

Cutaneous Reactions to Aluminum

Sara A. Kullberg, BA,*†‡ Jordan M. Ward, MD,§ Yujie Linda Liou, DO,¶ Amber Reck Atwater, MD,§
Sara Hylwa, MD,*|| Anne B. Neeley, MD,* and Erin M. Warshaw, MD, MS*‡||

Cutaneous exposure to aluminum may occur via contact with metal items, medications, and personal care products. Despite the widespread use of aluminum, allergic contact dermatitis is relatively rare. Sensitization is often incidentally identified during patch testing with aluminum-based chambers. This article presents several cases along with a literature review summarizing prevalence and clinical manifestations of cutaneous reactions to aluminum, recommendations for patch testing, sources of aluminum, and reproducibility of aluminum allergy over time.

SOURCES AND FUNCTION OF ALUMINUM

Aluminum is found in medications, immunizations, antiperspirants, food, cosmetics, jewelry, and electronics. It is also used in many manufacturing and construction industries.¹ Daily exposure to aluminum in humans is estimated to be between 0.06 mg (from inhalation of dust particles) and 3500 to 5300 mg (from consumption of aluminum antacids).^{2,3} Cutaneous exposure to aluminum may occur via elemental metal (with its associated soft, corrosion-resistant, recyclable properties) or aluminum salt (eg, aluminum sulfate, aluminum acetate, aluminum chloride hexahydrate).¹

CLINICAL CHARACTERISTICS OF ALUMINUM CONTACT ALLERGY

Exposure to aluminum is pervasive, yet aluminum allergy is surprisingly rare.⁴ The first case of aluminum contact allergy was reported in 1979 in a child who had previously undergone hyposensitization therapy for allergic rhinitis who presented with persistent axillary dermatitis from antiperspirants and, upon standardized patch testing, developed prominent “ringlike” reactions to aluminum Finn Chambers.⁵ This initial case exhibited 2 of the classic reactions patients with aluminum allergy can experience: (1) a ring or edge effect with the use of aluminum patch test chambers and (2) axillary vault dermatitis from antiperspirants.

*From the *Park Nicollet Contact Dermatitis Clinic; †University of Minnesota Medical School; and ‡Minneapolis Veterans Affairs Medical Center, Minneapolis, MN; §Department of Dermatology, Duke Health, Durham, NC; ¶University Hospitals Regional Hospitals, Richmond Heights, OH; ||Department of Dermatology, University of Minnesota, Minneapolis, MN.*

Address reprint requests to Sara A. Kullberg, BA, Park Nicollet Contact Dermatitis Clinic, 7550 34th Ave S, Ste #101, Minneapolis, MN 55450. E-mail: kull0057@d.umn.edu.

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In the 1990s, 376 cases of aluminum contact allergy in children were reported as a result of clinical trials of an acellular pertussis vaccine containing aluminum hydroxide.⁶ These children developed long-lasting, itchy, subcutaneous nodules and granulomas, weeks to months after being vaccinated. Subsequent patch tests with both metallic aluminum (empty Finn Chambers) and an aluminum salt (aluminum chloride hexahydrate, 2% petrolatum [pet]) were positive.⁶

Although the prevalence of other allergenic metals such as nickel, gold, cobalt, and chromium has been well described, less is known about the prevalence of aluminum contact allergy. In our clinics, we have encountered several patients with characteristic presentations (Table 1). In addition, a summary of published cases is included in Table 2.

Case 1

An atopic 6-year-old boy presented with eczematous dermatitis and vesicles involving the forearms, neck, and face. He completed patch testing with the North American Contact Dermatitis Group (NACDG) screening series and personal products applied to aluminum Finn Chambers. Final patch test results were difficult to interpret because of ring reactions at approximately half of the test sites; those sites that were confluent included lanolin, ethylhexyl dimethyl para-aminobenzoic acid, homosalate, isomyl methyl cinnamate, benzophenone-8, ketoprofen, nickel, and chloroxylenol. He was not initially tested to aluminum chloride hexahydrate because of lack of relevant clinical history; however, he later reported a history of intolerance to antiperspirants. Subsequently, the patient applied an empty aluminum Finn Chamber to his arm at home; an erythematous, circular, and papular reaction developed at 1 week (Fig. 1A). No current clinical relevance was identified.

Case 2

A 15-year-old boy presented for patch testing before Nuss bar placement for the correction of pectus excavatum. He was patch tested to the NACDG implant series in aluminum Finn Chambers. Final patch test results (Fig. 2A) on day 5 showed a very strong (+++) reaction to aluminum chloride hexahydrate (2% pet) and 11 doubtful (+/-) ring reactions thought to be due to allergy to the aluminum Finn

TABLE 1. Authors' Case Series

Author(s), Year Published, Country	Total No. Patients Patch Tested to Aluminum	No. (%) Patients Positive	Allergens Tested	Comments
Studies of >5 patients				
Hemmer et al, ⁷ 1996, Spain	1922	4/1922 (0.2%)	Aluminum chloride hexahydrate 2%	4 aluminum chloride hexahydrate-positive patients were negative to subsequent tests to aluminum chloride, aluminum acetate, aluminum phosphate, aluminum hydroxide, and potassium aluminum sulfate
Bergfors et al, ⁸ 2003, Sweden	740	369/720 children (51%) with itchy nodules and asymptomatic siblings 352/455 children (77%) with itchy nodules	-Metallic aluminum (empty Finn Chamber) -Aluminum chloride hexahydrate, 2% pet	-95.4% (n = 352) of aluminum-allergic patients had itchy subcutaneous nodules -17 aluminum-allergic patients had ≥ 1 aluminum-absorbed vaccine before patch testing -Time interval to subcutaneous nodule resolution: 37 mo in 154/627 followed (25%)
Lidholm et al, ⁶ 2013, Sweden	495	377/495 (76%)	-Metallic aluminum (empty Finn Chamber)	495 patients with vaccination-induced subcutaneous nodules; 76% patch test positive
Netterlid et al, ⁹ 2013, Sweden	205	8/205 (4%)	-Aluminum chloride hexahydrate, 2% pet -Metallic aluminum (empty Finn Chamber) -Aluminum chloride hexahydrate 2%, 10% (20% tested with doubtful first reading only)	-Aluminum patch testing was performed before initiation of ASIT in a randomized trial -4 patients unexposed to ASIT developed aluminum allergy; 4 patients exposed to ASIT developed aluminum allergy after 1 y of ASIT (ASIT was not shown to be a risk factor of aluminum allergy)
Siemund et al, ¹⁰ 2016, Sweden	205	72/205 (35%) tested positive to ≥ 1 baseline allergens	European Baseline Series (slightly modified; a total of 30 allergens not including aluminum)	-23 patients exposed to ASIT for 1 y developed subcutaneous nodules; unexposed patients did not develop subcutaneous nodules -Both aluminum contact allergy/itching nodules after ASIT were more common among children and atopic dermatitis patients -Adults and children, with and without elements of the atopic triad, before and after ASIT, were patch tested to a complete baseline series (30 allergens) -Increased prevalence of atopic dermatitis in patients with contact allergy (potential risk factor for sensitization) -Decreased prevalence of contact allergies in patients with ASIT exposure (potential immunomodulatory effect on sensitization)
Nielsen and Bang, ¹¹ 1954, Denmark	188	188/188 (100%)	Not reported	Clinical relevance not reported

