

The Sino-American Belt Study: Nickel and Cobalt Exposure, Epidemiology, and Clinical Considerations

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Background: Nickel and cobalt are common causes of metal allergy.

Objective: The objective of this study was to investigate nickel and cobalt exposure in belt buckles by testing 701 belts purchased in China and the United States and to consider the prevalence of nickel allergy and its relevance among Chinese patients.

Methods: Seven hundred one belt buckles purchased in China and the United States were tested for nickel and cobalt release. Six hundred thirty-one Chinese patients with suspected allergic contact dermatitis were patch tested and interviewed to determine clinical relevance of results. The Chinese and American literature was reviewed to investigate trends in nickel prevalence over the past decades.

Results: Sixty percent (n = 219) of belts purchased in China (n = 365) released nickel, and 0.5% (n = 2) released cobalt; 55.7% (n = 187) in the United States (n = 336) released nickel, and 0.9% (n = 3) released cobalt. Belt dermatitis was a significant clinical finding in 34.8% of Chinese nickel-allergic patients. Literature review suggests increasing nickel allergy prevalence in the United States and China.

Conclusions: Metallic belt buckles are an important source of nickel exposure to consumers. Belts from lowest socioeconomic vendors were more likely to release nickel. Belts with silver color and dark metallic color were more likely to release nickel and cobalt, respectively. Clinical findings show belt dermatitis in China to be a problem.

CAPSULE SUMMARY

- Allergic contact dermatitis can be caused by exposure to metallic items such as jewelry and belts.

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- This study finds nickel release in belts in both China and the United States to be frequent, establishing a connection between likelihood of metal allergen release and color/vendor socioeconomic class, and highlights the clinical significance of belt dermatitis in Chinese patients.
- Clinicians should be aware of common sources of metal allergen release, recognize clinical relevance of different sources of exposure, and educate patients on allergen avoidance.

Allergic contact dermatitis (ACD) is a T cell-mediated inflammatory process of the skin induced by cutaneous absorption of an allergen in a previously sensitized individual. Metal allergens, notably nickel and cobalt, account for a significant proportion of contact sensitization and ACD in the general population and among dermatitis patients.¹ Metal allergy is also a clinical challenge because it is considered a risk factor for hand eczema, a disorder resulting in poor quality of life and sick leave.² Metal allergy is a global public health issue. For example, in China, the overall prevalence of nickel allergy is 20.6% in female patients and 16.6% in males.³ In the United States, nickel and cobalt allergy prevalence rates are also high, being 19% and 8.4%, respectively, in dermatitis patients from the North American Contact Dermatitis Group.⁴ Furthermore, nickel is considered the most common contact allergen in American adults and children.^{5,6}



Figure 1. Allergic nickel dermatitis following prolonged skin contact to a metallic belt buckle.

Studies have identified important consumer sources of nickel exposure including earrings, hair clips, clothing fasteners, belts, jeans buttons, mobile phones, and toy makeup for children. Case reports have supported the clinical relevance of many of these sources of nickel exposure.^{7–14} On the other hand, cobalt release

seems to be infrequent from jewelry, hair clips, mobile phones, and work tools^{15,16} when using a novel cobalt spot test designed to test metallic items for cobalt release.¹⁷ For instance, in 2 recent studies, only about 1% of earrings (<1%) released cobalt in concentrations that may elicit cobalt dermatitis in cobalt-sensitized individuals.^{15,16} It is important that clinicians identify sources of nickel and cobalt exposure to improve clinical decisions and for effective patient education.

In this study, randomly purchased belt buckles were analyzed for nickel and cobalt release using spot tests. Belt dermatitis seems to be frequently encountered in a clinical setting (Fig. 1). Also, 631 Chinese patients with suspected ACD were patch tested with the European baseline series to estimate the nickel allergy prevalence in China and to determine the level of belt dermatitis. Finally, the development of nickel allergy in China between 1989 and 2011 and in the United States between 1972

TABLE 1. Proportion and Price Levels of Belts That Released Nickel and Cobalt in Amounts That May Cause Dermatitis in Allergic Individuals

