

Nickel and Cobalt Release From Children's Toys Purchased in Denmark and the United States

Peter Jensen, MD, PhD,* Dathan Hamann, MD,† Carsten R. Hamann, BA,‡ Morten S. Jellesen, MSc, PhD,§ Sharon E. Jacob, MD,‡||¶ and Jacob P. Thyssen, MD, PhD, DMSc*

Background: Nickel is the most common allergen detected by patch testing in children. There is an increasing number of cases in children who have not had exposure to piercing. Although the clinical relevance of nickel patch test reactions in children is sometimes uncertain, continued vigilance to identify new sources of nickel exposure in this age group is important. Recent case reports have described allergic nickel contact dermatitis in children following exposure to toys, but the magnitude of this problem is unknown.

Objective: The aim of this study was to evaluate nickel and cobalt release from children's toys.

Methods: We purchased 212 toys in 18 different retail and online stores in the United States and Denmark. Nickel and cobalt release was tested using the dimethylglyoxime and cobalt screening spot tests.

Results: A total of 73 toys (34.4%) released nickel, and none released cobalt.

Conclusions: Toys are a commonly overlooked source of nickel exposure and sensitization. Therefore, dermatologists, allergists, and pediatricians should consider the role of toys in their evaluation of children with dermatitis, and the parents of children with positive nickel patch test reactions should be told that toys may release nickel and be a potential chemical source in the manifestation of allergic contact dermatitis.

It is well known that adult dermatitis patients often exhibit positive nickel and cobalt patch test reactions. However, nickel and cobalt are also very common allergens detected in children worldwide.¹ Accordingly, 12.9% of 85 unaffected American

children younger than 5 years, 28% of children with dermatitis patch tested by the North American Contact Dermatitis Group, and 27% of 321 three-month-old to 36-month-old Italian children with dermatitis were found to be sensitized to nickel, respectively.²⁻⁵ Notably, the evidence in the literature indicates the presence of positive nickel patch tests with uncertain clinical relevance. For example, in American children, clinical relevance of the positive nickel patch test reactions was only identified in 26%.² Similarly, in French children aged 1 to 15 years, nickel patch test reactivity was common, but positive reactions rarely correlated with actual exposures.⁶ Furthermore, when nickel patch testing was performed in 304 asymptomatic 18-month-old Danish infants from the general population, as many as 9% had positive patch test reactions to nickel, despite no identified exposure source.⁷ When 21 of the same 26 children with positive nickel test reactions were reevaluated at age 3 and 6 years, only 2 children had persistent reactivity to nickel supporting that infant skin may have a propensity to show false-positive reactions.⁸ In line with this, a Danish study from 1963 with similar findings suggested that the nickel sulfate test concentrations should be lowered from 5% to 1% in young children.⁹ Collectively, patch test reactivity to nickel can sometimes be incorrectly read as positive in children, but nonetheless true nickel sensitization is prevalent, and there remain sources still to be detected.

Contact dermatology practitioners should be cognizant of allergen exposure sources in children with chronic dermatitis who

From the *Department of Dermato-Allergology, Gentofte University Hospital, Hellerup, Denmark; †Division of Dermatology, Department of Internal Medicine, Wexner Medical Center at The Ohio State University, Columbus ‡Loma Linda University School of Medicine, CA; §Department of Mechanical Engineering, Technical University of Denmark, Kongens Lyngby ||Department of Dermatology, Loma Linda University, and ¶Department of Dermatology, University of California, San Diego.

Address reprint requests to: Peter Jensen, MD, PhD, Department of Dermato-Allergology, Copenhagen University Hospital Gentofte, Niels Andersen Vej 65, DK-2900 Hellerup, Denmark. E-mail: peter.jensen@regionh.dk.

Conflict of interests: D. Hamann and C.R. Hamann are first-degree relatives of Curt Hamann, owner of SmartPractice (Phoenix, AZ), a company that produces and distributes nickel and cobalt spot tests. J.P. Thyssen and M.S. Jellesen developed and sold the cobalt spot test to Smarthealth and will receive annual royalties depending on net sales.

Funding sources: J.P. Thyssen is a Lundbeck Foundation fellow and is supported by an unrestricted grant.

Disclosure: S.E. Jacob served as an independent investigator on the Safety and Efficacy of TRUE Test (Smart Practice; Phoenix, AZ) Panels 1.1, 2.1, and 3.1 in Children and Adolescents, Pediatric Research Equity Act 1 trial. She is currently an investigator on the Pediatric Research Equity Act 2 trial at UCSD/Rady Children's Hospital and a consultant for Johnson & Johnson.

DOI: 10.1097/DER.0000000000000084

Copyright © 2014 American Contact Dermatitis Society. All Rights Reserved.

have a positive patch test reaction to nickel or cobalt. Nickel exposures documented in the United States and Europe include jewelry, hair clasps, clothing items, computers, cell phones, and keys.^{10–13} Cobalt exposures include magnets, jewelry, and clothing items.¹⁴ Cutaneous exposure to toys that contain and release nickel can indeed result in allergic nickel dermatitis (ACD), as illustrated in recent reports.¹⁵ In this study, we evaluated nickel and cobalt release from exposed metallic components on children's toys that had been randomly purchased from stores in Denmark and the United States. We present the results along with 3 clinical cases of ACD in children.

