

There is an association between contact allergy to aluminium and persistent subcutaneous nodules in children undergoing hyposensitization therapy

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Background: The development of persistent itchy nodules at the injection site following hyposensitization therapy with aluminium-precipitated antigen extract has been described in several reports. Occasionally, contact allergy to aluminium has been reported in individuals with such nodules.

Objectives: To investigate if hyposensitization therapy can induce contact allergy to aluminium and examine if there is any association between persistent subcutaneous nodules and aluminium allergy.

Patients/methods: Sixty-one children with allergic asthma and/or allergic rhinitis participated in the study of whom 37 had had hyposensitization therapy. The study consisted of a non-clinical part based on a questionnaire and a clinical part with a physical examination, self-assessment of itching, and patch testing. To secure an unbiased evaluation of possible reactions, the investigators were blinded.

Results: Contact allergy to aluminium was found in eight participants, all in the exposed group (8/37 versus 0/24, $P = 0.02$). Examination showed nodules on the upper arms in 13 participants, all in the group exposed to hyposensitization therapy. Nodules were over-represented in patients with contact allergy to aluminium.

Conclusions: There was a statistically significant association between contact allergy to aluminium and persistent subcutaneous nodules in children who had had hyposensitization therapy.

Key words: adjuvant; adverse reaction; allergic asthma; allergic contact dermatitis; allergic rhinitis; aluminium hydroxide; atopy; sensitization. © Blackwell Munksgaard, 2008.

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Contact allergy to aluminium has been considered as rare (1). Since 1980, it has been described in individuals with persistent itchy nodules following hyposensitizing therapy (2–6) and since 1985 after immunization (6–15). In the year 2000, Swedish authorities received oral reports from studies in the Gothenburg area in Sweden on an unexpectedly high frequency of persistent itchy subcutaneous granulomas at the site of injection of aluminium-containing vaccines in children, usually with a positive epicutaneous test to aluminium chloride hexahydrate. The lesions were first

observed after subcutaneous injections but occurred also after intramuscular injections (16). The authorities were concerned by these reports, and when a new booster diphtheria–tetanus vaccine was introduced, a prospective, cluster-randomized study on 25 000 school children was conducted by the Swedish Institute for Infectious Disease Control. However, no contact allergy to aluminium was detected (17).

Because of the Gothenburg reports, children who had been treated with hyposensitization therapy with aluminium-containing antigen

preparations at the Department of Paediatrics in Halmstad, Sweden, were enquired about adverse reactions. As many of the hyposensitized children reported persisting itchy nodules at the site of injection, a retrospective study was initiated. The over-riding aims were to investigate if aluminium allergy could be detected in hyposensitized children and if aluminium allergy was linked to persistent itchy nodules after hyposensitization therapy.

Materials and Methods

Design

A cross-sectional study of patients exposed/not exposed to hyposensitization therapy. All patients had the same diagnosis and had been treated at the same unit during the same period, i.e. 1993–2004.

The study consisted of two parts, a non-clinical part based on a questionnaire and a clinical part with a physical examination, self-assessment of itching, and patch testing. The logistics of the study are shown in Fig. 1.

Study population/participants

Two hundred and thirteen atopic children/young adults, 8–24 years of age, with allergic rhinitis and/or asthma according to a diagnostic code list were identified from the register at the Department of Paediatrics in Halmstad. In 2004, all children/young adults who had been offered and participated/not participated in hyposensitization therapy with aluminium-precipitated antigen extracts given subcutaneously in the arms were

invited to participate in the study. The two groups were labelled exposed and unexposed in this study.

A questionnaire was sent out with an information letter. The study consisted of a non-clinical part with participants who only consented to answer the questionnaire and a clinical part with participants who, in addition, agreed to give a medical history, undergo examination and patch testing.

Medical contraindications were limited to anaphylaxis during skin testing, pregnancy, ongoing immunosuppressive therapy, and acute infectious disease.

Before inclusion and after oral information about the study procedure, as well as inclusion and exclusion criteria, a written informed consent was obtained from the parents or the young adults.