Belt Testing	City	Vendor	No. Samples	Approximate Retail Price Range, US \$	% Ni ⁺ , n	% Co ⁺ , n
China	Beijing	Silk Street	58	2–8	77.6 (45)	1.7 (1)
	Beijing	Beijing Zoo Market 1	40	1–6	55.0 (22)	0 (0)
	Beijing	Beijing Zoo Market 2	33	1–6	51.5 (17)	0 (0)
	Beijing	Hot Wind Life	7	12–30	57.1 (4)	0 (0)
	Beijing	UNIQLO	14	18–35	42.9 (6)	0 (0)
	Beijing	Mango	5	12–45	0 (0)	20 (1)
	Beijing	H&M	4	20–40	0 (0)	0 (0)
	Shanghai	Wal-Mart	44	2–8	81.8 (36)	0 (0)
	Shanghai	580 Nanjing Rd, Market 1	94	2–6	76.6 (72)	0 (0)
	Shanghai	Biaoma Accessories	14	12–15	28.6 (4)	0 (0)
	Shanghai	Leather of Tibet	11	10–15	36.4 (4)	0 (0)
	Shanghai	Mickey Mouse Shop	11	3–8	0 (0)	0 (0)
	Shanghai	Baleno	4	9–15	75.0 (3)	0 (0)
	Shanghai	Zara	8	50–80	0 (0)	0 (0)
	Shanghai	H&M	6	25–45	0 (0)	0 (0)
	Shanghai	580 Nanjing Rd. Market 2	12	2–6	50.0 (6)	0 (0)
China total			365		60.0 (219)	0.5 (2)
US	Phoenix	Target	20	10–30	30.0 (6)	5.0 (1)
	Phoenix	Ross Dress for Less	21	25–60	47.6 (10)	0 (0)
	Phoenix	Old Navy	5	25–35	0 (0)	0 (0)
	Phoenix	Marshalls	41	20–70	60.1 (25)	0 (0)
	Phoenix	Wal-Mart	32	10–25	68.8 (22)	0 (0)
	Phoenix	Loehmann's	13	30–80	53.8 (7)	0 (0)
	Phoenix	Last Chance	39	20–150	38.5 (15)	2.6 (1)
	Phoenix	Phoenix Swap Meet	69	5–40	89.9 (62)	0 (0)
	Phoenix	Style for Less	11	20–30	81.8 (9)	0 (0)
	Phoenix	TJ Maxx	27	20–80	48.1 (13)	0 (0)
	Phoenix	Kmart	51	10–25	33.3 (17)	2.0 (1)
	Phoenix	Macy's	7	40–80	14.3 (1)	0 (0)
US total			336		55.7 (187)	0.9 (3)
Total			701		57.9 (406)	0.7 (5)

Sixteen and 12 vendors were visited in China and Phoenix, Ariz, to purchase random belts with metallic belt buckles.

TABLE 2. Outcome of Nickel and Cobalt Spot Testing of Belts and Stratified by the Socioeconomic Category of the Stores in Which They Were Purchased

China	Description	Clientele (Socioeconomic Class [SE]/Description)	Retail Price, US \$	No. Samples	% Ni ⁺	% Co ⁺
1	Upscale/mall	Upper SE class Chinese, foreign tourists	12–80	44	22.7	2.3
2	Chinese community	Middle-lower SE class Chinese	2–15	146	54.8	0.0
3	Counterfeit market	Tourists, mixed Chinese	1–8	175	75.0	0.6
US						
1	Fashion brands	Middle-upper SE class	20–150	164	48.8	0.6
2	Superstores	Variable	10–30	103	43.7	1.0
3	Swap meet	Middle-lower SE class	5–40	69	89.9	0.0

and 2006 was investigated by compiling patch test data from the literature.

MATERIALS AND METHODS

Metal Exposure Evaluation

Purchasing Strategy

A total of 701 belts with metallic buckles were purchased from 16 vendors in China (Beijing, 6 markets, $n = 161$; Shanghai, 8 markets, $n = 204$) and 12 vendors in the United States (Phoenix, 12 markets, $n = 336$) (Table 1). Chinese belt retailers were categorized according to socioeconomic impression: upscale foreign-owned stores, which had the highest prices ($n = 44$; US \$12–\$80); local Chinese community stores, which had low to moderate prices ($n = 146$; US \$2–\$15); and generic markets, which sold counterfeit Western brand merchandise ($n = 175$; US \$1–\$8) (Table 1). United States belt retailers were categorized into similar groups: the Phoenix Swap Meet, a large outdoor flea market with numerous various vendors ($n = 69$; US \$5–\$40); superstores such as Wal-Mart ($n = 103$; US \$10–\$30), and stores that sold fashion brands ($n = 164$; US \$20–\$150) (Table 2). Belt purchasing was conducted to maximize the variety of products tested. At any one vendor, only belts containing metallic components with potential for skin contact were purchased. Only 1 belt was purchased for every unique belt buckle, thus testing the greatest number of distinct buckles.