Goiset et al, ¹² 2018, France	97	21/97 (22%)	-Metallic aluminum (empty Finn Chamber) -Aluminum chloride hexahydrate, 2% pet	10/21 aluminum-allergic patients had a history of subcutaneous itchy nodules at likely previous vaccination sites
Bergfors and Trollfors, ¹³ 2013, Sweden	63	60/63 (95%)	-Metallic aluminum (empty Finn Chamber) -Aluminum chloride hexahydrate, 2% pet	-History of itchy subcutaneous nodules present in 63 patients; 95% were patch test positive -Time interval between vaccine and nodule development: 3 wk to 4 y -Risk of developing itchy nodules correlated with an increased number of aluminum-containing vaccines -Median resolution time of itchy subcutaneous nodules: 4.6 y (n = 24) and 6.3 y (n = 20) -“Probable” clinical relevance history of axillary dermatitis while using an aluminum-containing antiperspirant, which resolved after discontinuation -History of ASIT; resolution of axillary, chest, proximal upper extremities, and lower back dermatitis after discontinuing ASIT
Clemmensen and Knudsen, ⁵ 1980, Denmark	63	1/63 (2%)	-Aluminum sulfate, 2% aq -Aluminum chloride, 2% aq -Aluminum subacetate, 1% aq -Aluminum powder -Metallic aluminum (empty Finn Chamber) -Metallic aluminum (Finn Chamber with petrolatum)	-Risk of developing itchy nodules correlated with an increased number of aluminum-containing vaccines -Median resolution time of itchy subcutaneous nodules: 4.6 y (n = 24) and 6.3 y (n = 20) -“Probable” clinical relevance history of axillary dermatitis while using an aluminum-containing antiperspirant, which resolved after discontinuation -History of ASIT; resolution of axillary, chest, proximal upper extremities, and lower back dermatitis after discontinuing ASIT
Netterlid et al, ¹⁴ 2009, Sweden	61	8/61 (13%)	-Metallic aluminum (empty Finn Chamber) -Aluminum chloride hexahydrate, 2.0% and 10.0% -Aluminum chloride hexahydrate 15% only tested in patients with a doubtful reaction to aluminum at first reading	History of subcutaneous nodules present after ASIT in 13 of 61 patients; however, of the 13 patients with subcutaneous nodules, only 8 were allergic to aluminum
Bergfors et al, ¹⁵ 2014, Sweden	34	29/34 (85%)	-Metallic aluminum (empty Finn Chamber) -Aluminum chloride hexahydrate, 2% pet	-All 34 patients had itchy, subcutaneous granulomatous nodules -Itchy nodules appeared 2–52 wk after receiving aluminum-containing vaccine -Risk of developing itchy nodules correlated with an increased number of aluminum-containing vaccines received
Kaaber et al, ¹⁶ 1992, Denmark	23	23/23 (100%)	-Metallic aluminum (empty Finn Chamber) -Aluminum chloride 2%	-History of vaccination-induced subcutaneous nodules -Time interval to subcutaneous nodule resolution: 6 y in 24% of patients

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TABLE 1. (Continued)

Author(s), Year Published, Country	Total No. Patients Patch Tested to Aluminum	No. (%) Patients Positive	Allergens Tested	Comments
Siemund et al, ¹⁷ 2012, Sweden	21	21/21 (100%) All patients had previously tested positive for aluminum allergy 19/21 (91%) Aluminum chloride hexahydrate, aluminum lactate, and aluminum acetotartrate together reproduced the positive results	-Aluminum chloride hexahydrate (20%, 10%, 6.3%, 2%, 0.63%, 0.2% pet) -Aluminum hydroxide (6.5%, 2.1%, 0.65%, 0.21%, 0.065% pet) -Aluminum phosphate (10%, 3.2%, 1%, 0.32%, 0.1% pet) -Aluminum lactate (24%, 7.7%, 2.4%, 0.77%, 0.24% pet) -Alum (potassium aluminum sulfate) (39%, 12%, 3.9%, 1.2%, 0.39% pet) -Aluminum acetotartrate (25%, 8.8%, 2.9%, 0.91%, 0.29% aq) -Aluminum chloride hexahydrate 2%, 10%, 15%, 20% -Aluminum lactate 2.4%, 12% -Aluminum chloride hexahydrate 2% -Aluminum hydroxide 10%	-Patch testing with aluminum chloride hexahydrate 2.0%, empty Finn Chambers, and intradermal testing are insufficient methods for detecting contact allergy -Aluminum chloride hexahydrate 10.0% gave the highest number of positive reactions to aluminum
Siemund et al, ⁴ 2017, Sweden	21	21/21 (100%)		Clinical relevance not reported
Garcia-Patos et al, ¹⁸ 1995, Spain	10	5/10 (50%)		History of ASIT
Studies of <5 patients Hall, ¹⁹ 1944, United States	4	4/4	Aluminum filings	-Aircraft occupational exposure to aluminum dust, filings, and burrows -Persistent 1+ patch test reactions to aluminum filings -All patch tested because of itching from ASIT injection sites -2 patients with a history of axillary dermatitis with antiperspirant use -3 patients had positive patch test reactions to aluminum chloride hexahydrate; 1 had a doubtful reaction but positive use test to an aluminum-containing antiperspirant
Hindsen, ²⁰ 2005, Sweden	4	4/4	Aluminum chloride hexahydrate, 2% pet; aluminum hydroxide depot preparations (100,000 SQ-E/mL)	
Veien et al, ²¹ 1993, Denmark	3	3/3	Aluminum chloride, 2% aq	-All 3 children had previously experienced pruritic dermatitis at aluminum-containing vaccination site and were using Zedium toothpaste (containing 30%–40% aluminum oxide) -Pruritus and dermatitis resolved in all patients with toothpaste discontinuation; 2 patients flared with toothpaste reexposure.