Questionnaire

The questionnaire contained questions about atopic disease and exposure to aluminium and other metals (Table 1, far left column, items 1–13). Questions related to hyposensitization therapy were included for those who had obtained such therapy (Table 2, far left column, items 16–21).

Communication

The participants, and parents where applicable, were told not to communicate with the investigators performing the physical examinations and the patch test readings.

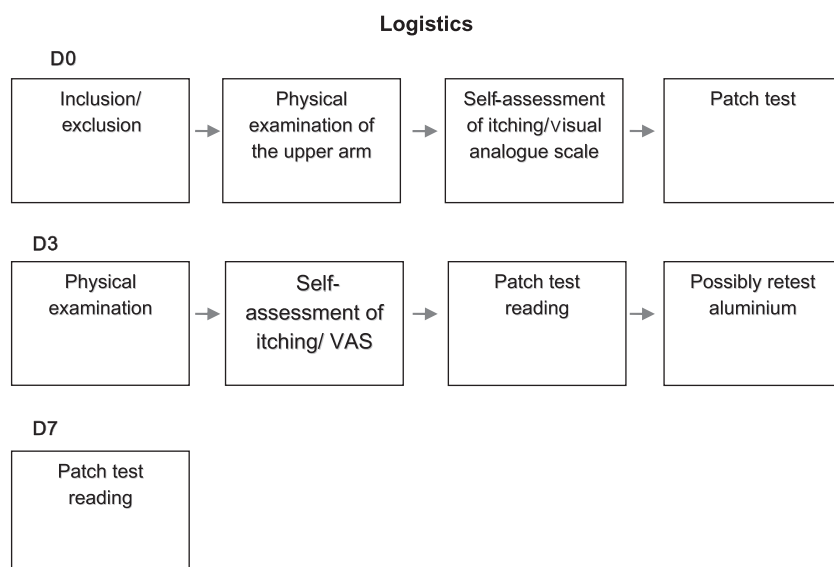


Fig. 1. The logistics of the study.

Table 1. Questionnaire results for exposed and unexposed study population (tested and not tested) in the survey group^{a,b}

	Exposed			Unexposed		
	Test (n = 37)	No test (n = 44)	Total (n = 81)	Test (n = 24)	No test (n = 40)	Total (n = 64)
Survey (n = 145)	Al ⁺ (n = 8)	Al [−] (n = 29)		Al [−]		
Age at study	16 (9–21)	15 (9–23)	16 (9–24)	13 (8–21)	14 (9–20)	14 (8–21)
Sex (% males)	3/8 (38)	16/29 (55)	22/44 (50)	12/24 (50)	22/40 (55)	34/64 (53)
Survey questions						
1. Atopic dermatitis	3/8 (38)	15/28 (54)	16/44 (36)	12/24 (50)	24/39 (62)	36/63 (57)
2. Skin exposure to metal	0/8 (0)	3/29 (10)	4/44 (9)	3/24 (13)	4/39 (10)	7/63 (11)
3. Ear piercing	4/4 (50)	11/29 (38)	19/44 (43)	9/24 (38)	17/40 (43)	26/64 (41)
4. Body piercing	1/7 (13)	1/29 (3)	4/42 (10)	1/24 (4)	0/40 (0)	1/64 (2)
5. Prolonged metal contact	3/8 (38)	16/29 (55)	15/43 (35)	9/24 (38)	14/39 (36)	23/63 (37)
6. Use of deodorants	7/8 (88)	21/29 (72)	34/44 (77)	16/24 (67)	25/40 (63)	41/64 (64)
Rash from deodorant	4/7 (57)	3/22 (14)	7/34 (21)	5/15 (33)	5/25 (20)	10/40 (25)
7. Eczema/skin problems	2/8 (25)	12/27 (44)	16/25 (39)	16/8 (67)	19/36 (53)	35/60 (58)
During pollen season	7/8 (88)	28/28 (100)	37/42 (88)	22/24 (92)	32/37 (87)	54/61 (92)
From pets	6/7 (86)	18/26 (69)	23/36 (64)	17/24 (71)	27/33 (82)	44/57 (77)
From dust mites	3/6 (50)	13/25 (52)	15/30 (50)	13/24 (54)	14/28 (50)	27/52 (52)
Other causes	4/5 (80)	8/21 (38)	15/28 (54)	9/21 (43)	10/23 (44)	19/44 (43)
9. Asthma	4/8 (50)	18/26 (69)	21/43 (49)	19/22 (86)	26/39 (67)	45/61 (74)
10. Antacids	0/8 (0)	2/29 (7)	4/44 (9)	1/24 (4)	6/39 (15)	7/63 (11)
11. Exposure to aluminium	0/6 (0)	3/17 (18)	2/32 (6)	2/14 (14)	7/25 (28)	9/39 (23)
12. Had recommended vaccinations	8/8 (100)	29/29 (100)	40/42 (95)	24/24 (100)	38/38 (100)	62/62 (100)
13. Had other vaccinations	1/8 (13)	6/27 (22)	12/42 (29)	8/21 (38)	3/35 (9)	11/56 (20)