METHODS

In the fall and winter of 2012/2013, a total of 212 toys were purchased from 18 retailers in the United States and Denmark. US retailers included www.amazon.com and 9 toy and thrift shops in San Bernadino County, California and Maricopa County, Arizona ($n = 63$). Toys were also purchased from 8 different toy stores in Copenhagen, Denmark ($n = 149$). We defined a toy as a product that is intended for use by a child for educational purposes or play. No jewelry was purchased. We selected and purchased toys with exposed metal components and assessed nickel and cobalt release with the nickel and cobalt spot tests. The dimethylglyoxime (DMG) nickel spot test was prepared by a hospital pharmacy in the Capital Region of Copenhagen. The test solutions were 1% DMG in alcohol and 10% ammonium hydroxide in water. The cobalt test based on nitroso R salt was prepared by the Department of Mechanical Engineering, Technical University of Denmark, Lyngby. These tests are both semiquantitative and become positive when about 10 and 8 ppm nickel and cobalt, respectively, are released in a solution.^{16,17} The nickel spot test is a DMG test containing water, ethanol, ammonium hydroxide, and DMG. The cobalt spot test contains water, sodium acetate, oxalic acid, and 1-nitroso naphthol 3,6-disulfonic acid disodium salt (nitroso R salt). We performed the tests by rubbing metallic toy surfaces with the activated tests' cotton tips for 30 to 60 seconds. When possible, cobalt and the nickel spot tests were performed on distinct metallic parts; otherwise, to minimize risk of false positives, cobalt release was tested first, followed by nickel.

A positive nickel test reaction was indicated by pink coloration of the cotton tip, whereas a negative test result was indicated by no color change of the cotton tip. A positive cobalt test reaction was indicated by an orange-red coloration of the cotton tip, whereas a negative test result was indicated by no color change of the cotton tip. Toys with brown or black discoloration of the cotton tip were washed in water and retested. Toys with doubtful reactions were retested. Persistent doubtful reactions were considered negative. Since the DMG test has a high specificity, but a moderate sensitivity, positive test reactions indicate that nickel is released in amounts that can cause nickel ACD in sensitized individuals.¹⁷ Although the cobalt spot test is very sensitive, becoming positive when very low amounts of cobalt

are released,¹⁶ the specificity of the cobalt spot test is currently unknown.

We recorded the cost of each toy; the store of purchase; the number of exposed metallic components on each toy; whether the toy was intended for girls, boys, or gender neutral; and finally, we graded the likelihood of skin contact with metallic components for each toy during normal play. "Definite" skin contact was defined as continuous skin contact with the metal component(s) (eg, a play tool made entirely of metal, such as a magnet or a metal mouth harmonica organ); "intermittent" was applied when the skin would only sometimes be in contact with the metal component (eg, a screw driver with a rubber handle, but where the child's index finger potentially would touch the metal to stabilize the tool during use); "uncommon/sporadic" was applied if the skin would only infrequently or sporadically touch the metallic component (eg, a ring on a toy otherwise made of plastic). The χ^2 test was used to test for associations between the different categories using IBM SPSS, version 20.0, Chicago, Ill. Two-sided values below 0.05 were considered statistically significant.

RESULTS

Of 212 toys (total cost, 3500 US \$/19,250 DKK), 81.6% ($n = 173$) cost 20 US \$ or less, 14.6% ($n = 31$) cost 20 to 40 US \$, and 3.8% ($n = 8$) cost more than 40 US \$. We rated presumed skin contact as definite for 58.5% ($n = 124$), intermittent for 39.2% ($n = 83$), and uncommon/sporadic for 2.3% ($n = 5$) of the toys. Most toys were gender neutral (58.5%, $n = 124$), whereas 27.4% ($n = 58$) were intended for girls, and 14.1% ($n = 30$) were intended for boys.

Table 1 shows the DMG test (nickel release) results of 149 toys purchased in 8 different stores in Copenhagen, Denmark. The toys ranged in price from 1 to 39 US \$ apiece and had a total of 200 exposed metal components of which 76 (38%) gave positive DMG test results. Table 2 shows the DMG test results of the 63 toys purchased from 10 different retailers in the United States. These toys all cost below 20 US \$ a piece and had a total of 105 exposed metallic components of which 54 (51.4%) tested positive with the DMG spot test.

In total, 73 (34.4%) of the 212 toys had at least 1 DMG test positive metallic component. Of the 149 toys purchased in Denmark, 41 (27.5%) were DMG test positive compared with 32 (50.8%) of the 63 toys purchased in the United States. A total of 39 (31%) of the 124 toys with definite skin contact gave positive DMG test reactions. Moreover, 34 (41%) of the 83 toys with intermittent skin contact gave positive DMG test reactions. None of the 212 toys gave positive cobalt spot test reactions.

Table 3 shows the relationship between the DMG test outcome, gender distribution, purchase price, and the likelihood of skin contact. There was no difference between the proportions testing DMG positive and negative with regards to purchase price and likelihood of skin contact with exposed metallic components. However, a significantly higher proportion of gender-neutral toys gave positive DMG test results.

