include excited skin syndrome (also known as angry back syndrome), active sensitization through exposing the child to new allergens, and rarely anaphylaxis. Appropriate pretesting of patients may mitigate some of these complications.

The chemicals in the baseline series depend on which patch test is being used. The European baseline series used in 2006 included potassium dichromate, 4-phenylenediamine base (PPD), thiuram mix, neomycin sulfate, cobalt chloride, benzocaine, nickel sulfate, clioquinol (chinoform and vioform), colophonium, parabens mix, N-Isopropyl-N-phenyl-4-phenylenediamine, lanolin alcohol, mercapto mix, epoxy resin, *Myroxylon pereirae* resin, 4-tert-Butylphenol formaldehyde resin, mercaptobenzothiazole, formaldehyde, fragrance mix (cinnamic alcohol, cinnamic aldehyde, hydroxycitronellal, amylcinnamaldehyde, geraniol, eugenol, isoeugenol, oakmoss absolute), sesquiterpene lactone mix (alantolactone, dehydroxosus lactone, costunolide), quaternium-15 (Dowicil 200), primin, Cl+Me-isothiazolinone (Kathon CG, 100 ppm), budesonide, tixocortol pivalate, methyldibromo glutaronitrile, methylisothiazolinone, fragrance mix II, and textile dye mix. Most test substances were single compounds, but some of the tests were mixtures of closely-related chemicals.

The T.R.U.E.® Test allergens (29 allergens+) do not include sesquiterpene lactone, primin, or methyldibromo glutaronitrile. The North American Contact Dermatitis Group (NACDG) Standard Screening Tray includes a greater range of allergens. It does not include clioquinol, primin, or thiomersal. The International Standard Series (2001) does not contain cobalt, benzocaine, clioquinol, parabens, N-Isopropyl-N-phenyl-4-phenylenediamine, sesquiterpene lactone, primin or tixocortol, but imidazolidinyl urea is included.

7.1. Pediatrics

As the causative allergens differ between children and adults, it is advisable to use pediatric-specific patch test series for children [15, 33]. It is important to avoid water and sweat on the testing area, which is particularly challenging in the pediatric age group. Measurement as well as interpretation of the test results require training and experience, and consideration of clinical relevance. False positive reactions may result from high concentrations of allergens applied at the test site and active dermatitis at the test site [50].

8. LABORATORY STUDIES

Laboratory tests are usually not necessary in the evaluation of patients with suspected ACD. At times, laboratory tests are useful in the exclusion of other disorders with similar clinical features. For example, a potassium hydroxide (KOH) examination of scrapings from the border of an eruption should be considered if a fungal infection is suspected.

9. SKIN BIOPSY

Lesions of ACD, ICD, and atopic dermatitis (AD) or eczema share similar clinical features [55]. Eosinophils are more commonly observed in AD than in ICD or ACD. No other significant differences have been found regarding patterns of epidermal appearances, dermal infiltrates, or immunophenotyping. Dermal eosinophils are more often associated with AD, necrotic epidermal keratinocytes with ICD, and focal parakeratosis with ACD. Hence, the differentiation of ACD, ICD, and AD is based on clinical features and results of allergy tests. Histopathology does not reliably differentiate between ICD, ACD, and AD, but helps to exclude other conditions, such as tinea, dyshidrotic eczema, psoriasis, or T-cell lymphoma. In ACD, spongiosis is the dominant feature and the epidermis is of normal thickness. Exocytosis of eosinophils and lymphocytes into the spongiotic foci is an additional feature of ACD.

10. COMPLICATIONS

ACD is a common dermatologic disorder associated with disability and chronicity [56]. The disorder has an adverse effect on QoL, particularly in psychological wellbeing and social functioning [56-58]. QoL of patients with ACD could be quantified [57]. A modified questionnaire based on Skindex-16 QoL scores demonstrated that ACD has significant adverse effects on life quality and emotional impacts, especially when the face and the hands are affected, or occupationally related [56, 59]. Early diagnosis of the disease can improve QoL outcomes in patients with ACD. It is important to note that individuals who elected to change jobs because of their skin condition reported worse QoL than those who retained their current positions [60]. According to a modified questionnaire for QoL, there were no gender-related differences in QoL scores [60]. Non-Caucasians, younger individuals, and industrial workers reported significant QoL impairment with ACD. However, the questionnaire was not designed for the pediatric age group.

A 17-question survey instrument is available to assess the impacts of ACD on QoL. Though not designed for use in children with ACD, the questionnaire can assess the specific and most problematic aspects of individuals with ACD [61].

One research group validated a novel QoL instrument for ACD [62]. The index can be reliably used to assess changes in QoL over time.

In some dark-skinned individuals, areas of hypopigmentation or hyperpigmentation may develop from ACD. Rarely, ACD can be complicated by secondary bacterial infection.