Al⁺, patch tested positive to aluminium; Al[−], patch tested negative to aluminium; No test, only participated in the questionnaire survey.

^a‘Do not know’ – answers are not included.

^bMedian value, range in brackets, or number of positive answers of total with percentage in brackets. All unexposed patients were tested negative to aluminium.

Physical examination

A physical examination with visual inspection and palpation of the injection places, i.e. both upper arms, was performed before the patch testing and immediately before the first patch test reading by the same investigator to assess if there were any subcutaneous nodules or any signs of scratching. To secure an unbiased evaluation of possible reactions on the sites of injection, the investigator was blinded not only to all data collected but also to notes regarding exposure to hyposensitization therapy and to the result of the patch test.

Definition of persistent nodule with or without itching

A nodule at the injection site is defined by the presence of a discrete or well-demarcated soft tissue mass or lump THAT IS firm AND is located at the injection site (for this investigation the upper arms). In the absence of abscess formation AND erythema AND warmth (18).

Self-assessment

On two occasions after the physical examinations, before the application of the patch test and before the first patch test reading, respectively, the par-

ticipant was asked to make a self-assessment of the intensity of the itching on both upper arms on a visual analogue scale.

Patch testing

The patch testing was performed with the European baseline test series (19), slightly modified and supplemented with aluminium preparations and antigen extracts used for hyposensitization therapy. The antigen extracts were honey bee venom, yellow jacket venom, three trees (alder, birch, and hazel), a five-grass pollen mixture, mugwort (*Artemisia vulgaris*), cat dander, dog dander, and two *Dermatophagoides* mite preparations, all being Alutard SQ 100 000 SQ-E/ml manufactured by ALK-Abelló, Copenhagen, Denmark. Each of these preparations contains aluminium hydroxide, 4.0 mg/ml. The allergens were tested in IQ chambers (25 µl of liquid test preparations was micropipetted onto the IQ chambers) on a non-woven adhesive tape (Chemotechnique Diagnostics, Vellinge, Sweden). The tests were applied to the upper part of the back and left for 2 D. Aluminium chloride hexahydrate in petrolatum (pet.) at 2.0%, 10.0%, and 15.0% w/w prepared at our laboratory and together with an empty Finn Chamber[®] (diameter 8 mm; Epitest Ltd Oy,