Fischer and Rystedt, ²² 1982, Sweden	2	1/2	Patch test: Finn Chamber Al-test Al-foil Aluminum chloride $\times$ 6H₂O, 2% and 5% (both aq and pet); aluminum acetotartrate, 1% aq Intracutaneous: aluminum hydroxide, 0.1% aq	-2 patients with diffuse reactions to Finn Chambers were retested to various preparations of aluminum -The only patient who demonstrated contact sensitivity to aluminum (positive reaction to Finn Chamber, all preparations of aluminum chloride, intracutaneous aluminum hydroxide) reported a history of axillary dermatitis with the use of antiperspirants
Meding et al, ²³ 1984, Sweden	2	2/2	-Metallic aluminum (empty Finn Chamber) -Al-test -Aluminum foil -Aluminum chloride hexahydrate 2%, 5% -Aluminum acetotartrate 1% -Metallic aluminum (empty Finn Chamber; both patients) -Aluminum chloride 0.5%, 1%, 2% (only 1 patient)	Both patients used topical aluminum acetotartrate 1% for venous leg ulcer and dermatitis
Dwyer and Kerr, ²⁴ 1993, United Kingdom	2	2/2	-Aluminum foil -Aluminum chloride hexahydrate 2%, 5% -Aluminum acetotartrate 1% -Metallic aluminum (empty Finn Chamber; both patients) -Aluminum chloride 0.5%, 1%, 2% (only 1 patient)	"Unknown" clinical relevance; vaccinations completed without adverse effects
McFadden et al, ²⁵ 1989, Norway	1	0/1 (patch test) 1/1 (intradermal provocation)	Finn Chamber Aluminum chlorhydroxide, 10 aq Aluminum chloride, 2% aq Aluminum sulfate, 2% aq 0.3 mL total (buffered solution of 2% aq disodium hydrogen-phosphate-12-hydrate and 10% aq aluminum chloride)	-Presented with swelling/scaling inside tattoo (specifically areas of violet ink); symptoms initiated 4 wk after tattoo placement and had persisted for 20 wk in duration -Negative patch testing; positive intradermal provocation (granuloma) -Excisional biopsy tissue examination with scanning electron microscopy indicated the presence of titanium and aluminum in violet-colored tattoo tissue -Energy dispersive x-ray microanalysis of excisional biopsy of granuloma showed single pigment particle peak for aluminum, the only inorganic element that tested positive with intradermal provocation
Helgesen and Austad, ²⁶ 1997, Norway	1	1/1	Empty Finn Chamber Aluminum powder (100%) in pet	-Contact urticaria due to Norwegian coin exposure -Patch testing with both aluminum materials resulted in erythema and infiltration within a few hours -Skin biopsy: urticarial vasculitis; IF: complement deposits and fibrin in dermal vessels -Resolved with cetirizine
Peters et al, ²⁷ 1998, Germany	1	1/1	Aluminum filings in pet	-Hand/antecubital fossae dermatitis -Worked in machine construction plant; used compressed air pistol to blow metal filings out of aluminum threads (Al particles impelled into hands)

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TABLE 1. (Continued)

Author(s), Year Published, Country	Total No. Patients Patch Tested to Aluminum	No. (%) Patients Positive	Allergens Tested	Comments
Schwarze et al, ²⁸ 2000, France	1	0/1 (patch test) 1/1 (intradermal provocation)	European standard, relevant chemicals, pigment (does not specify) Aluminum silicate (concentration not reported)	-Erythematous lesions on both eyelids 6 d after blepharopigmentation -Negative patch testing; positive intradermal testing on the buttocks to aluminum silicate -Biopsy 4 mo post intradermal testing on positive test site consistent with delayed-hypersensitivity granulomatous reaction
Purello-D'Ambrosio et al, ²⁹ 2000, Spain	1	1/1	Not reported	Hospital worker with hand eczema and occupational exposure to aluminum; further details not available
Frederiksen and Tofte, ³⁰ 2004, Denmark	1	1/1	Not reported	History of vaccination-induced subcutaneous nodule
Bruze et al, ³¹ 2008, Sweden	1	1/1	-Metallic aluminum (empty Finn Chamber)	History of ASIT and subcutaneous nodules at injection sites
Garg et al, ³² 2010, United Kingdom	1	1/1	-Aluminum chloride hexahydrate 2%, 10% -Aluminum chloride hexahydrate, 2% pet -Metallic aluminum (empty Finn Chamber)	+++ reaction to aluminum chloride hexahydrate; negative reaction to metallic aluminum History of bilateral axillary dermatitis in the setting of aluminum-containing deodorant; complete resolution of dermatitis with avoidance of aluminum-containing deodorant
Beveridge et al, ³³ 2012, United States	1	1/1	-Aluminum chloride 3.5%, 1.7%, 0.35%	History of vaccination-induced subcutaneous nodules
Lauren et al, ³⁴ 2016, United States	1	1/1	-Metallic aluminum (empty Finn Chamber)	History of subcutaneous nodules at previous vaccination sites
King and Moffitt, ³⁵ 2018, United Kingdom	1	1/1	-Metallic aluminum (empty Finn Chamber)	"Probable" clinical relevance due to history of dermatitis to aluminum-containing antiperspirants; patient was also allergic to multiple fragrances, which can also be present in deodorants
Gordon et al, ³⁶ 2018, United States	1	1/1	-Pure aluminum, unknown concentration, pet	History of subcutaneous nodules at previous vaccination sites
Deleuran et al, ³⁷ 2019, Denmark	1	1/1	-Aluminum chloride hexahydrate, 2% pet -Aluminum chloride hexahydrate, 2% pet	"Unknown" clinical relevance; vaccinations completed without adverse effects

ASIT, allergen-specific immunotherapy; aq, aqueous; pet, petrolatum.

