

High prevalence of contact allergy in adolescence: results from the population-based BAMSE birth cohort

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Summary

Background. Contact allergy is common among adults. However, little is known about the prevalence in adolescents.

Objectives. To assess the prevalence of allergy to common contact allergens in Swedish adolescents in the general population.

Participants and methods. The BAMSE cohort is a population-based birth cohort with the main aim of studying the risk factors for asthma, rhinitis, and atopic dermatitis. Patch testing was performed at the 16-year follow-up. The test (TRUE Test[®]) was applied at home, and removed 2 days later by nurses, who recorded and photographed the results. Dermatologists made final assessments on the basis of photographs and protocols.

Results. Two thousand two hundred and eighty-five participants (88% of all 16-year follow-up participants) were patch tested; 15.3% had at least one positive reaction. Contact allergy was more common in girls than in boys (17.0% versus 13.4%, $p = 0.018$). Sensitization to nickel was most common (7.5%), followed by sensitization to fragrance mix I (2.1%) and *p*-tert-butylphenol formaldehyde resin (1.9%). Nickel allergy was more frequent in girls (9.8% versus 4.9%, $p < 0.001$). Solitary sensitization to cobalt was more common than co-sensitization to nickel and cobalt.

Conclusions. The prevalence of contact allergy in adolescents is of almost the same high magnitude as in adults. The applied method was feasible in the population-based setting.

Key words: adolescents; epidemiology; fragrances; metals; patch test; plastics.

Approximately 15–20% of adults in the general population have contact allergy (1). Small children and adolescents also suffer from contact allergy and allergic contact dermatitis. However, little is known about how frequent contact allergy is among adolescents in the general population. Although studies of contact allergy in children and adolescents have been published, most are based on patients recruited from dermatological

specialist care (2–4). Moreover, diagnostic patch testing is time-consuming and laborious, and relatively few large patch test studies of the general population have been performed. A population-based study performed in Denmark in 1995–1996 showed a prevalence of contact allergy of 15.2% in schoolchildren aged 12–16 years, with 8.6% being sensitized to nickel (5). Nickel allergy was studied in teenagers in Sweden in 2000–2004,

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and a prevalence of 9.9% was found (6). Nickel allergy in adults and adolescents has been shown to be significantly associated with hand eczema (7, 8). Results from the population-based BAMSE birth cohort imply a 1-year prevalence of hand eczema of 5.2% among adolescents, and a strong association between atopic dermatitis in childhood and hand eczema in adolescence, but the cause of the hand eczema was not analysed (9, 10).

There are regional differences in exposure to contact allergens and in contact allergy to specific substances, nickel being the most prominent example. The prevalence of nickel allergy in dermatitis patients is lower in Denmark, Germany and Sweden than in Italy, Poland and the United Kingdom (11). An important explanation for this is variation in compliance with the EU restriction on nickel release and some previous national legislation (11–16). Among adults, there is a well-known female predominance of contact allergy, driven by nickel (13, 17). However, it is not clear to what extent this predominance already exists in childhood, as both patient studies and population-based studies show diverging results (18–20). More knowledge is also needed concerning which contact allergens adolescents are sensitized to today.

The present study is part of the prospective birth cohort named the BAMSE project (Children, Allergy, Milieu, Stockholm, Epidemiological Survey), the main aim of which is to study lifestyle and environmental risk factors for the development of atopic dermatitis, asthma, and rhinitis (21). The BAMSE cohort is internationally unique, as the adolescents have been followed since birth with repeated questionnaires. This large cohort provides an opportunity to explore contact allergy among adolescents in Sweden at a population level.

The main aim of the present study was to assess the prevalence of and sex difference in contact allergy to common contact allergens in Swedish 16-year-olds.

Materials and Methods

The BAMSE cohort and 16-year follow-up

The BAMSE cohort is a closed population-based birth cohort for which the children were recruited consecutively at birth and followed prospectively up to 16 years of age (21). The Swedish birth register was used to identify all children born in the time-span 1994–1996 in pre-defined areas of Stockholm, Sweden. The parents of all of the children were invited to take part, and 4089 children were included, corresponding to 75% of the eligible children.