TABLE 1. DMG Test Results of Toys Purchased in 8 Random Stores in Denmark

Toy No.	Type of Toy	Price (Low, Medium, High)	Store	No. Toy Parts	No. Positive Components, Nickel	No. Positive Components, Cobalt	Presumed Skin Contact (Definite, Intermittent, Uncommon)	Sex (Boy, Girl, Both)
1	Magnets	Low	1	1	0	0	Definite	Both
2	Binoculars	Medium	1	1	1	0	Definite	Both
3	Mini golf game	Low	1	1	1	0	Intermittent	Both
4	Magnets	Low	1	2	1	0	Definite	Both
5	Pin point	Medium	1	1	1	0	Definite	Both
6	Drum	Medium	1	1	1	0	Intermittent	Both
7	Music box	Medium	4	1	1	0	Definite	Girl
8	Metal box	High	4	1	1	0	Definite	Both
9	Balance ball	Low	4	1	1	0	Definite	Both
10	Magnets	Low	4	1	1	0	Definite	Both
11	Spinning top	Low	4	1	1	0	Definite	Both
12	Tools	Medium	3	4	1/4	0	Definite	Boy
13	Drum	Medium	4	1	1	0	Definite	Both
14	Doll	Low	4	1	1	0	Intermittent	Both
15	Xylophone	Medium	4	1	1	0	Definite	Both
16	Spinning top	Medium	4	1	1	0	Definite	Both
17	Skate board	Medium	5	3	1/3	0	Definite	Boy
18	Binoculars	Low	2	1	1	0	Definite	Both
19	Picnic set	Medium	4	1	1	0	Definite	Girl
20	Rattle	Low	4	1	1	0	Definite	Both
21	Music box	Low	4	1	1	0	Definite	Girl
22	Shovel	Low	4	1	1	0	Definite	Both
23	Tools	Low	4	5	4/5	0	Definite	Boy
24	Key chain	Low	4	1	1	0	Definite	Both
25	Foldable pocket comb	Low	4	1	1	0	Intermittent	Boy
26	Tools	Medium	4	8	8/8	0	Definite	Boy
27	Tools	High	4	5	1/5	0	Definite	Boy
28	Shovel	Low	4	1	1	0	Definite	Both
29	Key chain	Low	6	1	1	0	Intermittent	Both
30	Hair clasp	Low	4	1	1	0	Definite	Girl
31	Key chains	Medium	4	4	4/4	0	Intermittent	Girl
32	Key chain	Low	7	1	1	0	Intermittent	Girl
33	Purse	Medium	7	1	1	0	Intermittent	Girl
34	Purse	Low	8	1	1	0	Intermittent	Girl
35	Key chain	Low	8	1	1	0	Intermittent	Girl
36	Magician rings trick	Medium	7	4	4/4	0	Definite	Both
37	Diary	Low	6	1	1	0	Intermittent	Girl
38	Tweezers	Low	6	1	1	0	Definite	Both
39	Diary	Low	8	1	1	0	Intermittent	Girl
40	Key chain	Low	6	1	1	0	Intermittent	Both
41	Key chain	Low	7	1	1	0	Intermittent	Both
42	Magnets	Low	6	10	10/10	0	Definite	Both
43	Loom	Low	1	1	0	0	Uncommon	Girl
44	Pistol	Low	1	1	0	0	Definite	Boy
45	Basket	Low	1	1	0	0	Definite	Girl
46	Cube puzzle	Medium	1	1	0	0	Intermittent	Both
47	Microscope	High	1	1	0	0	Uncommon	Both
48	Rods	Medium	1	1	0	0	Intermittent	Both
49	Acrobat ball	Medium	1	1	0	0	Intermittent	Both
50	Plane tools	High	1	1	0	0	Uncommon	Boy
51	Metal box	Low	1	1	0	0	Definite	Both

(Continued on next page)

TABLE 1. (Continued)