Table 2. Treatment and questionnaire results for the exposed group^a

	Al ⁺ (n = 8)	Al ⁻ (n = 29)	No test (n = 44)	P value (Al ⁺ versus Al ⁻)
Age at start of treatment (years)	14 (8–17)	9 (4–16)	12 (5–17)	0.006
Strength ^b	27 (9–62)	45 (0–126)	30 (3–65)	0.17
Dose (aluminium hydroxide in mg) ^c	110 (36–250)	181 (0–503)	119 (13–258)	0.13
Number of injections ^d	35 (12–66)	56 (8–163)	38 (5–81)	0.16
At least one contact allergy ^e	5/8 (63)	8/29 (28)	—	0.12
Questions				
16. Itching/nodules	7/7 (100)	21/28 (75)	32/42 (76)	>0.3
18. Is itching/nodules aggravated by				
Upper respiratory/other infection	1/2 (50)	0/7 (0)	3/17 (18)	>0.3
Pollen season	4/5 (80)	3/11 (27)	14/24 (58)	0.19
Contact with flowers	2/4 (50)	0/10 (0)	4/19 (21)	>0.3
Vaccination	0/5 (0)	0/15 (0)	3/17 (18)	>0.3
19. Atopic dermatitis ^f	1/1 (100)	3/6 (50)	2/13 (15)	>0.3
20. Allergy shock ^g	2/7 (29)	5/28 (18)	5/42 (12)	>0.3
21. Heredity				
Atopic dermatitis	5/8 (63)	16/29 (55)	21/42 (50)	>0.3
Other skin problems/eczema	4/8 (50)	20/28 (71)	17/42 (40)	>0.3
Hay fever	5/8 (63)	21/29 (72)	32/42 (76)	>0.3
Asthma	4/8 (50)	21/29 (72)	19/41 (46)	>0.3

^aMedian value, range in brackets, or number of positive answers of total with percentage in brackets.

^bTotal injected volume of antigen extract with 100 000 SQ units/ml.

^cOnly based on the injected volume of antigen extract with the strength 100 000 SQ units/ml containing 4.0 mg/ml aluminium hydroxide.

^dNumber of injections with 100 000 SQ units/ml.

^eAluminum positive not included.

^fAggravation of atopic dermatitis during hyposensitization therapy.

^gExperienced allergy shock during hyposensitization therapy.

Tuusula, Finland) were used to diagnose aluminium allergy. All participants were tested with an empty Finn Chamber and aluminium chloride hexahydrate at 2.0% and 10.0%. The 15.0% aluminium chloride hexahydrate preparation was only tested on those who had a doubtful reaction to any aluminium preparation on the first reading.

In this article, the patch results with aluminium preparations and antigen extracts are presented.

Patch test reading

To evaluate the patch test reactions unbiased, the dermatologist reading the patch test was blinded not only to all data collected but also to notes regarding exposure to hyposensitization therapy and to the result of the physical examination. The patch test reading was performed according to International Contact Dermatitis Research Group guidelines (20) on D3 and D7. The retest with 15.0% aluminium chloride hexahydrate was only read once on D7, i.e. 4 days after the application on D3.

Calculation of treatment dose

The children/young adults who had received hyposensitization therapy had been treated in accordance to standardized guidelines, with antigen extracts containing aluminium hydroxide (21). The amount of aluminium hydroxide given was calculated individually.

Statistical calculations

The non-parametric Mann–Whitney *U*-test was used when comparing ordinal and continuous outcome variables between two independent groups, for example, aluminium-positive (Al⁺) and aluminium-negative (Al⁻) individuals. When comparing binary outcome variables, for example, frequencies of Al⁺ and Al⁻, we used Fisher's exact test (two groups) and Chi-squared test (more than two groups). Trends in binary proportions were tested using Cochran–Armitage trend test. All statistical analyses were performed using SPSS 15.0 for Windows (SPSS Inc., Chicago, IL, USA) or STAT-XACT-6 (Cytel Software Corp., Cambridge, MA, USA). Exact methods for *P*-value calculations were used throughout. We considered *P* values below 0.05 as statistically significant. The number of individuals with nodule/s and itching was separately compared between the exposed group, individually or combined for subjects with and without hypersensitivity to aluminium, and the unexposed group on D0 but also with regard to the course of the nodule/s and itching (alleviated, unchanged, and aggravated) during the patch test procedure.

Ethics

The regional ethical review board in Lund approved the study on 31 August 2004 (Dnr 410/2004). Written informed consent was obtained from the parents and/or the young adults.