TABLE 2. Previously Published Cases of Aluminum Contact Allergy

Patient	Age, y	Sex	Location of Dermatitis	Aluminum Allergy		Pertinent Positive Patch Test Results	Pertinent Negative Patch Test Results	Clinical Relevance of Aluminum Contact Allergy
				Incidentally Identified	Aluminum Tested			
1	6	M	Forearms, neck, face	Yes	Empty aluminum chamber	-Ring reactions at multiple aluminum chamber sites -Erythematous, papular reaction to empty aluminum chamber		Past (antiperspirants)
2	15	M	None present	No	Aluminum chloride hexahydrate, 2% pet	-Ring reactions at multiple aluminum chamber sites -Very strong (+++) reaction to aluminum chloride hexahydrate, 2% pet		None
3	47	M	Hands and arms	Yes	-Empty aluminum chamber -Aluminum chloride hexahydrate, 2% pet -Aluminum powder, 100%	-Ring reactions at multiple aluminum chamber sites -Erythematous, papular reaction to empty aluminum chamber -Erythematous, papular reaction to aluminum chloride hexahydrate, 2% pet	Aluminum powder, 100%	Past (aluminum pipes)
4	20	F	Face, forearms, legs	Yes	Empty aluminum chamber	-Ring reactions at multiple aluminum chamber sites -Erythematous, circular papule at empty aluminum chamber		None
5	8	F	Genital	Yes	-Aluminum chamber with and without petrolatum -Aluminum chloride hexahydrate, 2% pet -Aluminum powder, 100% -Aluminum hydroxide, 10% pet	-Mild (+) ring reactions at every aluminum chamber site except for corticosteroids -Erythema at empty aluminum chamber -Mild (+) reactions to aluminum chloride hexahydrate 2% pet and aluminum powder, 100%	-Corticosteroids -Plastic chamber -Aluminum hydroxide, 10% pet	Past
6	14	F	Arms, posterior neck, back, chest, abdomen	Yes	Aluminum chamber	-Diffuse rim or ring effect at patch test sites using aluminum chambers -Positive reaction to aluminum inferred	Ring reactions absent with plastic chambers	None
7	30	F	Bilateral eyelids	Yes	None	Diffuse rim reactions at almost all patch test sites		Possible (antiperspirant)
8	2	M	Right leg with subcutaneous nodules	No	-Aluminum chloride hexahydrate (2% pet and 10% aq) -Aluminum hydroxide (10% pet) -Empty Finn Chamber	-Strong/very strong (++ and +++) reactions to all 4 formulations of aluminum tested -Plastic IQ chambers were used for testing given patient age and high suspicion of aluminum allergy	-Plastic chamber -Vaccine preservatives	Definite

F, female; M, male.

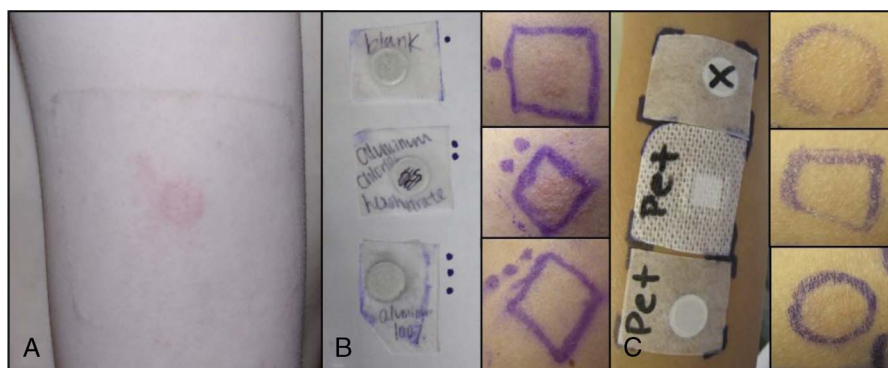


Figure 1. At-home patch test to aluminum preparations. A, Positive reaction to empty aluminum-based chamber in case 1. B, Patch test reactions to empty aluminum-based chamber (positive); aluminum chloride hexahydrate, 2% petrolatum (positive); and aluminum powder, 100% (negative), in case 3. C, Patch test reactions to aluminum-based chamber without petrolatum (top, doubtful positive), plastic chamber without petrolatum (middle, negative), and aluminum-based chamber with petrolatum (bottom, doubtful positive) in case 5.

Chambers; no clinical relevance was identified. The standard Nuss bar does not contain aluminum, and therefore its use was recommended over the alternative titanium implant (titanium, aluminum, vanadium).

Case 3

A 47-year-old atopic man presented with pruritic, vesicular, bilateral hand and arm dermatitis; patch testing was performed with aluminum Finn Chambers. Final reading revealed papules in a ring pattern at more than half of the patch test sites (Fig. 2B). In addition, he had several reactions with a confluent, edematous appearance distinct from the background ring reactions, interpreted as true-positive reactions including strong (++) reactions to fragrance mix II, formaldehyde 2%, and coco glucoside and mild (+) reactions to methylisothiazolinone/

methylchloroisothiazolinone, cinnamic aldehyde, decyl glucoside, and captan. An empty Finn Chamber and aluminum chloride hexahydrate (2% pet) and aluminum powder (100%) (both tested in plastic IQ chambers) were subsequently tested (Fig. 1B). Erythematous papular reactions developed to both the empty Finn Chamber and aluminum chloride hexahydrate, but the aluminum powder was negative. Aluminum allergy was confirmed, but no current clinical relevance was identified (only past relevance as he reported a distant history of dermatitis on his hands after handling aluminum pipes in his work).

Case 4

A 20-year-old atopic woman presented with severe dermatitis of the face, forearms, and legs, which had resulted in several hospitalizations. Patch testing revealed multiple ring reactions (Fig. 2C). At home,