Toy No.	Type of Toy	Price (Low, Medium, High)	Store	No. Toy Parts	No. Positive Components, Nickel	No. Positive Components, Cobalt	Presumed Skin Contact (Definite, Intermittent, Uncommon)	Sex (Boy, Girl, Both)
52	Rattle	Low	1	1	0	0	Definite	Both
53	Yo-yo	Low	1	1	0	0	Definite	Both
54	Bottle	Low	1	1	0	0	Intermittent	Both
55	Bucket	Low	1	1	0	0	Definite	Girl
56	Puzzle	Low	1	1	0	0	Definite	Both
57	Flashlight	Low	1	1	0	0	Definite	Boy
58	Toolkit	Medium	1	4	0	0	Definite	Boy
59	Golf club	Low	2	1	0	0	Definite	Both
60	Dart game	Medium	3	1	0	0	Intermittent	Both
61	Arrows	Low	3	1	0	0	Definite	Both
62	Cookware	Medium	3	1	0	0	Definite	Both
63	Crane	Medium	5	1	0	0	Definite	Both
64	Pointing pen	Low	5	1	0	0	Definite	Both
65	Cookware	Low	4	1	0	0	Definite	Both
66	Abacus	Low	4	1	0	0	Definite	Both
67	Soccer game	High	3	1	0	0	Intermittent	Boy
68	Soccer game	High	3	1	0	0	Intermittent	Boy
69	Safe	Low	4	1	0	0	Definite	Both
70	Jewelry	Low	4	1	0	0	Definite	Girl
71	Patch	Low	4	1	0	0	Intermittent	Both
72	Wallet	Low	3	1	0	0	Intermittent	Girl
73	Brush	Low	3	1	0	0	Definite	Both
74	Key ring	Low	3	1	0	0	Intermittent	Both
75	Scissors	Low	3	1	0	0	Definite	Girl
76	Rattle	Low	3	1	0	0	Definite	Both
77	Train	Low	3	1	0	0	Intermittent	Boy
78	Race track	High	3	1	0	0	Intermittent	Boy
79	Dollhouse	High	4	1	0	0	Definite	Girl
80	Soccer game	Medium	2	1	0	0	Intermittent	Boy
81	Musical instruments	Medium	3	3	0	0	Definite	Both
82	Soccer game	Low	2	1	0	0	Definite	Boy
83	Tools	Low	2	1	0	0	Definite	Both
84	Pen	Low	2	1	0	0	Intermittent	Both
85	Bell	Low	2	1	0	0	Intermittent	Both
86	Balls	Low	2	1	0	0	Definite	Both
87	Harmonica	Low	2	1	0	0	Definite	Both
88	Wallet	Low	2	1	0	0	Definite	Girl
89	Scissors	Low	2	1	0	0	Definite	Girl
90	Earrings	Low	4	1	0	0	Definite	Girl
91	Rings	Low	4	2	0	0	Definite	Girl
92	Birthday train	Medium	4	1	0	0	Intermittent	Both
93	Rattle	Low	4	1	0	0	Definite	Both
94	Spring	Low	4	1	0	0	Definite	Both
95	Bell	Low	4	1	0	0	Definite	Both
96	Necklace	Low	4	1	0	0	Definite	Girl
97	Key chain	Low	4	1	0	0	Definite	Girl
98	Puzzle	Low	4	1	0	0	Definite	Both
99	Mask	Medium	1	1	0	0	Definite	Boy
100	Belt	Low	1	1	0	0	Definite	Boy
101	Bell	Low	4	1	0	0	Definite	Both

(Continued on next page)

TABLE 1. (Continued)

Toy No.	Type of Toy	Price (Low, Medium, High)	Store	No. Toy Parts	No. Positive Components, Nickel	No. Positive Components, Cobalt	Presumed Skin Contact (Definite, Intermittent, Uncommon)	Sex (Boy, Girl, Both)
102	Necklace	Low	4	1	0	0	Definite	Girl
103	Bike	Medium	5	1	0	0	Definite	Boy
104	Rattle	Low	5	1	0	0	Definite	Both
105	Rattle	Low	5	1	0	0	Definite	Both
106	Key chain	Low	4	1	0	0	Definite	Girl
107	Bracelet	Medium	4	2	0	0	Definite	Girl
108	Wristwatch	Medium	4	2	0	0	Definite	Girl
109	Charm bracelet	Low	4	1	0	0	Definite	Girl
110	Key chain	Low	4	1	0	0	Definite	Boy
111	Brushes	Low	4	3	0	0	Definite	Both
112	Key chain	Low	4	1	0	0	Definite	Girl
113	Bike	Low	5	1	0	0	Definite	Boy
114	Back-scratcher	Low	2	1	0	0	Definite	Both
115	Scissors	Low	4	1	0	0	Intermittent	Both
116	Bracelet	Low	4	1	0	0	Definite	Girl
117	Scissors	Low	4	1	0	0	Intermittent	Both
118	Jewelry clay blades	Low	4	3	0	0	Definite	Girl
119	Brushes	Low	6	3	0	0	Definite	Both
120	Rivets	Low	6	1	0	0	Intermittent	Both
121	Key chain	Low	4	1	0	0	Intermittent	Girl
122	Purse	Low	7	1	0	0	Intermittent	Girl
123	Cookware	Low	7	2	0	0	Definite	Both
124	Dice in a can	Low	5	1	0	0	Intermittent	Both
125	Gun	Low	5	1	0	0	Intermittent	Boy
126	Low energy dispersion magnifier	Low	5	1	0	0	Intermittent	Both
127	Bracelet	Low	7	1	0	0	Intermittent	Girl
128	Key chain	Low	8	1	0	0	Intermittent	Girl
129	Key chain	Low	7	1	0	0	Intermittent	Girl
130	Bracelet	Low	7	1	0	0	Definite	Girl
131	Key chain	Low	7	1	0	0	Intermittent	Girl
132	Necklace	Low	5	1	0	0	Definite	Girl
133	Necklace	Low	6	1	0	0	Definite	Girl
134	Key chain	Low	7	1	0	0	Intermittent	Girl
135	Key chain	Low	7	1	0	0	Intermittent	Girl
136	Charm	Low	6	1	0	0	Definite	Girl
137	Bracelet	Low	6	1	0	0	Definite	Girl
138	Key chain	Low	7	1	0	0	Intermittent	Girl
139	Card tricks device	Medium	7	1	0	0	Intermittent	Both
140	Skateboard	Medium	5	1	0	0	Intermittent	Boy
141	Train	Low	6	1	0	0	Intermittent	Boy
142	Key chain	Low	7	1	0	0	Intermittent	Boy
143	Car	Medium	5	1	0	0	Intermittent	Boy
144	Charm	Low	6	1	0	0	Definite	Girl
145	Bracelet	Low	7	1	0	0	Definite	Girl
146	Diary	Low	8	1	0	0	Intermittent	Both
147	Purse	Low	6	1	0	0	Intermittent	Girl
148	Key chain	Low	7	1	0	0	Intermittent	Both
149	Mouse trap game	Low	6	1	0	0	Intermittent	Both