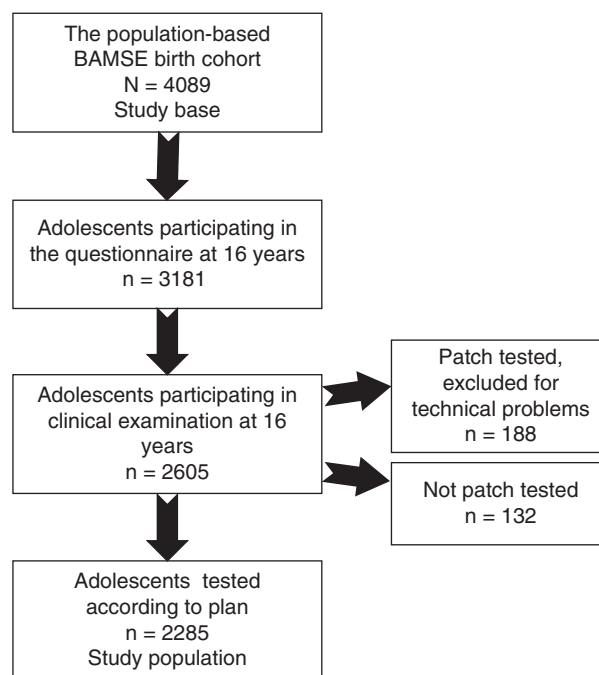


Fig. 1. Flow-chart showing the original cohort and how the final study population was arrived at.

The study population of the present study was defined as shown in Fig. 1. Both parental and adolescent questionnaires concerning asthma, rhinitis, atopic dermatitis and environmental factors were used at the age of 16 years. If either the adolescent or parent answered the questionnaire, the adolescent was asked to participate in a clinical examination to assess physical development, lung function, IgE sensitization, and, for the first time, contact allergy by patch testing, performed between January 2011 and March 2013.

Before the clinical examination, each participant received, by mail, ready-to-apply patch test tapes (TRUE Test® panels; Mekos Laboratories AS, Hillerød, Denmark) and written instructions. Self-adhesive fabrics (Mefix®; Mölnlycke Health Care, Göteborg, Sweden; two pieces, 5 × 30 cm²) were enclosed for 75% of the participants, to be applied across the upper and lower parts of the test panels to ensure skin contact, as some test panels had fallen off at the beginning of the study. TRUE Test® panels 1 and 2, and a specially prepared panel 3, were used, giving, in total, 30 test substances covering 24 of the 28 compounds of the European baseline series at the time of the study (Table 2 and Table S1). The test was applied at home on the back by someone assisting the participant.

At the clinical examination, 2 days after application of the test (D2), trained nurses inspected, marked and

removed the tapes, and 1 hr later they read, registered and photographed the results. The training (by M.M.) emphasized how to distinguish positive reactions from other reactions. The photography conditions were standardized concerning illumination, background, distance, and camera settings (by the Karolinska University Hospital photographer). The photographs included an overview and close-ups in cases of visible reactions. Final assessment of all tests was made under coded conditions by two dermatologists together (C.F.W., C.L., M.L., and M.M.), first independently and then in consensus, on the basis of photographs and protocols by the nurses. In the final assessment, the test results were scored as positive, negative, or inconclusive owing to technical problems (e.g. camera failure, patch test panels fallen off, or patches with insufficient skin contact). The minimum criteria for a positive reaction were homogeneous erythema and infiltration according to ICDRG criteria, corresponding to the current European Society of Contact Dermatitis guideline (22, 23). Test sites scored as negative included reactions not fulfilling the criteria for a positive reaction. This design was similar to that of previous population-based studies in Denmark (24, 25).

Ethical approval

The study was approved by the Regional Ethical Review Board in Stockholm, Sweden. The Declaration of Helsinki principles were followed, and all parents gave their written informed consent for their children to participate in the clinical examination. This was confirmed by the adolescents at the clinical examination.