Results

In total, we offered 213 children/young adults to participate in the study. One hundred and forty-five (63%) participated and of those, 61 (42%) were patch tested. The numbers in the various groups are given in Fig. 2.

We received no answer from 58 (27%), 28 exposed and 30 unexposed to hyposensitization therapy, while 10 (4%), 3 exposed and 7 unexposed to hyposensitization therapy, did not want to participate in the study (Fig. 2).

Major reasons not to participate in the clinical part were lack of time and moving away from the study area.

In general, the answers to the questionnaire did not differ markedly from each other (Table 1). However, the prevalence of asthma (question 9) varied significantly ($P = 0.034$) between the exposed and the unexposed groups, and also the prevalence of occupational and non-occupational exposure to aluminium (question 11, specified by the participants as exposure to brewery work, cans, kitchen utensils, handicraft, bicycles, engines, and aluminium rims) ($P = 0.008$). Asthma and aluminium exposure were more common in the unexposed group.

Contact allergy to aluminium was found in eight participants, all in the exposed group (8/37 versus 0/24, $P = 0.02$). The patch test reactions to aluminium chloride hexahydrate in pet. and to an empty Finn Chamber are given in Table 3. The

only individual testing positively to an empty Finn Chamber was the participant with the strongest reactions to both aluminium chloride hexahydrate at 2.0% and 10.0%. All eight aluminium-hypersensitive patients tested positively to 10.0%, while only three tested positively to 2.0%. Three of the patients testing positively to 10.0% had a doubtful reaction to aluminium chloride hexahydrate at 2.0%. To diagnose contact allergy to aluminium, the second reading after 1 week was only necessary for one patient who tested positively to 10.0% (Table 3, individual 3). No additional contact allergy to aluminium was detected with the retest procedure. No correlation was found between injected dose of aluminium hydroxide and aluminium contact allergy. There were no positive reactions to the antigen extracts.

Before the patch testing, examination showed nodules on the upper arms in 13 participants, all in the group exposed to hyposensitization therapy (13/37 versus 0/24, $P < 0.001$). Nodules were over-represented in patients with contact allergy to aluminium (6/8 = 75% versus 7/29 = 24% $P = 0.013$). The nodules in 3 of the 13 patients before patch testing remained unchanged, while the remaining 10 patients had enlarged nodules when examined just before the first patch test reading. Furthermore, nodules appeared between the patch test application and the first reading in four exposed individuals, but in none of the unexposed individuals (4/24 versus 0/24, $P = 0.11$).