Low, 0 to 20 US \$; medium, 20 to 40 US \$; high, more than 40 US \$. Store 1: Toys, Hørsholm; store 2: Tiger, Lyngby; store 3: Toys 'r' us, Gentofte; store 4: Grønært Shop, Lyngby; store 5: BR, Lyngby; store 6: Panduro Hobby, Lyngby; store 7: Bahne, Lyngby; store 8: Arnold Busck, Lyngby.

TABLE 2. DMG Test Results of Toys Purchased in 10 Random Stores in the United States

Toy no.	Type of Toy	Price (Low, Medium, High)	Store	No. Toy Parts	No. Positive Components, Nickel	No. Positive Components, Cobalt	Presumed Skin Contact (Definite, Intermittent, Uncommon)	Sex (Boy, Girl, Both)
150	Figure with metal tie	Low	9	1	1	0	Definite	Both
151	Car	Low	9	1	1	0	Intermittent	Both
152	Fish with key chain	Low	9	1	1	0	Intermittent	Both
153	Binoculars	Low	9	1	1	0	Intermittent	Both
154	Claw grabber	Low	10	1	1	0	Definite	Both
155	Make-up case	Low	11	1	1	0	Intermittent	Girl
156	Key chain skateboard	Low	11	1	1	0	Intermittent	Both
157	Denim doll clothing	Low	11	2	1/2	0	Intermittent	Girl
158	Transformer Bot Shots Battle Game	Low	12	2	2/2	0	Intermittent	Boy
159	Key chain	Low	12	1	1	0	Intermittent	Both
160	Latches board	Low	13	10	10/10	0	Definite	Both
161	Skateboard ramp and grind bar	Low	13	1	1	0	Definite	Both
162	Tambourine	Low	13	4	4/4	0	Intermittent	Girl
163	Van	Low	13	1	1	0	Intermittent	Both
164	Rattle with bells	Low	13	4	4/4	0	Definite	Girl
165	Little tikes tambourine	Low	13	4	4/4	0	Intermittent	Both
166	Puzzle box and Lunchbox	Low	13	2	2/2	0	Definite	Both
167	Train Engine Take and Play	Low	14	2	2/2	0	Intermittent	Both
168	Train Engine	Low	14	1	1	0	Intermittent	Both
169	Train express	Low	14	1	1	0	Intermittent	Both
170	Tractor trailer with hay	Low	13	1	1	0	Intermittent	Both
171	Sailor key ring	Low	14	1	1	0	Intermittent	Both
172	Car	Low	15	1	1	0	Intermittent	Both
173	Car	Low	15	1	1	0	Intermittent	Both
174	Whistle	Low	16	1	1	0	Definite	Both
175	Whistle	Low	16	1	1	0	Definite	Both
176	Hex Bug Ant	Low	17	2	2/2	0	Definite	Both
177	Railroad track	Low	16	1	1	0	Intermittent	Both
178	Magnets	Low	16	2	1/2	0	Definite	Both
179	Magic nickels magic trick	Low	16	1	1	0	Definite	Both
180	Toy railroad track ties	Low	16	1	1	0	Definite	Both
181	Adjustable mini skateboard set	Low	18	2	1/2	0	Intermittent	Both
182	Transforming ball with metal springs and screws	Low	9	1	0	0	Uncommon	Boy
183	Gold/blue ninja man	Low	9	1	0	0	Intermittent	Boy
184	Transforming ball with metal springs and screws	Low	9	2	0	0	Uncommon	Boy
185	Remote-controlled car with metal antennae	Low	9	1	0	0	Intermittent	Both
186	Cement mixer	Low	9	1	0	0	Intermittent	Both
187	Doll clothes	Low	11	3	0	0	Definite	Girl
188	Skateboard	Low	12	2	0	0	Intermittent	Both
189	Princess tambourine	Low	12	4	0	0	Definite	Girl

(Continued on next page)

TABLE 2. (Continued)