Statistical analysis

Groups were compared by use of the χ^2 -test for non-parametric data. Differences were considered to be significant at $p < 0.05$. The prevalence proportions were defined as all positive reactions divided by the total number of patch tested adolescents. The study population and the study base (original cohort) were compared on a number of different background factors and 95% confidence intervals were computed. All data were analysed with the statistical package STATA™ Statistical Software (release 11.1; Stata-Corp, College Station, TX, USA).

Results

Study population

In total, 2285 adolescents (median age 16.7 years, range 15.8–18.9 years; 0.9% were aged 18 years when tested);

of these, 1199 girls (52.5%) and 1086 boys (47.5%) were included in the patch test study, representing 88% of the 2605 who participated in the 16-year follow-up (Fig. 1). The background characteristics of the individuals in the study population ($n = 2285$) and in the study base (original BAMSE birth cohort) ($n = 4089$) were considered to be comparable, despite somewhat lower participation among boys and somewhat higher participation among white-collar workers in the study population (Table 1).

Prevalence of contact allergy

A total of 2285 patch tests were assessed, and 15.3% of the subjects showed at least one positive patch test reaction. The highest frequencies of positive reactions were seen to nickel (7.5%), fragrance mix (hereby called fragrance mix I, to avoid confusion with fragrance mix II) (2.1%), and *p*-tert-butylphenol formaldehyde resin (PTBP-FR) (1.9%). Girls were sensitized significantly more often than boys (17.0% versus 13.4%, $p = 0.018$). With respect to single allergens, the sex differences were significant for nickel (9.8% versus 4.9%, $p < 0.001$). Sensitization to *Myroxylon pereirae* (balsam of Peru) was more common in boys than in girls (0.7% versus 0.1%, $p = 0.024$), although this result was based on few positive reactions. Positive reactions were seen to 29 of 30 test substances. Detailed data for all test substances are given in Table 2.

We assigned the test substances to seven groups: metals, adhesive chemicals, fragrances, topical drugs, hair dyes, preservatives, and rubber chemicals (Tables 2 and 3). The group 'adhesive chemicals' also contains plastic chemicals. Metals were the most frequent sensitizers (8.9%), followed by adhesive chemicals (2.6%) and fragrances (2.4%). Girls were sensitized to metals significantly more often than were boys (11.6% versus 6.3% $p < 0.001$), and the difference was driven by nickel (Table 2).

Of the patch tested adolescents, 2.0% (46/2285) were sensitized to more than one allergen. Forty were sensitized to two substances, 3 were sensitized to three substances, and 3 were sensitized to four substances. Of the subjects sensitized to cobalt, 34.6% were co-sensitized to nickel. Sensitization to metals is illustrated by the Venn diagram in Fig. 2.

Discussion

This population-based study confirms that adolescents are sensitized to frequently occurring contact allergens at almost the same high rate as adults. Nearly 2300 girls and boys in Sweden were patch tested for contact allergy at the

Table 1. Comparison of selected background factors to show the representativeness at 16 years of age between the study population (n = 2285) and the study base (original BAMSE cohort) (n = 4089)

	Study population (n = 2285), % (n)	95%CI	Study base (n = 4089), % (n)
Male sex	47.5 (1086)	45.5–49.6	50.5 (2065)
Parental history of AD, asthma, or rhinitis ^a	44.4 (1015)	42.8–46.9	43.1 (1746)
Parental smoking at baseline: yes	20.0 (455)	18.4–21.7	21.0 (855)
Socioeconomic status ^b : white-collar worker	84.7 (1910)	83.3–86.2	82.7 (3323)
Infantile eczema ^c	15.4 (345)	13.9–16.9	15.1 (594)
Young mother ^d : yes	7.3 (167)	6.2–8.4	7.8 (319)

Significant differences are in bold

AD, atopic dermatitis; CI, confidence interval.

^aDoctor's diagnosis of asthma and asthma medication and/or doctor's diagnosis of hay fever in combination with furred pets and/or pollen allergy and/or doctor's diagnosis of eczema (contact allergy among parents excluded) at baseline in any parent.