Belt Spot Testing and Evaluation

Belts were inspected for metal parts that had potential to contact the skin. These areas were spot tested with the dimethylglyoxime

(DMG)–based Reveal Nickel Spot Test and the Reveal Cobalt Spot Test (SmartPractice, Phoenix, Ariz). Test solutions were applied to cotton-tipped applicators, and metallic parts were rubbed vigorously for 30 seconds. The cotton tip was then held against a white background for correct interpretation. For the Nickel Spot Test, a positive reaction was indicated by pink coloration of the cotton tip. A negative reaction was indicated by no color change of the cotton tip. For the Cobalt Spot Test, which is a yellow solution that colors the white cotton tip yellow, a positive reaction was indicated by red or orange coloration of the cotton tip. A negative reaction was indicated by no color change of the cotton tip (Fig. 2). Nickel and cobalt spot tests were done on separate areas to prevent false-positive reactions. Belts with doubtful reactions, defined by an applicator with discoloration that was not pink, red, or orange, were cleaned with water and retested. If doubtful reactions persisted, the belt was considered negative.

Investigating Color

Belt buckles were classified according to approximate color: silver, dark metallic, gold, copper, or mixed (defined as colors not belonging to any of the other groups or a combination of different colors) to determine whether metal release was associated with a particular color (Fig. 3).

Statistical Methods

The χ^2 test and the Fisher exact test were used to test for significant differences between categories and patient populations when appropriate. These tests were performed with SPSS software version 15 (SPSS Inc, Chicago, Ill). A standard linear regression was used to assess trends in allergy prevalence, performed by Microsoft Excel 2007 (Microsoft Inc, Redmond, Wash).



Figure 2. Examples of positive cobalt and nickel spot test reactions indicating cobalt and nickel release in sufficient amount to elicit allergic dermatitis in sensitized individuals. Left, (Cobalt) A positive reaction as indicated by an orange-red coloration of the yellow cotton stick. Right, (Nickel): A positive reaction as indicated by pink coloration of a white cotton stick.



Figure 3. Belt color categorization examples. Belts of each color are shown. From left: dark metallic, copper, gold, and silver.

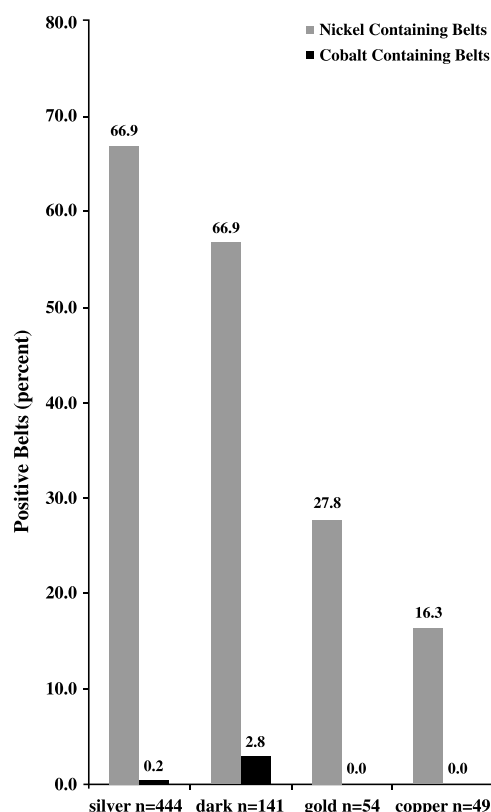


Figure 4. Association between the outcomes of cobalt and nickel spot testing and color. Silver-colored belts were more likely to release nickel than belts of any other color (P values when compared with other colors were, respectively, 0.028 for silver-dark, <0.001 for silver-gold, and <0.001 for silver-copper). Dark metallic belts were significantly more likely to release cobalt than remaining color categories ($P = 0.013$).

Clinical Evaluation

The study was approved by the local ethics committee, and informed consent was obtained from all participants. A total of 631 consecutive patients with suspected ACD, aged 5 to 85 years old, were patch tested at the Peking University Third Hospital between May 2009 and September 2010. The population included 186 male and 445 female patients. All patients were ethnically Han Chinese. Patch testing was performed with European baseline series containing 5% nickel sulfate hexahydrate in petrolatum and using IQ Chambers (Chemotechnique Diagnostics, Vellinge, Sweden). Allergens in IQ Chambers were applied to the upper back, and the results were read at 48 and 96 hours according to International Contact Dermatitis Research Group criteria. With each patient, evaluation of possible relevant sources of nickel exposure was conducted by careful history taking and location of dermatitis.