Toy no.	Type of Toy	Price (Low, Medium, High)	Store	No. Toy Parts	No. Positive Components, Nickel	No. Positive Components, Cobalt	Presumed Skin Contact (Definite, Intermittent, Uncommon)	Sex (Boy, Girl, Both)
190	Noise magnets	Low	12	1	0	0	Definite	Both
191	Remote-controlled car with metal antenna	Low	13	1	0	0	Intermittent	Both
192	Remote-controlled car with metal antenna	Low	13	2	0	0	Intermittent	Both
193	Spinner	Low	13	2	0	0	Definite	Both
194	Stuffed animal leopard key chain	Low	13	1	0	0	Intermittent	Both
195	Toy car with wrench	Low	13	1	0	0	Definite	Both
196	Hot wheels hot rod	Low	13	1	0	0	Intermittent	Both
197	Toy ice scoop	Low	13	1	0	0	Definite	Both
198	Princess rattle with chimes	Low	13	3	0	0	Intermittent	Girl
199	Large slinky	Low	13	1	0	0	Definite	Both
200	Driftblade Ultraspin	Low	14	1	0	0	Definite	Boy
201	Rat-ified racer	Low	14	2	0	0	Definite	Both
202	Sports Fun Junior Pro Golf	Low	15	2	0	0	Definite	Both
203	Twirler	Low	16	1	0	0	Definite	Both
204	Gyroscope	Low	16	2	0	0	Definite	Both
205	Jumbo Jacks	Low	16	2	0	0	Definite	Both
206	Harmonica	Low	16	1	0	0	Definite	Both
207	Metal Kazoo	Low	16	1	0	0	Definite	Both
208	Motorcycle	Low	17	2	0	0	Definite	Both
209	Robot	Low	17	2	0	0	Definite	Both
210	Handcuffs	Low	18	1	0	0	Definite	Both
211	Mini slinky	Low	18	1	0	0	Definite	Both
212	Puzzle set and box	Low	18	1	0	0	Definite	Both
					54/105 (51.4%)			

Low, 0 to 20 US \$; medium, 20 to 40 US \$; high, more than 40 US \$. Store 9: Redlands Thrift, Redlands, CA; store 10: Walmart, Colton, CA; store 11: 99 Cent Bargain, Colton, CA; store 12: Dollar Tree–Phoenix 13/Good Will, Phoenix, AZ; store 14: Target, Phoenix, AZ; store 15: Big Lots, Phoenix, AZ; store 16: Amazon.com; store 17: Radio Shack, Phoenix, AZ; store 18: Family Dollar, Phoenix, AZ.

CASES

All the patients described below were seen and treated at the Contact Dermatitis Clinic, University of Miami by S.E.J.

1. A 1-year-old boy with atopic dermatitis (AD) and perioral and generalized dermatitis was found to have a positive patch test reactions to *Myroxylon pereirae* (1+), fragrance mix 1 (1+), nickel sulfate (1+), and propylene glycol (1+). On follow-up, the patient had improved only slightly with the prescribed avoidance regimen. When the boys' favorite toy, his parents' key fob, was avoided, he had rapid and significant clearance of his dermatitis. Notably, his AD became manageable with emollient therapy.
2. A 3-year-old boy with AD and dermatitis on his hands, feet, and abdominal skin had positive patch test reactions to cocamidopropyl betaine (1+), nickel sulfate (2+), cinnamic aldehyde (1+), and geraniol (1+). He experienced some

improvement on a sensitive skin regimen avoiding fragrances, formaldehyde, and cocamidopropyl betaine. However, significant improvement of his dermatitis was noted when his metallic toys (namely, metal cars and generic slinky) were specifically avoided.

3. A 2-year-old boy with AD and dermatitis on both forearms presented for evaluation. Patch testing showed a 2+ reaction to nickel sulfate only. The child often played with a set of nickel-releasing toy keys, and dermatitis resolved when the keys were removed.

DISCUSSION

A search for new sources of nickel exposure in children is crucial to address and limit nickel sensitization and dermatitis, particularly as clinical relevance is often difficult to establish. An increasing number of recognized cases of sensitization to nickel has

TABLE 3. DMG Test Results Stratified by Sale Price, Presumed Skin Contact During Normal Play, and Typical Gender That Would Play With the Toy

	DMG Test Negative	DMG Test Positive	P
Price			0.356
Low, n = 173	67.1% (n = 116)	32.9% (n = 57)	
Medium, n = 31	54.8% (n = 17)	45.2% (n = 14)	
High, n = 8	75% (n = 6)	25% (n = 2)	
Skin contact			0.096
Definite, n = 124	68.5% (n = 85)	31.5% (n = 39)	
Intermittent, n = 83	59% (n = 49)	41% (n = 34)	
Uncommon, n = 5	100% (n = 5)	0	
Intended for:			0.040
Boys, n = 30	80% (n = 24)	20% (n = 6)	
Girls, n = 58	72.4% (n = 42)	27.6% (n = 16)	
Both genders, n = 124	58.9% (n = 73)	41.1% (n = 51)	
Total (n = 212)	65.6 (n = 139)	34.4 (n = 73)	

Price: low, 0 to 20 US \$; medium, 20 to 40 US \$; high, more than 40 US \$.

Presumed skin contact: definite—continuous skin contact with metal (toy entirely made of metal); intermittent—skin only sometimes in contact with metal (such as a screw driver with rubber handle and metal tip); uncommon—only sporadic skin contact.

been noted in younger children who have not had exposure to piercings, suggesting additional potentially relevant sources of nickel exposure.¹⁸ Inspired by the observation of Hsu and Jacob¹⁵ that children's toys indeed can release sufficient amounts of nickel to cause nickel contact dermatitis, we evaluated a large sample of toys that had exposed metallic components purchased in Denmark and the United States.