^bSocioeconomic groups according to Statistics Sweden.

^cDoctor's diagnosis of eczema and/or typical symptoms of eczema before 1 year of age.

^dMother's age below 25 years at birth of the child.

16-year follow-up of the BAMSE birth cohort. We found that allergy to nickel is the most frequent contact allergy in both girls and boys of the general population, and that the sex difference, with a female predominance, already exists in adolescence. The patch test system used (TRUE Test[®]) and the method of application were feasible in the population-based setting.

Of the adolescents in the study, 15.3% had at least one positive patch test reaction. The frequency of sensitization is in line with results for adults in the population (1). The highest frequencies of positive reactions were seen with nickel (7.5%), fragrance mix I (2.1%), PTBP-FR (1.9%), cobalt (1.2%), and *p*-phenylenediamine (1.1%). The results of our study on adolescents in Sweden are in line with the previously reported very high prevalence of nickel allergy in children, adolescents, and adults, in dermatitis patients, and in the population, particularly in females (2–8). This highlights the importance of making the EU nickel restriction and other preventive measures more effective to avoid sensitization and dermatitis among sensitized children, adolescents, and adults.

Allergy to fragrance mix I substance(s) was the second most common in this study, at a level consistent with other reports on adults and adolescents (3, 26, 27). It is likely that fragrance allergy is even more frequent than we found, as the TRUE Test[®] at the time of the study did not include fragrance mix II (six additional fragrance allergens), which became part of the European baseline series in 2008. Sensitization to *M. pereirae* was significantly more common in boys. We do not know the reason for this, but consider there might be sex-related differences in exposure to cosmetics or chemical products containing substances that cross-react with *M. pereirae* (28). Improved ingredient labelling would be beneficial

for the adolescents who are aware that they are sensitized, and reduced use of perfumed products during childhood would reduce the risk of sensitization.

Allergy to PTBP-FR was also common in adolescents in this study. This allergy has not been shown to be so prevalent in previously published population-based studies [0.9% in a study performed in 1995–1996 (5); 1.4% in 2000–2001 (29)], with the exception of one, where the prevalence was exceedingly high (13.8%) (18). Because of the late development of some reactions in previous studies, patch test sensitization has been suggested as an explanation (29). However, the reactions in our study were recorded on D2, not late. The formulation and concentration of PTBP-FR in TRUE Test[®] have not been altered (M Nielsen, pers comm, Smart Practice, 22 May 2015). We suggest that the slightly increasing prevalence of PTBP-FR allergy in young people may reflect increasing skin exposure. PTBP-FR is often present in shoe materials, watch straps, and sports gear, and is a well-known cause of foot eczema (30). Among other contact allergens that cause foot eczema are chromium, colophonium, and rubber chemicals.

Girls were sensitized significantly more often than boys. With respect to single allergens, the difference between the sexes was significant for nickel. It is known that the higher risk of nickel allergy in girls and women is related to differences in nickel exposure from jewellery, clothing, and other fashion items. Ear piercing and earrings have often been highlighted as important causes of nickel allergy (31, 32), but are probably now less important in countries where compliance with the nickel restriction is fairly good (12, 33).

Sensitization to cobalt was not associated with sensitization to nickel to the same high degree as is often

Table 2. Patch test substances (TRUE Test®) listed by frequency of positive test reactions on D2 in Swedish 16-year-old adolescents in the population-based BAMSE birth cohort (n = 2285)