Epidemiological Evaluation

Literature searches were performed to determine the median prevalence of nickel allergy in China^{3,18} and the United States.^{19,20} New literature searches were performed not only in medical jour-

nals accessible at www.pubmed.com but also in medical journals and textbooks printed in Chinese. Search terms included *contact dermatitis*, *nickel dermatitis*, *contact allergy*, *nickel allergy*, *metals*, *patch testing*, *prevalence*, *frequency*, *epidemiology*, *United States*, *China*, *Hong Kong*, and *Taiwan*.

RESULTS

Exposure Evaluation

In China, 219 (60%) of 365 belts were nickel spot test positive, and 2 (0.5%) were cobalt spot test positive. In the United States, 187 (55.7%) of 336 belts were nickel positive, and 3 (0.9%) were cobalt positive (Table 1). A significant difference in the proportion of belts that released nickel was identified when stratification was performed by socioeconomic shop category (Table 2). Hence, in China, belts from the counterfeit markets were significantly more likely to release nickel than those from other stores ($P < 0.001$). Belts from the upscale stores were, however, significantly less likely to release nickel than belts from the other stores when these were combined ($P < 0.001$). A similar trend was found in the United States; belts purchased from the swap meet were significantly more likely to release nickel than belts purchased from other stores ($P < 0.001$). Significant differences in the proportion of belts that released nickel were also found between different colors. Silver-colored belts were more likely to release nickel than belts of other colors (P values when compared with other colors were, respectively, 0.028 for silver-dark, <0.001 for silver-gold, and <0.001 for silver-copper). Regarding cobalt release,

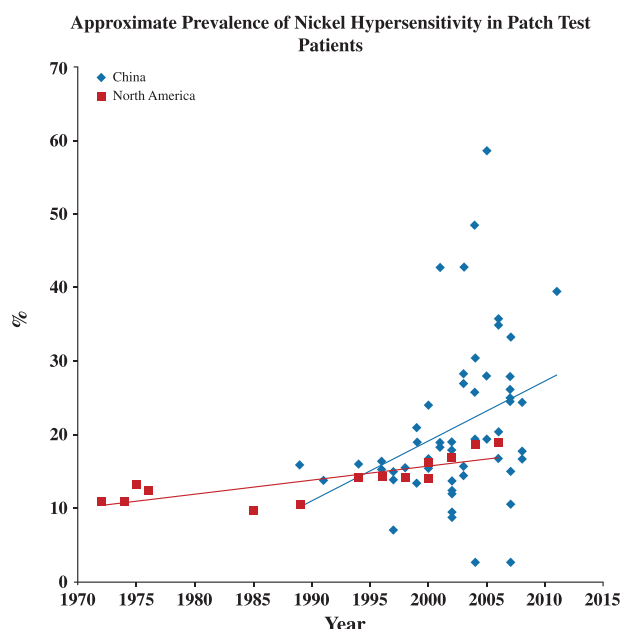


Figure 5. The prevalence of nickel allergy in Chinese dermatitis patients by testing date from 1989 to 2011 and the prevalence of North American dermatitis patients by study completion date from 1972 to 2006.

dark metallic belts were significantly more likely to release cobalt than remaining color categories ($P = 0.013$) (Fig. 4).

Clinical Findings

Among 631 Chinese dermatitis patients, 96 were patch test positive to nickel sulfate (15.2% of all patients; 18.2% of female patients and 8.1% of male patients). There was a significant difference in positive patch test result between sexes ($P > 0.05$). The prevalence of nickel patch test reactivity was significantly higher for patients aged 20 to 40 years (20%) when compared with patients younger than 20 years (4%) ($P < 0.05$) and patients older than 40 years (10.5%) ($P < 0.05$). Clinically relevant sources of nickel exposure were indentified in 69 (71.9%) of the 96 nickel patch test–positive patients. Some patients had multiple sources of exposure, and we found that 49 female patients (71.0%) were found to have nickel ACD due to metallic jewelry, whereas metallic belt buckles accounted for 24 cases (38.4%) in total. Other sources of nickel ACD such as spectacle frames, zippers, and watches accounted for 14 cases (20.2%).