Respectively, 27.5% and 50.8% of toys with metallic parts purchased in Denmark and the United States released excessive amounts of nickel when tested with the DMG nickel spot test. This test becomes positive when nickel is released in amounts that can cause ACD in sensitized individuals.¹⁷ No associations were found regarding price and intended gender, suggesting that all pediatric consumers seem to be equally at risk. Three cases were presented to emphasize that excessive nickel release from toys indeed can have significant clinical consequences. Notably, all 3 children also had met the Hanifin and Rajka criteria for AD. Previous studies have linked the high prevalence of nickel allergy to AD, and nickel allergy has even been suggested as an independent minor criteria for the Hanifin and Rajka criteria.¹⁹ The link between nickel allergy and AD could likely be explained by the shared association with loss-of-function mutation in the filaggrin gene because filaggrin deficiency enhances the penetration of nickel ions through a histidine-depleted stratum corneum.²⁰ We recommend that the parents of nickel sensitized children should be educated in the use of the DMG test to screen toys and other items that may release nickel, especially in those who also carry the diagnosis of AD. In addition, parents should be aware that their personal items such as keys and cell phones often contain and release nickel.¹³ Their use as child distraction-entertainment devices is therefore not recommended because they, as illustrated in case report 1, can elicit ACD. A limitation of our study was that we did not quantify nickel release by using more advanced chemical tests, such as for example, the EN1811 1-week sweat test

where the metallic item is dispersed in artificial sweat for 1 week before nickel release is estimated.

Approximately 10 years ago, representatives from the Nickel Development Institute and the Nickel Producers Environmental Research Association met with the Consumer Product Safety Commission to encourage the United States to adopt legislation similar to the 1994 European Nickel Directive, which is now included in the Regulation on Registration, Evaluation, Authorization, and Restriction of Chemicals. This European regulation dictates that certain consumer products intended to be in prolonged skin contact should not release more than 0.5 µg nickel/cm² per week as this limit was predicted to limit nickel allergy and dermatitis.²¹ Indeed, since the implementation of this regulation, a change in the epidemiology of nickel allergy and dermatitis has been observed in European adults.²² Nevertheless, despite having been stabilized, the prevalence of nickel allergy is still very high.²³

The United States Consumer Product Safety Commission shared concern over the need for limiting nickel release from articles that would come in direct and prolonged contact with the skin, but they could not commit to action at that time (personal communication with CPSC, SJ December 2013). Nickel in toys in the United States is therefore currently not under specific regulation. Furthermore, although standards have been developed that recommend avoiding the use of strong sensitizers (toys would not be exempt from this), nickel is not specifically mentioned. Likewise, in Canada, Section 26 and Schedule 3 of the *Toys Regulations* states that "Substances that are excessively corrosive, excessively irritating, or excessively strong sensitizers are not permitted for use in toys if they can come in contact with the skin" (<http://www.hc-sc.gc.ca/cps-spc/pubs/indust/toys-jouets/index-eng.php>). Notably, nickel is also not specifically mentioned in this regulation.

At present, children's toys are not covered by the European Union (EU) Nickel Directive. However, the German Federal

Institute for Risk Assessment suggested in 2010 that the limit for nickel release specified in the Registration, Evaluation, Authorization, and Restriction of Chemicals regulation should also apply to toys with metal components, which may come into extensive contact with children's skin for extended time (<http://www.bfr.bund.de/cm/349/contact-allergens-in-toys-health-assessment-of-nickel-and-fragrances.pdf>). This proposal is consistent with the intention of the EU Toy Directive 2009/48/EF (<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2009:170:0001:0037:EN:PDF>), which states that toys must be shaped and manufactured in a manner that imposes no harmful effects on human health due to release of chemical compounds. The Toy Directive also states that nickel containing stainless steel is safe in toys. Importantly, the limits of nickel release from toys sold in EU member states are now restricted to 75 mg/kg ($\approx$ parts per million), 18.8 mg/kg, and 930 mg/kg, respectively, from the following: (1) dry, brittle, powderlike, or pliable toy material; (2) liquid or sticky toy material; (3) scraped-off toy material.

Unfortunately, with the relatively high nickel release concentrations allowed by the Toy Directive, DMG test positive toys from this study, although capable of eliciting nickel ACD, could theoretically be in compliance with the directive, as the DMG test becomes positive when about 10 ppm nickel concentrations are present. Importantly, skin contact with DMG test–positive metallic items can result in ACD in nickel-sensitized individuals.²⁴ The conclusion is that exposure to toys releasing nickel in amounts that result in a positive DMG test should be minimized because they clearly pose a risk for the child in terms of nickel sensitization and subsequent ACD.

So far, when the cobalt spot test has been utilized in market surveys, it has only very infrequently detected significant cobalt release from jewelry, belt buckles, cell phones, and work tools.²⁵ Based on the results from the present study, we postulate that children's toys likely do not represent a significant risk of cobalt sensitization, as they do for nickel. Nonetheless, cobalt patch test reactivity is commonly reported in American children with dermatitis with reaction rates reported as high as 18%.² Because some of these could be irritant in nature and falsely be read as positive reactions, more investigation is needed with repeat patch testing on the subjects to determine the reproducibility and clinical relevance of these reactions.