Substance	Group	Prevalence, % (no. positive/no. tested) ^a			p
		All	Girls	Boys	
Nickel sulfate	Metal	7.50 (167/2236)	9.80 (115/1177)	4.90 (52/1062)	< 0.001
Fragrance mix I	Fragrance	2.10 (47/2245)	1.79 (21/1175)	2.43 (26/1070)	0.288
PTBP-FR	Adhesive chemical	1.88 (41/2183)	1.90 (22/1157)	1.85 (19/1026)	0.932
Cobalt chloride	Metal	1.17 (26/2226)	1.20 (14/1168)	1.13 (12/1058)	0.888
p-Phenylenediamine	Hair dye	1.08 (24/2222)	1.11 (13/1173)	1.05 (11/1049)	0.892
Colophonium	Adhesive chemical	0.45 (10/2241)	0.60 (7/1175)	0.28 (3/1066)	0.265
Lanolin alcohol	Topical drug	0.35 (8/2255)	0.42 (5/1182)	0.28 (3/1073)	0.567
<i>Myroxylon pereirae</i>	Fragrance	0.35 (8/2256)	0.08 (1/1180)	0.65 (7/1076)	0.024
MCI/MI	Preservative	0.32 (7/2209)	0.34 (4/1169)	0.29 (3/1040)	0.730
Potassium dichromate	Metal	0.31 (7/2264)	0.37 (4/1086)	0.28 (3/1078)	0.627
Carba mix	Rubber chemical	0.27 (6/2211)	0.17 (2/1165)	0.38 (4/1046)	0.342
Epoxy resin	Adhesive chemical	0.27 (6/2254)	0.30 (3/1180)	0.30 (3/1074)	0.908
Tixocortol-21-pivalate	Topical drug	0.27 (6/2264)	0.34 (4/1182)	0.18 (2/1082)	0.478
Formaldehyde	Preservative	0.22 (5/2224)	0.17 (2/1172)	0.29 (3/1052)	0.569
Mercapto mix	Rubber chemical	0.22 (5/2226)	0.09 (1/1172)	0.38 (4/1054)	0.143
Ethylendiamine-2HCl	Topical drug	0.22 (5/2242)	0.34 (4/1175)	0.09 (1/1067)	0.216
MDBGN	Preservative	0.18 (4/2267)	0.00 (0/1186)	0.37 (4/1081)	0.036
Mercaptobenzothiazole	Rubber chemical	0.14 (3/2203)	0.09 (1/1166)	0.19 (2/1037)	0.496
Thiomersal	Preservative	0.14 (3/2221)	0.09 (1/1167)	0.19 (2/1054)	0.505
Diazolidinyl urea	Preservative	0.13 (3/2255)	0.08 (1/1179)	0.19 (2/1076)	0.511
Caine mix	Topical drug	0.13 (3/2259)	0.18 (2/1084)	0.09 (1/1075)	0.568
Thiuram mix	Rubber chemical	0.09 (2/2209)	0.09 (1/1162)	0.10 (1/1047)	0.941
Budesonide	Topical drug	0.09 (2/2267)	0.17 (2/1186)	0.00 (0/1081)	0.177
Hydrocortisone-17-butyrate	Topical drug	0.09 (2/2267)	0.08 (1/1186)	0.09 (1/1081)	0.948
Paraben mix	Preservative	0.05 (1/2206)	0.09 (1/1186)	0.00 (0/1040)	0.349
Black rubber mix	Rubber chemical	0.05 (1/2219)	0.09 (1/1171)	0.00 (0/1048)	0.344
Imidazolidinyl urea	Preservative	0.04 (1/2253)	0.00 (0/1178)	0.09 (1/1075)	0.295
Quinoline mix	Topical drug	0.04 (1/2257)	0.08 (1/1181)	0.00 (0/1076)	0.340
Neomycin sulfate	Topical drug	0.04 (1/2260)	0.00 (0/1185)	0.09 (1/1075)	0.293
Quaternium-15	Preservative	0.00 (0/2185)	0.00 (0/1160)	0.00 (0/1025)	–
Any positive reaction	–	15.33 (350/2285)	17.01 (204/1199)	13.44 (146/1086)	0.018

MCI/MI, methylchloroisothiazolinone/methylisothiazolinone; MDBGN, methyldibromo glutaronitrile; PTBP-FR, p-tert-butylphenol formaldehyde resin.