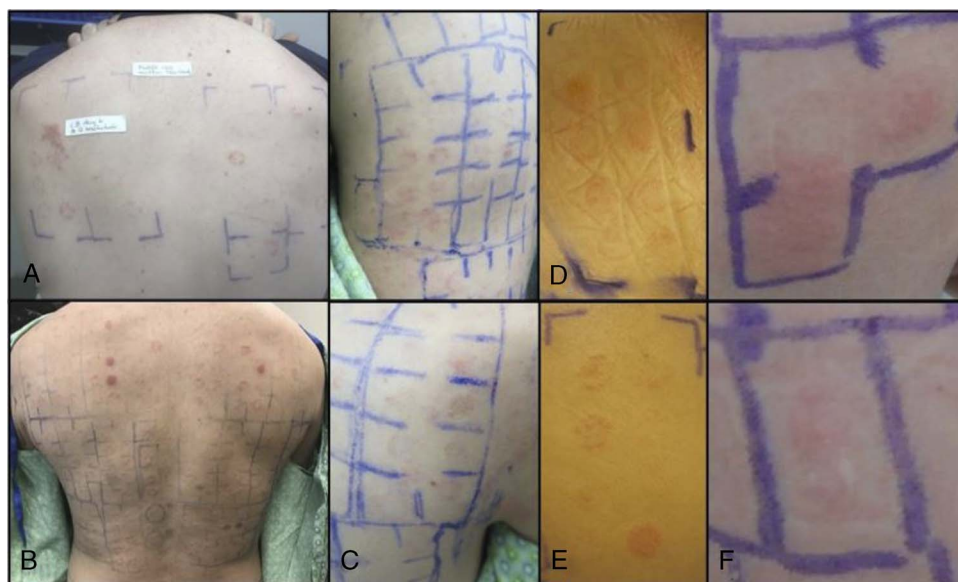


Figure 2. Patch testing with aluminum-based chambers resulted in multiple erythematous macules and papules, with some in a ring pattern. (A) Case 2, (B) case 3, (C) case 4, (D) case 5, and (E) case 7. (F) Patch test reactions at 48-hour reading to 2 concentrations of aluminum chloride hexahydrate (top photograph, 10% aq [top right] and 2% petrolatum [bottom left]) and aluminum hydroxide 10% petrolatum (bottom photograph) from case 8.

she applied an empty Finn Chamber, which resulted in erythematous, circular papules, suggesting aluminum allergy. No clinical relevance was identified. She subsequently underwent successful patch testing with plastic chambers.

Case 5

An 8-year-old girl with genital dermatitis was tested with the NACDG screening series and a supplemental panel in Finn Chambers. Final reading revealed mild (+) reactions at every patch test site, except for corticosteroids (Fig. 2D). Testing was repeated with petrolatum in a Finn Chamber, petrolatum in a plastic chamber, and an empty Finn Chamber. A doubtful (+/-) reaction was noted for the 2 Finn Chamber preparations, and the plastic chamber was negative (Fig. 1C). Additional patch testing was performed with aluminum chloride hexahydrate (2% pet), aluminum powder (100%), and aluminum hydroxide (10% pet), all prepared in plastic chambers. Mild (+) reactions developed to aluminum chloride hexahydrate and aluminum powder. No current relevance was identified. Later, she successfully underwent repeat patch testing using plastic chambers.

Case 6

A 14-year-old girl presented with worsening atopic dermatitis, which was initially limited to the inner arms but had spread to involve the posterior neck, back, chest, and abdomen. She underwent patch testing with Finn Chambers; the final reading was notable for a significant number of reactions demonstrating a rim or ring effect, with only coco glucoside and captan exhibiting confluence. All allergens initially demonstrating the rim or ring effect were retested with the use of plastic IQ chambers and were negative. No current relevance was identified.

Case 7

A 30-year-old atopic woman presented with pruritic, eczematous bilateral eyelid dermatitis. She completed patch testing with the NACDG screening series, several additional screening series, and personal products using Finn Chambers. Final patch test results were difficult to interpret because of multiple ring reactions at almost all patch test sites (Fig. 2E). Confluence suggested positive reactions to phenylenediamine, benzophenone-4, lidocaine, ammonium persulfate, pramoxine, benzyl salicylate, α -isomethyl ionone, and nickel sulfate hexahydrate. She was initially not tested to aluminum because of lack of relevant clinical history; however, she later reported a history of intolerance to antiperspirants containing aluminum.

Case 8

A 2-year-old boy presented with a 6-month history of persistent pruritic subcutaneous nodules on his right leg, which corresponded to specific injection sites of aluminum-containing vaccinations administered 3 to 4 months before nodule development. Interestingly, his right leg symptoms flared with an acute upper respiratory tract infection. His sister had a history of delayed-onset subcutaneous nodules after aluminum-containing vaccinations, although hers were asymptomatic and gradually resolved without treatment. Patch

testing was performed to all potential components of the patient's vaccines, including preservatives, antibiotics, and 4 different formulations of aluminum. Results revealed reactions to all 4 aluminums tested, including aluminum chloride hexahydrate (2% pet, +++), aluminum chloride hexahydrate (10% aqueous [aq], +++), aluminum hydroxide (10% pet, ++), and an empty Finn Chamber (as is, ++). In addition, he had a mild (+) reaction to gentamycin and a borderline (+/-) reaction to neomycin. He was advised to continue vaccinations as scheduled and seek aluminum-free alternatives whenever possible. Planned treatment of granulomas included intralesional triamcinolone.

SOURCES OF ALUMINUM AND ASSOCIATED CLINICAL REACTIONS

Vaccines

Aluminum plays an important role as an adjuvant in vaccinations, particularly for viral/bacterial inactivated vaccine antigens, bacterial toxoids, and polysaccharides.³⁸ Salts used in vaccinations include aluminum hydroxide, aluminum phosphate, alum (potassium aluminum sulfate), and mixed aluminum salts.³⁹ It was initially thought that aluminum enhances the immune response to vaccinations by preventing elimination of antigens at the inoculation site (depot effect); more recently, aluminum has also been found to activate antigen-presenting cells, cytokines, macrophages, and complement proteins.^{38,40-43} As a result, aluminum was used as an adjuvant, reducing the amount of antigen per human vaccine dose and number of scheduled vaccinations.³⁸ In the United States, the Centers for Disease Control and Prevention maintains a list of excipients used in vaccines^{44,45}; there are currently 24 aluminum-based vaccines including DTap, hepatitis A, hepatitis B, human papillomavirus, Td/Tdap, and some pneumococcus and meningococcus.^{38,39}

After vaccination, a localized inflammatory response to the antigen-adjuvant solution results in erythema and swelling, which usually resolves within a few days; rare hematomas may occur.³³ Vaccination-induced subcutaneous granulomatous nodule formation in children has been reported with frequencies of 0.35% to 1.18%, with a median duration of 18 to 49 months.¹⁵ In Sweden, between 77% and 95% of postvaccination pruritic nodules were associated with positive patch tests to aluminum.^{8,13} Patients with contact allergy to aluminum may present several months after vaccination with pruritic, often lichenified, subcutaneous nodules with overlying excoriations and occasional discoloration and hypertrichosis at the site of the vaccination.^{15,16}

The development of persistent, painful, and pruritic nodules or granulomas at the site of aluminum-containing injections is considered to represent type IV hypersensitivity.^{15,46} In a prospective cohort study of more than 4700 children who had received either a diphtheria-tetanus-pertussis-polio-*Haemophilus influenzae* type b vaccine (Infanrix, Pentavac) alone or with a pneumococcal conjugate (Prenar), both containing an aluminum adjuvant, 38 children had

itchy granulomas; of the 34 children patch tested, contact allergy to aluminum was verified in 85%.¹⁵