10.1. Pediatrics

No disease-specific QoL in the pediatric age group has been developed owing to the fact that ACD is more a disease of young adults. The weak point is that these scores are short-term scores and often subjective and symptom-based. PADQLQ (Pediatric Allergic Disease Quality Life Questionnaire) is a composite allergy score recently found to reflect disease severity in ACD [63]. Thus far, no trial has used PADQLQ for pediatric patients with ACD.

11. MANAGEMENT

The fundamental step in managing ACD is recognition and accurate diagnosis, followed by identification of the culprit and the source of the chemical [49, 64, 65]. Allergen avoidance is the cornerstone of management. The recognition is permanent once the immune system registers the allergen. Parents should be educated about avoidance of the offending product and the use of an alternative, allergen-free product.

Topical mid- or high-potency corticosteroids (*e.g.*, triamcinolone or clobetasol 0.05%) are the mainstay of treatment for lesions less than 20% of the body area. The medication should be used judiciously and according to the prescribed directions. Prolonged use of topical corticosteroid should be avoided as prolonged use of the medication may lead to skin atrophy, striae, telangiectasia, depigmentation, subcutaneous adipose tissue atrophy, rosacea, perioral dermatitis, steroid acne, and folliculitis [66, 67]. Percutaneous absorption of steroids may result in systemic side effects, which include hypothalamic-pituitary-adrenal suppression, Cushing's syndrome, osteopenia/osteoporosis, glaucoma, cataracts, and growth retardation. Topical calcineurins, such as tacrolimus and pimecrolimus, are reasonable alternatives in patients whose eruption involves the face, genitalia, or flexural areas and when topical corticosteroids have been used for a prolonged period of time.

Generally, severe or extensive (>20% of the total body surface area) cases of ACD may require treatment with systemic corticosteroids (*e.g.*, oral prednisone). Long-term use of systemic corticosteroids should be discouraged because of the associated morbidity. Depending on the duration of the use, systemic corticosteroids may have to be gradually tapered, with dosing schedules ranging from 12 to 20 days to prevent the relapse of the eruption (while the chemical allergen still remains in the skin).

The distress caused by ACD may be ameliorated by wearing cotton clothing to reduce frictional skin irritation. Soaps with perfumes and dyes must be avoided. Symptomatic treatments can provide short-term relief of pruritus. Cool compresses can be used to ease the pruritus. In ACD due to contact with poison ivy, cool oatmeal baths and calamine lotion when used additionally may relieve pruritus. Oral sedative antihistamines, such as hydroxyzine or diphenhydramine, may be used in more severe cases of ACD to relieve the intense itching. Topical antihistamines are not advised as there might be treatment-associated contact dermatitis from the topical antihistamines. Although the symptoms of ACD usually resolve without treatment in two to four weeks, specific medication may hasten the healing and reduce the discomfort if the trigger is avoided.

Some patients with chronic ACD recalcitrant to treatment with topical and systemic corticosteroids may benefit from phototherapy using ultraviolet-A (PUVA) plus psoralen. Rarely, patients with severe ACD resistant to other therapies may require immunosuppressive agents (*e.g.*, mycophenolate). Preliminary studies have shown that biologics, such as dupilumab and infliximab, may be of use in the treatment of recalcitrant ACD [68].

12. PROGNOSIS

The prognosis depends on how well the affected person can avoid the allergen. ACD may persist if the allergen cannot be identified and avoided. The prognoses of occupational and nonoccupational contact dermatitis, ICD, and ACD are similar and often poor [69, 70]. Only a few studies on the prognosis of occupational contact dermatitis have shown that a job change by the affected individual may lead to the clearance of dermatitis. Occupational ACD can evolve into persistent occupational dermatitis. Chromium and compositae ACD often have a poor prognosis. Repeat patch testing over time may help identify additional aggravating allergens.

CONCLUSION

ACD is highly prevalent among children. Patients with ACD experience sociopsychological and QoL burdens more than those in the general population. Children as well as their caregivers are especially vulnerable to the burden of ACD. Localized acute ACD lesions are often treated with mid- or high-potency topical corticosteroids. Extensive or severe ACD may require systemic steroid therapy. Patch testing should be considered if treatment fails to ascertain the diagnosis or specific contact allergen.

AUTHORS' CONTRIBUTIONS

Professor Kam Lun Hon is the principal author, while Professor Alexander K.C. Leung, Dr. James Wesley Cheng, Dr. David Luk, Dr. Agnes S.Y. Leung, and Dr. Mark J. Koh are coauthors. All the authors contributed to drafting and revising of the manuscript, and approved the final version submitted for publication.

LIST OF ABBREVIATIONS

ACD	=	Allergic Contact Dermatitis
AD	=	Atopic Dermatitis
DC	=	Dendritic Cell
ICD	=	Irritable Contact Dermatitis
IL	=	Interleukin

LC = Langerhans Cell

PADQLQ = Pediatric Allergic Disease Quality Life Questionnaire

QoL = Quality of Life

TRUE = Thin-layer Rapid Use Epicutaneous

CONSENT FOR PUBLICATION

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CONFLICT OF INTEREST

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