^aThe numbers tested and finally assessed varied slightly between substances, owing to technical problems.

described in adult dermatitis patients (17, 34). Cobalt sensitization alone was more common than co-sensitization with nickel in the present study, and approximately half of the adult patients with cobalt allergy in a recent study were likewise not sensitized to nickel (C Lidén, et al. in manuscript, 2015). This highlights the need to increase our knowledge about sources of exposure and sensitization to cobalt, including products with cobalt-containing alloys, hard metals, platings, pigments, and drying agents (34–36).

The preservative methylchloroisothiazolinone (MCI)/methylisothiazolinone (MI) is an extremely potent sensitizer, and its use is severely restricted in cosmetics (15 ppm in rinse-off cosmetics; banned in leave-on cosmetics). The prevalence of allergy to MCI/MI was modest in the present study (0.3%). However, it should be recalled

that, since 2005, MI alone has been allowed in cosmetics at a much higher concentration (100 ppm), and that MI at 50 ppm in liquid soap has been shown to cause allergic contact dermatitis (37). An alarming increase in MI allergy has been noted when MI alone (at higher concentration than in the MCI/MI test substance) has been used for testing (38, 39). MI has been included in the European baseline series since 2015 (40). The prevalence of contact allergy to MCI/MI and MI is thus most likely underestimated in this study.

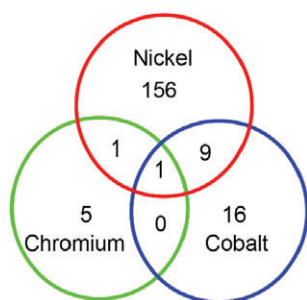
The prevalence of allergy to the preservative methyldibromo glutaronitrile (MDBGN) was low (0.18%) in the present study. We suggest that this is because of actions taken to reduce exposure from cosmetics. A rapid increase in allergy to MDBGN in the 1990s caused much concern. This resulted in a ban on MDBGN in cosmetic

Table 3. Groups of patch test substances (TRUE Test®) and positive reactions on D2 in Swedish 16-year-old adolescents in the BAMSE birth cohort

Group ^a	Prevalence			<i>p</i>
	All (%)	Girls (%)	Boys (%)	
Metals	8.9	11.6	6.3	< 0.001
Adhesive chemicals	2.6	2.7	2.4	NS
Fragrances	2.4	1.9	3.1	NS
Topical drugs	1.2	1.6	0.8	NS
Hair dyes	1.1	1.1	1.0	NS
Preservatives	1.1	0.8	1.4	NS
Rubber chemicals	0.8	0.5	1.1	NS

NS, not significant.

^aAn explanation of substance assignment to groups is given in Table 2.

**Fig. 2.** Distribution of number of positive patch test reactions to metals (nickel, cobalt, and chromium) (*n* = 200), showing solitary and concomitant reactivity in adolescents with allergy to metals (*n* = 188).

products (in 2005 for leave-on products and in 2008 for rinse-off products) when the participants were aged 10–13 years. Since then, the use of MDBGN in Sweden has been largely phased out for chemical products, including detergents (41, 42).

The strengths of this study include its population-based design, large size, and high participation rates. A failure analysis performed in 2002 showed that heredity for atopic disease did not differ between non-responders and responders, although parental smoking was more common among non-responders (21). The difference in parental smoking indicates that the original BAMSE cohort had a higher socioeconomic status than the eligible subjects (43).

A limitation of our study is that patch test readings were performed only once (on D2 after application and 60–70 min after removal of the test panels). It is known that this will result in underestimation of the true prevalence of contact allergy. However, it is not considered to result in false positives or overestimation when guideline

reading criteria are adhered to (23). Thus, these results represent minimum figures. In diagnostic patch testing of dermatitis patients, the recommendation is to perform at least two readings, on D3 or D4 and around D7, so as not to miss slowly developing test reactions (23, 44). It is not known exactly how large is the proportion of reactions that we missed by reading tests on D2 only, as this may vary with test concentrations, test systems, test sites, etc. A previous study that tested schoolgirls with nickel by the use of TRUE Test® and reading on D2 and D4 suggests that we may have missed 19–30% of positive reactions to nickel (45).