Some authors hypothesize that aluminum hypersensitivity reactions are mediated through epidermal dendritic cells and that this complication can be avoided by intramuscular injection.³³ This theory is supported by the report of an aluminum patch test–positive patient who developed a nodule after a subcutaneous vaccination containing aluminum but did not develop symptoms with the same subsequent vaccination performed intramuscularly.³⁰ Importantly, experts agree that the small risk of injection site nodules does not outweigh the benefit of disease prevention from vaccines.^{12,30,36}

The US Food and Drug Administration has determined that the recommended schedule of vaccines for infants results in no more than 4.335 mg of aluminum in the first year of life.^{38,47} On the basis of minimal risk levels established by the Agency for Toxic Substances and Disease Registry, the aluminum body burden in infants from both diet and vaccines during their first year would be unlikely to exceed safe aluminum burden thresholds (1 mg/kg per day).⁴⁷

In addition, the Global Advisory Committee on Vaccine Safety, an advisory board for the World Health Organization, has stated that there is no scientific evidence of harm related to aluminum–adjuvant vaccines, specifically denying links with autism and other autoimmune/inflammatory neurological diseases.⁴⁸ Additional reports dispute the theoretical association between human papillomavirus vaccine and macrophagic myofasciitis (a rare muscle inflammatory disease that presents with aluminum salt inclusions).^{48,49}

Allergen-Specific Immunotherapy

Several reports describe itchy nodules at the site of allergen-specific immunotherapy (ASIT) injections using aluminum-precipitated antigen extracts.²⁰ A cross-sectional study compared more than 60 children with asthma or allergic rhinitis who were either exposed (ASIT) or unexposed (no ASIT). Patch tests demonstrated aluminum contact allergy in 8 of the exposed patients.¹⁴ A separate, randomized, controlled, single-blind multicenter study involved patch testing of 205 children and adults patch tested before and during ASIT using the European Baseline Series supplemented with aluminum (aluminum chloride hexahydrate 2.0%, 10.0%, and 20.0% pet and an empty Finn Chamber). Four of the initially aluminum patch test–negative patients became positive after immunotherapy.⁹

Antiperspirants

Common forms of aluminum used in antiperspirants include aluminum chloride, aluminum chlorohydrate, aluminum zirconium trichlorohydrate gly, and aluminum zirconium tetrachlorohydrate gly; these complexes react with electrolytes found in sweat and form plugs in sweat gland ducts, preventing excretion of sweat. A common presentation of aluminum contact allergy is axillary vault dermatitis due to antiperspirants; many case reports describe this clinical scenario.^{20,22,32,35}

Concern about topical application of aluminum originates from its potential association with breast cancer. This topic was first

hypothesized by Darbre,⁵⁰ who suggested a link between breast cancer occurrence in the upper outer quadrant and application of antiperspirant in this area. This researcher documented higher amounts of aluminum accumulating in human breast tissue than in blood. Although overall studies have remained inconclusive, investigators have documented that aluminum can lead to genomic instability, as well as inappropriate proliferation, increased migration, and invasion of breast epithelial cells.⁵⁰ In addition, as a metalloestrogen, aluminum chlorohydrate can increase estrogen receptor α protein levels and overall estrogen signaling.^{50,51} A retrospective study comparing 209 breast cancer patients with 209 healthy controls revealed a significant association between self-reported use of antiperspirant more than once daily when younger than 30 years and both aluminum content in the breast and breast cancer.⁵² Importantly, this type of study is limited by recall bias.

Several studies have investigated the cutaneous absorption of aluminum from daily antiperspirant use. Pineau et al⁵³ measured transdermal uptake of aluminum chlorohydrate with *in vitro* Franz diffusion cells, evaluating 3 different formulations: 14.5% roll-on aluminum chlorohydrate emulsion, 21.2% aluminum chlorohydrate “stick,” and 38.5% aluminum chlorohydrate aerosol. After 24 hours of skin contact, the aluminum assays demonstrated insignificant transdermal absorption, less than 0.07% of the aluminum deposited on intact human skin samples. Stripped skin samples, evaluated with the stick formulation only, demonstrated significantly increased uptake of aluminum (11.50 vs 1.81 $\mu\text{g}/\text{cm}^2$) as compared with healthy skin, suggesting possible clinical relevance for shaved axillae and other damaged skin. A separate study performed by Flarend et al⁵⁴ evaluated absorption of aluminum chlorohydrate via radiolabeling of ²⁶Al isotopes and found that only 0.012% of skin-applied aluminum was absorbed. Comparing these 2 intradermal studies with an estimated 2.5% of gut-exposed aluminum (via food) absorbed, these represent insignificant exposure.

Other Personal Care Products and Medical Uses

Other than antiperspirants, there are a few other sources of aluminum, in personal care products and medicaments. Systemic contact dermatitis was reported in 3 children previously sensitized to aluminum from vaccinations with subsequent exposure to toothpaste containing 30% to 40% aluminum oxide.²¹ Aluminum was introduced into sunscreens to prevent agglomeration of particles (eg, titanium dioxide); more recently, theoretical concerns have been raised of UV-induced pro-oxidant reactions to aluminum, leading to skin cancer.⁵⁵ Aluminum functions in cosmetics both as a pigment and as a thickening agent. We were unable to identify any reports of patients with clinically relevant dermatitis from aluminum-containing sunscreen or makeup products.^{6,56}

Aluminum is also found in several medicaments. The most common are aluminum-containing antacids. Topical aluminum chloride hexahydrate is used for hemostasis during minor procedures and hyperhidrosis treatment; colloidal aluminum hydroxide suspensions and aluminum hydroxide gels are used during surgical treatment of peptic ulcers or bowel fistulas.^{6,57–59} After ingestion, aluminum

hydroxide has the ability to neutralize gastric contents, as well as bind bile acids in the gut.⁶⁰ Historically, aluminum acetotartrate, 1% aq, was used as a topical medicament for eczema and venous leg ulcers. Meding et al²³ described 2 patients treated with aluminum acetotartrate who were patch test positive to the Al-test; aluminum acetotartrate, 1% aq; an empty Finn Chamber; aluminum foil; and aluminum chloride hexahydrate, 2% and 5% pet.