This is the first market survey that investigates nickel release from children's toys. We recommend that dermatologists, allergists, and pediatricians consider the role of toys in the evaluation of children suspected with nickel sensitization and AD, despite previous studies which have documented that clinical relevance of positive nickel reactions can sometimes be difficult to determine. The parents of children with positive patch test reactions to nickel should be educated on the potential for nickel exposure through metallic toys. The prevalence of nickel allergy has continued to increase among American children affected with dermatitis, from 25% in 1992 to 93% to 36% in 2003 to 2004.²⁶ Our results suggest that toys could play a role in this development. A regulatory

initiative to limit the use of nickel-releasing alloys in children's toys could be important in reducing nickel exposure in children.

REFERENCES

1. Simonsen AB, Deleuran M, Mortz CG, et al. Allergic contact dermatitis in Danish children referred for patch testing—a nationwide multicentre study. *Contact Dermatitis* 2014;70(2):104–111.
2. Zug KA, McGinley-Smith D, Warshaw EM, et al. Contact allergy in children referred for patch testing: North American Contact Dermatitis Group data, 2001–2004. *Arch Dermatol* 2008;144(10):1329–1336.
3. Belloni Fortina A, Romano I, Peserico A, et al. Contact sensitization in very young children. *J Am Acad Dermatol* 2011;65(4):772–779.
4. Weston WL, Weston JA, Kinoshita J, et al. Prevalence of positive epicutaneous tests among infants, children, and adolescents. *Pediatrics* 1986;78(6):1070–1074.
5. Bruckner AL, Weston WL, Morelli JG. Does sensitization to contact allergens begin in infancy? *Pediatrics* 2000;105(1):e3.
6. Roul S, Ducombs G, Taieb A. Usefulness of the European standard series for patch testing in children. A 3-year single-centre study of 337 patients. *Contact Dermatitis* 1999;40(5):232–235.
7. Johnke H, Norberg LA, Vach W, et al. Reactivity to patch tests with nickel sulfate and fragrance mix in infants. *Contact Dermatitis* 2004;51(3):141–147.
8. Mortz CG, Kjaer HF, Eller E, et al. Positive nickel patch tests in infants are of low clinical relevance and rarely reproducible. *Pediatr Allergy Immunol* 2013;24(1):84–87.
9. Marcussen PV. Primary irritant patch-test reactions in children. *Arch Dermatol* 1963;87:378–382.
10. Heim KE, McKean BA. Children's clothing fasteners as a potential source of exposure to releasable nickel ions. *Contact Dermatitis* 2009;60(2):100–105.
11. Thyssen JP, Menné T, Johansen JD. Nickel release from inexpensive jewelry and hair clasps purchased in an EU country—are consumers sufficiently protected from nickel exposure? *Sci Total Environ* 2009;407(20):5315–5318.
12. Hamann D, Hamann C, Li LF, et al. The Sino-American belt study: nickel and cobalt exposure, epidemiology, and clinical considerations. *Dermatitis* 2012;23(3):117–123.
13. Hamann D, Scheman AJ, Jacob SE. Nickel exposure from keys: alternatives for protection and prevention. *Dermatitis* 2013;24(4):186–189.
14. Cheong SH, Choi YW, Choi HY, et al. Nickel and cobalt release from jewellery and metal clothing items in Korea. *Contact Dermatitis* 2014;70(1):11–18.
15. Hsu JW, Jacob SE. Children's toys as potential sources of nickel exposure. *Dermatitis* 2009;20(6):349–350.
16. Thyssen JP, Menné T, Johansen JD, et al. A spot test for detection of cobalt release—early experience and findings. *Contact Dermatitis* 2010;63(2):63–69.
17. Thyssen JP, Skare L, Lundgren L, et al. Sensitivity and specificity of the nickel spot (dimethylglyoxime) test. *Contact Dermatitis* 2010;62(5):279–288.
18. Czarnobilska E, Obtulowicz K, Dyga W, et al. Contact hypersensitivity and allergic contact dermatitis among school children and teenagers with eczema. *Contact Dermatitis* 2009;60(5):264–269.
19. Huber A, Fartasch M, Diepgen TL, et al. Occurrence of contact allergies in atopic eczema. Relation to simultaneously detected atopic markers [in German]. *Derm Beruf Umwelt* 1987;35(4):119–123.

20. Ross-Hansen K, Ostergaard O, Tanassi JT, et al. Filaggrin is a predominant member of the denaturation-resistant nickel-binding proteome of human epidermis. *J Invest Dermatol* 2014;134(4):1164–1166.
21. Thyssen JP. Nickel and cobalt allergy before and after nickel regulation—evaluation of a public health intervention. *Contact Dermatitis* 2011; 65(Suppl 1):1–68.
22. Garg S, Thyssen JP, Uter W, et al. Nickel allergy following European Union regulation in Denmark, Germany, Italy and the U.K. *Br J Dermatol* 2013;169(4):854–858.
23. Schnuch A, Schwitulla J. Decrease in nickel allergy in women after the second EU nickel directive. *Contact Dermatitis* 2013;69(4):253–256.
24. Menné T, Brandup F, Thestrup-Pedersen K, et al. Patch test reactivity to nickel alloys. *Contact Dermatitis* 1987;16(5):255–259.
25. Thyssen JP. Cobalt sensitization and dermatitis: considerations for the clinician. *Dermatitis* 2012;23(5):203–209.
26. Rietschel RL, Fowler JF, Warshaw EM, et al. Detection of nickel sensitivity has increased in North American patch-test patients. *Dermatitis* 2008; 19(1):16–19.