However, this test regime was considered to be essential to ensure a high participation rate. The participants only needed to come in once, and 2285 of 2605 adolescents successfully completed the patch testing. Patch testing with reading on D2 only was a necessary compromise that gave important results and was feasible in our population-based setting.

Assessment of patch test results (positive or non-positive) was performed by experienced patch testers, on the basis of digital photographs and recordings by specially trained nurses. The approach was applied in previous studies in Denmark (24, 25). Patch test rating based on photographs only has also been validated and found to be largely valid, particularly concerning the distinction between positive and non-positive reactions, as in our study (46, 47).

It was not possible to include assessment of the relevance of positive patch test reactions (past, present or unknown relevance) on the basis of history of dermatitis and exposure in the 16-year follow-up, where contact allergy was only one of many outcomes studied. However, data on contact allergy in relation to hand eczema, atopic dermatitis, IgE sensitization and genetic markers will be analysed and presented later.

Nickel is still, despite the EU restriction on nickel, which has been in force since 2000, the most common cause of contact allergy, along with fragrances and (in this study) PTBP-FR, cobalt, and *p*-phenylenediamine. The large difference in nickel allergy between the sexes, with a female predominance, already exists in adolescence. This might be a result of higher exposure, starting in childhood. External generalization to the general population of northern Europe is probably valid, because of the large and well-defined cohort, provided that the study limitations are kept in mind.

Conclusion

The prevalence of contact allergy is high among adolescents in the population, and in line with findings in adults.

A positive patch test reaction does not always mean that the subject will develop allergic contact dermatitis, but subjects with contact allergy are at risk of developing allergic contact dermatitis if exposed to the chemical at a concentration exceeding an individual threshold level. Patch testing and contact allergy should therefore always be considered in children and adolescents with eczema.

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the other nurses are acknowledged for assistance with patch testing.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Detailed information on patch test substances (TRUE Test®) used in the Swedish BAMSE birth cohort at the age of 16 years, 2011 to March 2013. Panels 1 and 2 were regular panels, and panel 3 was specially prepared for the study.

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High prevalence of contact allergy in adolescence: results from the population-based BAMSE birth cohort

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Table S1. Detailed information on patch test substances (TRUE Test[®]) used in the Swedish BAMSE birth cohort at the age of 16, 2011 - March 2013. Panels 1 and 2 were regular panels and panel 3 was specially prepared for the study

Panel no.	Substance no.	Substance	Conc. mg/cm ²	No. ingredients in mixes and alternative names
1	1	Nickel sulfate	0.2	
	2	Lanolin alcohol	1.0	
	3	Neomycin sulfate	0.23	
	4	Potassium dichromate	0.023	
	5	Caine mix	0.63	n=3
	6	Fragrance mix I	0.43	n=8
	7	Colophonium	0.85	
	8	Epoxy resin	0.05	
	9	Quinoline mix	0.19	n=2
	10	<i>Myrolylon pereirae</i>	0.8	balsam of Peru
	11	Ethylenediamine·2HCl	0.05	
	12	Cobalt chloride	0.02	
2	13	<i>p</i> -tert-butylphenol formaldehyde resin	0.05	PTBP-FR
	14	Paraben mix	1.0	n=5
	15	Carba mix	0.25	n=3
	16	Black rubber mix	0.075	n=3
	17	Methylchloroisothiazolinone/methylisothiazolinone	0.004	MCI/MI
	18	Quaternium-15	0.1	
	19	Mercaptobenzothiazole	0.075	
	20	<i>p</i> -Phenylenediamine	0.09	
	21	Formaldehyde	0.18	
	22	Mercapto mix	0.075	n=3
	23	Thiomersal	0.008	
	24	Thiuram mix	0.025	n=4
3	25	Diazolidinyl urea	0.55	Germall II
	26	Imidazolidinyl urea	0.6	Germall 115
	27	Budesonide	0.001	
	28	Tixocortol-21-pivalate	0.003	
	29	Hydrocortisone-17-butyrate	0.02	
	30	Methyldibromo glutaronitrile	0.005	MDBGN