Tattoos

In an in vitro quantitative chemical analysis study investigating the composition of 30 tattoo inks using scanning electron microscopy, 87% of these inks identified aluminum as an ingredient, making the overall frequency of exposure to those undergoing tattoo placement relatively high.⁶¹ Granulomatous reactions to aluminum-containing tattoo pigments have been documented in 2 patients; scanning electron microscopy and energy dispersive x-ray microanalysis demonstrated intradermal particles containing aluminum, and intradermal tests with either aluminum silicate or aluminum chloride were positive.^{25,28}

Elemental Exposures

A comprehensive literature search found few reports of occupational allergic contact dermatitis to aluminum. Hall¹⁹ described 4 aluminum patch test–positive aircraft workers with dermatitis most prominent on the flexor surfaces of the forearms and wrists associated with exposure to aluminum dust, filings, and burrings. In addition, there have been reports of a hospital attendant and a machine construction plant worker becoming sensitized to aluminum through workplace exposures.^{27,29}

TYPE I IMMEDIATE HYPERSENSITIVITY REACTIONS TO ALUMINUM

Helgesen and Austad²⁶ reported a patient with aluminum contact urticaria due to cutaneous exposure to Norwegian coins (up to 0.01% aluminum). Testing with empty Finn Chambers on the patient's

forearm and back resulted in erythema at 2 hours and infiltration at 5 hours. In addition, pure aluminum powder in petrolatum led to infiltration and erythema at 1 hour and erosions at 3 hours. A skin biopsy showed urticarial vasculitis, and immunofluorescence demonstrated complement deposits and fibrin in the dermal vessels. The patient's symptoms completely resolved with the use of 10 to 20 mg cetirizine daily for 5 days.²⁶ We did not find any cases of anaphylaxis to aluminum.

PATCH TEST MATERIALS

Like other metal salts, aluminum salts are “problematic” antigens in which improper concentrations and/or vehicles may lead to false-positive or irritant reactions. Many experts recommend testing with both metallic aluminum (an empty Finn Chamber) and aluminum chloride hexahydrate 2% pet.^{1,62} Importantly, false negatives may occur in adults at this concentration; current recommendations for diagnosing aluminum allergy include testing to both an empty Finn Chamber and aluminum chloride hexahydrate (2% pet for children younger than 8 years and 10% for adults).¹

A variety of different aluminum salts and mediums have been used for patch testing in the past. A comprehensive review performed by Siemund¹ and Netterlid et al⁹ discusses historical patch testing with multiple salts in various concentrations (Table 3). Intradermal testing has also been performed to diagnose aluminum allergy, traditionally using 0.1% to 0.5% aluminum hydroxide in 0.5% sodium chloride or water, with a final reading 2 to 3 days later.¹

If aluminum allergy is suspected, plastic chambers should be used for patch testing. Because of the higher frequency of aluminum allergy in children, some contact dermatitis clinics routinely use plastic chambers for children (generally younger than 16–18 years) undergoing patch testing.

LOSS OF ALLERGY OVER TIME

It is unclear whether aluminum sensitivity diminishes over time or whether aluminum reactions have a high nonreproducible rate

TABLE 3. Compounds and Concentrations of Aluminum Used for Patch Testing*

Aluminum Compound	Vehicle	Concentration(s) (% wt/wt)
Aluminum chloride hexahydrate	aq and pet	0.1, 0.5, 1.0, 2.0, 5.0, 10.0
Aluminum hydroxide	aq and pet	0.5, 10.0
Aluminum subacetate	aq	1.0, 2.0
Aluminum acetotartrate	aq	1.0
Aluminum sulfate	aq	2.0
Aluminum acetate	aq	2.0, 1.3
Aluminum sulfide	aq	2.0
Potassium aluminum sulfate	aq and pet	0.98, 1.98, 3.93
Aluminum phosphate	pet	0.25, 0.5, 1.0
Aluminum oxide	aq and pet	10.0
Aluminum powder	aq and as is	2.0
Aluminum metal/sheet		
Empty Finn Chamber		

*Adapted from Siemund's¹ *Contact Allergy to Aluminum* doctoral dissertation.

TABLE 4. Studies Investigating Loss of Aluminum Contact Allergy Over Time

Author(s)	No. Patients Retested	Aluminum Tested	Nonreproducible (%)	Comments
Siemund et al, ⁴ 2017	21	-Aluminum chloride hexahydrate 32% pet, 10% pet, 3.2% pet, 1% pet, 0.32% pet, 0.1% pet, 0.032% pet, 0.01% pet -Aluminum lactate 38% pet, 12% pet, 3.8% pet, 1.2% pet, 0.38% pet, 0.12% pet, 0.038% pet, 0.012% pet -Empty aluminum chamber -Aluminum chloride hexahydrate, 2% pet	-Overall: 4/21 (19%) not reproducible on retesting with either aluminum salt -36/84 (43%) were not reproducible with aluminum chloride hexahydrate -49/84 (58%) were not reproducible with aluminum lactate 186/241 (77%)	-Each previously aluminum-allergic patient was retested with 4 serial dilutions of each salt on 4 occasions for a total of 84 serial dilution tests per salt. -Patch test reactivity can vary over time, with potential for false negatives -if there is a strong suspicion for aluminum contact allergy, retesting should be considered. All doubtful (+/-) reactions were considered negative; loss of allergy was positively associated with no longer having an itchy granuloma, being older in age, an increased time span from sensitization to repeat testing, and having a lower strength positive reaction on initial testing. When results were reviewed again in 2018, a decrease in the strength of reactions to both metallic aluminum and aluminum chloride hexahydrate 2% was observed. Only 5 individuals had the same reaction strength over time. 7/1922 patients had an initial positive reaction (+/- to +++) to aluminum chloride hexahydrate, 2% aq; 0/7 had a positive reaction to the subsequent series of aluminum salts or empty aluminum chamber.
Lidholm et al, ^{6,63} 2013 and 2018	241			
Hemmer et al, ⁷ 1996	7	Initial testing: -Aluminum chloride hexahydrate, 2% aq Subsequent series: -Aluminum chloride 2% aq, 1% aq, and 0.5% aq -Aluminum acetate 1.34% pet, 0.67% pet, and 0.33% pet -Aluminum phosphate 1.0% pet, 0.5% pet, and 0.25% pet -Aluminum hydroxide 0.5% pet -Potassium aluminum sulfate 3.93% pet, 1.96% pet, 0.98% pet, 3.93% aq, 1.96% aq, and 0.98% aq -Empty aluminum chamber	0/7 (100%)	
Kaaber et al, ¹⁶ 1992	4	Not reported	2/4 (50%)	Disappearance of itching and granulomas occurred with the loss of aluminum allergy in 2 of 4 patients; 1 patient's granuloma and itching resolved but still had a positive patch test to aluminum.
Nielsen and Bang, ¹¹ 1954	188	Not reported	111/188 (59%)	