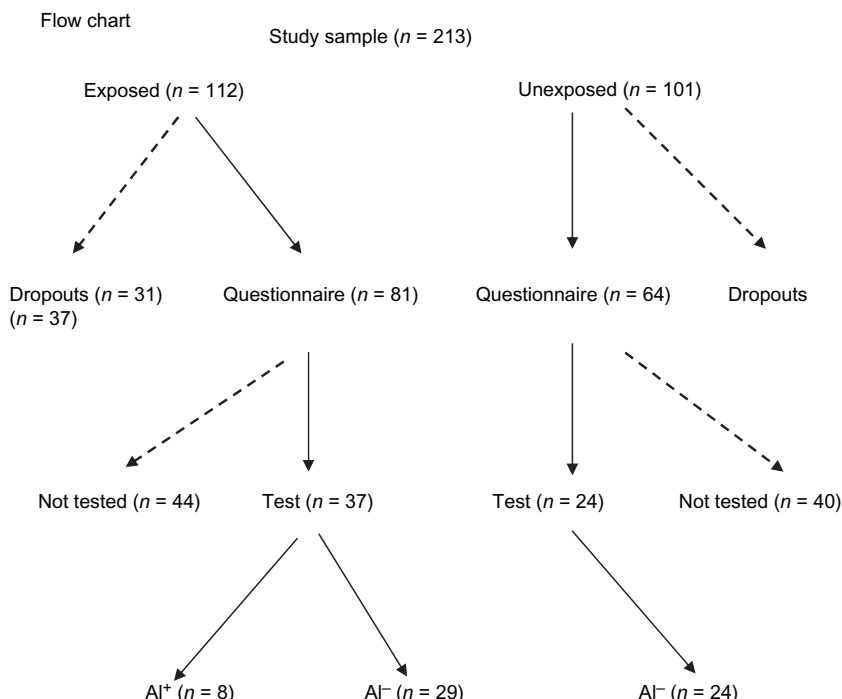


Fig. 2. A flow chart over the exposed and unexposed groups, shown in number of subjects. Al^+ , patch tested positive to aluminium and Al^- , patch tested negative to aluminium.

Table 3. Results of patch testing with aluminium chloride hexahydrate and presence of nodule/s and itching on the upper arm/s before the patch testing on D0 and at the patch test reading on D3

Patch test procedure^a

Individual	Aluminium test preparations						Nodule ^{b,c}		Pruritus ^{d,e}	
	2% pet.		10% pet.		Finn Chamber [®]		D0 ^b	D3 ^c	D0 L/R ^d	D3 L/R ^e
	D3 ^a	D7	D3	D7	D3	D7				
1	+	?	++	+	?	–	+	++	+/+	++/++
2	–	–	+	–	–	–	+	++	+/+	++/+
3	?	?	?	+	–	–	+	++	+/+	++/++
4	++	++	+++	++	++	–	+	++	–/–	–/–
5	?	+	++	+	–	–	+	++	+/+	+/+
6	–	–	++	?	–	–	–	–	+/+	++/++
7	–	?	++	+	–	–	–	–	–/+	–/+
8	?	–	++	+	–	–	+	++	+/+	++/++
9	–	–	?	?	–	–	–	–	+/+	+/+
10	–	?	?	?	–	–	–	–	–/–	–/–
11	–	?	?	?	–	–	+	+	–/+	–/+
12	–	?	?	?	–	–	–	+	–/–	+/+
13	–	–	?	–	–	–	–	–	–/–	–/–
14	?	–	?	–	–	–	–	–	+/+	(+)/–
15	–	–	?	?	–	–	+	++	+/+	++/++
16	–	–	–	–	–	–	+	+	–/–	–/–
17	–	–	–	–	–	–	–	+	–/–	–/–
18	–	–	–	–	–	–	–	+	–/+	–/–
19	–	–	–	–	–	–	+	+	–/–	+/+
20	–	–	–	–	–	–	–	+	–/–	+/–
21	–	–	–	–	–	–	+	++	–/–	+/+
22	–	–	–	–	–	–	+	++	+/+	+/+
23	–	–	–	–	–	–	+	++	–/+	–/–
24	–	–	–	–	–	–	–	–	+/+	+/+
25–37	–	–	–	–	–	–	–	–	–/–	–/–
38	–	–	?	–	–	–	–	–	+/+	++/++
39	?	–	?	–	–	–	–	–	–/–	+/–
40	–	–	?	–	–	–	–	–	–/+	+/(+)
41	–	–	–	–	–	–	–	–	+/+	–/(+)
42	–	–	–	–	–	–	–	–	+/+	–/–
43	–	–	–	–	–	–	–	–	+/+	+/+
44	–	–	–	–	–	–	–	–	+/+	+/–
45	–	–	–	–	–	–	–	–	+/+	(+)/(+)
46–61	–	–	–	–	–	–	–	–	–	–

1–37, exposed individuals; 38–61, unexposed individuals; pet., petrolatum.

^a+, ++, +++: positive patch test reactions with an allergic morphology; ?, doubtful patch test reaction; –, negative patch test reaction.

^bD0: +, presence of subcutaneous nodule/s; D0: – no subcutaneous nodule/s.

^cD3: +, new subcutaneous nodule/s if – on D0; unchanged nodule/s if + on D0; D3: ++, enlarging of nodule/s present on D0; D3: –, no subcutaneous nodule/s.