TABLE 5. Select Aluminum-Free Deodorants (Using American Contact Dermatitis Society Contact Allergen Management Program and Online Manufacturer Ingredient Listings)⁶⁴

AHAVA
Roll-On Mineral Deodorant (Regular or Men's)
Arm & Hammer
Essentials Natural Deodorant Stick, Fresh
ARROW PROTECT
Aluminum-Free Deodorant
AXE
All-Day Fresh Deodorant Body Spray Anarchy for Her
Daily Fragrance Body Spray
Dark Temptation Body Spray
Gold Temptation Body Spray
Biossance
Squalane + Bamboo Deodorant
Blume
Hug Me Deodorant
Brut
Deodorant Spray, Classic Scent
Curie
Natural Deodorant, White Tea
Dove
0% Aluminum (Cucumber & Green Tea, Coconut & Pink Jasmine, Pomegranate & Lemon Verbena)
Men+Care Deodorant Stick, Extra Fresh
Men+Care Deodorant Stick, Clean Comfort
Earth Science
Liken Plant, Unscented
Freedom
Natural Deodorant, Bergamot Mint
Jack Black
Pit CTRL Aluminum-Free Deodorant
kai
Rose Deodorant
Megababe
Rosy Pits Aluminum-Free Deodorant
milk + honey
Regular Strength Deodorant, All Scents
Baking Soda-Free Deodorant, Lavender & Tea Tree
Native
Teen Deodorant, All Scents
Women's Deodorant, All Scents
Men's Deodorant, All Scents
Sensitive Deodorant, Unscented*
Sensitive Deodorant, All Scents
Old Spice
Aluminum-Free Deodorant for Men Stick, Classic Fresh
Classic Stick Deodorant, Original Scent
Body Spray, All Scents
Fresher Collection Men's Deodorant, All Scents
Red Zone Collection Men's Deodorant Stick (Champion, After Hours, Aqua Reef, Pure Sport, Swagger)
Primally Pure

(Continued on next page)

TABLE 5. (Continued)

Blue Tansy Deodorant
Schmidt's
Water + Wood Deodorant
Natural Deodorant for Sensitive Skin, All Scents
Sebamed
Men's Deodorant, Balsam Sensitive and Deo Sensitive
Secret
Aluminum-Free Deodorant, All Scents
Speed Stick
Deodorant for Men, Ocean Surf
Regular Deodorant
Tarte
Clean Queen Vegan Deodorant
Tom's of Maine
Long Lasting Natural Deodorant Stick (Unscented, Fresh Apricot)
Mineral Confidence Deodorant Crystal Roll-On, Fragrance Free
Original Care Deodorant Stick, Unscented
Vanicream
Deodorant*

*Fragrance-free/botanical-free.

compared with other allergens. In a 1954 study, Danish patients underwent repeat testing 2 to 19 years after a positive patch test to aluminum; 111 of 188 positive reactions (59%) were not reproducible.¹¹ Lidholm et al⁶ retested 241 children with previously identified reactions to 2% aluminum chloride hexahydrate 5 to 9 years later, and 186 (77%) were negative; a negative test result was associated with older age, longer time elapsed from first aluminum-absorbed vaccine dose, less severe cutaneous reactions, and resolution of vaccination site itching.

In contrast, Siemund et al⁴ found that, when 21 previously positive adults were subsequently tested to an equimolar dilution series

TABLE 6. Homemade Deodorant Recipes (Fragrance-Free/Botanical-Free)***Recipe 1: Ingredients**

¾ cup arrowroot powder/cornstarch
¼ cup baking soda
4–6 tbsp melted coconut oil

Instructions

1. Combine baking soda and arrowroot powder/cornstarch.
2. Add 4 tbsp of melted coconut oil and mix with a fork—continue adding coconut oil until the deodorant reaches the consistency you would prefer.
3. Transfer mixture to a jar with a tight-fitting lid.

Recipe 2: Ingredients

¾ cup arrowroot powder/cornstarch
¼ cup food grade diatomaceous earth
7–9 tbsp melted coconut oil

Instructions

1. Combine diatomaceous earth and arrowroot powder/cornstarch.
2. Add 6 tbsp of melted coconut oil and mix with a fork—continue adding coconut oil until the deodorant reaches your preferred consistency.
3. Transfer mixture to a jar with a tight-fitting lid.

*See Dessinger⁶⁵ for further details.

of aluminum chloride hexahydrate and aluminum lactate in petrolatum 4 times during an 8-month period, they demonstrated increased reproducibility. This suggests that single-occasion repeat patch testing to evaluate for aluminum allergy may result in false negatives. Siemund et al⁴ also proposed that it is possible that aluminum patch tests initially interpreted as positive could have been false positives or irritant reactions, which are especially common with higher concentrations of aluminum salts (eg, aluminum chloride 15%–20% pet). A summary of studies focused on these issues is presented in Table 4.

Management of Aluminum Allergy

Management of aluminum contact allergy is based on avoidance. For aluminum, this includes evaluation of antiperspirants, medications, clasps/buttons/pins, inks/tattoos, sunscreens, implants, metal contactants (eg, aluminum foil, cans),²³ and various occupational exposures. Aluminum-free allergen extracts are options for aluminum-allergic patients requiring immunotherapy.¹ Barriers (eg, gloves) may be used for metal exposures.

For patients experiencing clinically relevant contact allergy to aluminum with persistent axillary dermatitis, aluminum-free deodorants as well as homemade recipes are available (Tables 5 and 6). Some natural “aluminum-free” deodorants are formulated with “natural deodorant crystals” including potassium alum or ammonium alum. Alum salts contain aluminum sulfate; tolerance to these alum salts in individuals allergic to aluminum is unclear. In patients who experience persistent itchy nodules or granulomas, topical steroids, colloid bandages, and intralesional corticosteroid injections may be helpful.¹

SUMMARY

Aluminum exposure is ubiquitous, but allergy is relatively rare. Classic presentations of aluminum allergy include diffuse ring reactions to aluminum Finn Chambers during patch testing, itchy subcutaneous nodules or granulomas soon after vaccinations or ASIT, and axillary dermatitis from antiperspirants. In individuals referred for patch testing who are suspected of having aluminum allergy, patch testing with plastic chambers is recommended. Aluminum allergy is typically confirmed by a positive patch test reaction to an empty Finn Chamber or aluminum chloride hexahydrate (2% pet for children younger than 8 years and 10% for adults). Some studies have shown patterns of decreasing allergenicity to aluminum over time; clinical implications of this require further study.

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