^dD0: +/+, itching on both the left (L) and the right (R) upper arms; D0: –/–, no itching.

^eD3: +/+, new itching on both arms if –/– on D0; unchanged itching if +/+ on D0; D3: ++/++, aggravated itching on both arms; D3: (+)/(+), decreased itching on both arms; D3: –/– no itching.

In 100% of those individuals with the strongest contact allergy to aluminium (reactors positive to both 10% and 2%), nodules were present, while the corresponding figures for those with positive reactions only to 10%, with doubtful reactions or negative reactions, were 60%, 29%, and 23%, respectively (Fig. 3, $P = 0.007$, Cochran–Armitage trend test).

Itching on at least one upper arm was present in 15 (41%) exposed and 7 (29%) unexposed individuals ($P > 0.3$, Table 3). In the exposed group, itching was found to be significantly more prevalent in individuals with aluminium allergy (7/8 = 88% versus 8/29 = 29%, $P = 0.0038$). A

similar level of significance ($P = 0.0103$) was obtained for itching when the aluminium-positive group was compared with the unexposed group. In 12 participants, all, but 2 in the exposed group, reported aggravated itching after the patch test and five of those belonged to the aluminium-positive group. Reduced itching was noted in three exposed and four unexposed individuals. The difference between exposed and unexposed individuals with respect to alleviated, unchanged, and aggravated itching did not reach statistical significance ($P = 0.075$, Table 3). However, aggravated itching was more common in the exposed aluminium-hypersensitive participants

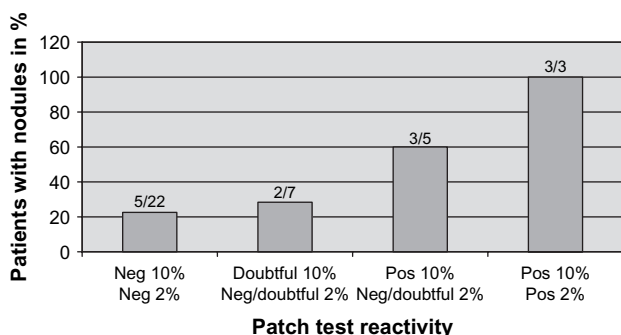


Fig. 3. The association between the presence of nodule/s and patch test reactivity to aluminium in the 37 exposed individuals. The figures above the bars represent the number of individuals with nodule/s of the number of individuals with a certain patch test reactivity, e.g. 5/22 means that nodule/s were detected in five individuals of those 22 who tested negatively to both aluminium chloride hexahydrate at both 10.0% and 2.0%. Neg, negative; pos, positive.

compared with exposed non-allergic and unexposed individuals ($P = 0.016$ and $P = 0.003$, respectively).

Furthermore, when comparing only the participants who were exposed, there were some striking differences between positive and negative reactors (Table 2). The children with aluminium allergy were significantly older ($P = 0.006$) than the children without aluminium allergy when they started the hyposensitization treatment. There also seemed to be some tendencies for lower doses (110 versus 181 mg in median, $P = 0.13$) and higher prevalence of at least one other contact allergy ($5/8 = 63\%$ versus $8/29 = 28\%$, $P = 0.12$) in the aluminium-hypersensitive group. In this group, there was also a significantly higher frequency ($P = 0.047$) of rash after using deodorant (Table 1).

Discussion

Surprisingly, in this small cohort of exposed and unexposed individuals, a statistically significant difference in contact allergy to aluminium was found between exposed and unexposed individuals. In the exposed group, no statistical correlation between dose and contact allergy could be shown, but strikingly, there was a tendency pointed towards a lower dose and the development of contact allergy to aluminium (Table 2). Whether this finding is due to a 'healthy worker effect', hyposensitization, an initially contracted contact allergy to aluminium or has any other explanation is not known. Age at start of treatment might be an important factor in developing contact allergy to aluminium, but our result differs from children having pertussis vaccines containing aluminium hydroxide (22).

The development/presence of persisting itching nodules at the injection sites after hyposensitization therapy with aluminium-precipitated antigen extract has been described in reports, sometimes associated with aluminium allergy (3–16). We were able to show that nodules at the site of injection are strongly associated with hyposensitization therapy with aluminium-precipitated antigen and also with contact allergy to aluminium.

Traditionally, contact allergy to aluminium has been diagnosed by patch testing with aluminium chloride hexahydrate in pet. at 2% and an empty Finn Chamber, which is made of elemental aluminium (1). In this study, 10% aluminium chloride hexahydrate was required to confirm aluminium contact allergy in five (63%) patients. Of these five patients, all suffered from itching of at least one arm, three had nodules at the injection sites and two had experienced an axillary rash from deodorants.

This study strongly indicates that hyposensitization therapy with aluminium-precipitated antigens may induce contact allergy to aluminium. The association between contact allergy to aluminium and the presence of itching nodules at the injection sites is most likely a manifestation of such allergy. An important question is whether itchy nodules can appear without aluminium allergy. It is possible that the seven exposed individuals with nodules before the patch test but without a positive aluminium patch test also had an aluminium contact allergy not diagnosed with the used preparations to diagnose aluminium allergy. Interestingly, this interpretation is supported by the indicated dose–response relationship between the degree of contact allergy to aluminium and the presence of nodules.

Also the appearance of new nodules and enlargement of nodules existing before patch testing, as well as the aggravation of itching at the injection sites during patch testing, were associated with aluminium allergy. Theoretically, there are at least two major possible explanations for the enlargement/aggravation. One explanation is that any positive patch test reaction to any sensitizer in the baseline patch test series would cause an enlargement/aggravation as a consequence of the induced allergic contact dermatitis (positive patch test reaction). However, there was no association between aggravation and other contact allergies except for aluminium (in manuscript). The other explanation is penetration of aluminium from the test preparations in the test chamber through the skin and subsequent absorption into the blood, resulting in a systemically induced aggravation. The extent of the penetration of aluminium chloride hexahydrate and aluminium hydroxide through the skin is not known, but patch testing with another metal salt,

gold sodium thiosulfate, resulted in a 10-fold increase of the blood level of gold (23).

Is aluminium allergy a new phenomenon or is it an old phenomenon that has been largely overlooked? It is likely that it is not an old phenomenon as a substantial part of the aluminium allergy reported in the literature (2, 5–9, 11–16) and found in this study was diagnosed by an empty Finn Chamber and the 2% pet. preparation with aluminium chloride hexahydrate. Over the years, thousands of patients at our department in Malmö have been tested with these without detection of any aluminium allergy. If it is a new phenomenon, what can then explain the allergy? Is there a change in the exposure pattern? Yes, we think so. In Sweden, hundreds of children with itchy nodules and contact allergy to aluminium have recently been found in children having been treated with vaccines containing aluminium hydroxide (15, 16). Previously, vaccines containing aluminium phosphate were used in Sweden without any known/negligible problem with contact sensitization. Besides differences in doses of aluminium salts used, differences in physicochemical properties of various aluminium salts as well as differences in the manufacturing process of antigen preparations and vaccines with possible significance for the bioavailability of aluminium ions in the tissue may help explain the new situation.

Paradoxically, treatment of type-I allergy induces another type of allergy, namely contact allergy (type-IV) to aluminium. This is unacceptable unless the aluminium contact allergy is not clinically relevant. However, the itchy nodules are a manifestation of the aluminium allergy. Furthermore, there was a statistically significant overrepresentation of deodorant intolerance in those who are aluminium hypersensitive. Aluminium salts are used as antiperspirants and are found in virtually all deodorants/antiperspirants on the Swedish market. The contact allergy to aluminium may also be relevant in many other situations as elemental aluminium and aluminium compounds are ubiquitous. Prospective, randomized, and controlled studies should be performed in patients undergoing hyposensitization therapy to explore and establish the sensitization rate to aluminium and the association between contact allergy to aluminium and clinical manifestations.

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