Epidemiological Findings

Stratification by year of publication for Chinese articles and by study end date for United States articles showed an increase in nickel allergy (Fig. 5). Retrieved nickel patch test studies for China covered the period 1989 to 2008.³ A total of 54 new studies were identified, adding 26 studies to the 28 studies that were identified and listed in our previous publication.^{21–46} When the prevalence of nickel allergy was stratified by year of publication, an increasing reported prevalence of nickel allergy was observed, and a linear regression found a significant increase in prevalence ($P = 0.0133$) (Fig. 5). In the United States, a total of 14 studies were identified, adding 3 studies to the 11 studies identified and listed in a previous publication that found a significant increase from 1970 to 2002 ($P < 0.0001$).²⁰

DISCUSSION

This study identified excessive nickel release from more than half of 701 belts randomly purchased from stores and vendors in China and the United States. Our findings support conclusions from relatively small nickel release studies conducted previously in the United States (25/47 positive), the Netherlands (3/9 positive), and Korea (2/2 positive), which also showed that high proportions of belt buckles released too much nickel.^{10,47,48} Also, we showed that allergic nickel dermatitis manifested as periumbilical dermatitis was explained by exposure to belts in about 38% of Chinese nickel-allergic patients, emphasizing that nickel exposure from belts is indeed a clinical problem. No clinical data were available from American dermatitis patients, but we acknowledge that belt nickel dermatitis occurs frequently in patients in Europe as well as the in United States. The DMG test becomes positive when $0.5 \mu\text{g}$

nickel/cm² per week or greater is released from an item, a concentration that results in allergic nickel dermatitis in most nickel-allergic patients.⁴⁹ The DMG test was recently validated, and it appeared to be specific (98%) but only moderately sensitive (60%).⁵⁰ Thus, probably more than the 58% total nickel positive belts actually released nickel in concentrations, which may result in allergic nickel dermatitis. Nickel-releasing potential of belts after long-term use was not evaluated in this study. Deterioration of the top plating, polish, or paint may expose the consumer to nickel- or cobalt-releasing alloys commonly found in underlying layers.

For the first time, we have shown that nickel release was significantly more frequent from belts with a silver appearance when compared with belts with a dark metallic, gold, or copper appearance (Figs. 3, 4). Nickel-allergic individuals should be particularly careful about purchasing silver metallic belts and possibly silver metallic jewelry in general. Despite silver belts most commonly releasing nickel, belts in all color categories released nickel. Hence, consumers cannot rely on color to avoid excessive nickel exposure. Also, inexpensive belts from both China and the United States released excessive amounts of nickel significantly more often than more expensive belts (Table 2). This finding resembled similar studies performed for earrings in Europe and the United States.^{7,51,52} These findings underscore that nickel-allergic patients should not only be informed by their physicians to be careful when purchasing metallic consumer items, especially from street vendors, but also be instructed how to perform a nickel spot test. Also, it can be argued that public information campaigns should be directed at vendors as well as the general public to limit the nickel allergy problem.

We found a marked and similar increase in nickel allergy in patch-tested dermatitis patients from China and the United States (Fig. 5). It should be noted that sex and age stratification was not performed, and confounding variables were not assessed. At present, there is no nickel regulation in the United States, although such restrictions have been proposed by concerned researchers and clinicians.⁵³ The epidemiology of nickel allergy in China, as illustrated not only by the increase displayed in Figure 5 but also by the high prevalence of nickel allergy in 20- to 40-year-old Chinese dermatitis patients, suggests that the regulation may not be adequately followed or enforced.

The above findings are interesting to compare to epidemiological data from Europe where a nickel directive was introduced in 1994. Such regulation has been linked to reductions in the prevalence of nickel allergy,⁵⁴ although prevalence seems to have stabilized at a relatively high level.⁵⁵ A Swedish study showed that excessive nickel release from metallic consumer items, including jewelry and belts, decreased significantly after the legislation implementation.⁵⁶ Also, research conducted in Denmark, the first country to regulate nickel, showed a significant decrease in nickel allergy in young female dermatitis patients and women from the general population after nickel regulation.^{54,57} Furthermore, public awareness of the nickel problem seemed to have success limiting nickel exposure in Sweden, where a nationwide

health campaign on nickel allergy was conducted in 1999. This may explain why nickel release from earrings seems to be more frequent in Germany, England, Poland, and Denmark when compared with Sweden despite all countries being covered by the EU Nickel Directive.⁵¹ Nevertheless, the proportion of earrings that released nickel in excessive amounts was much higher in samples from unregulated countries, including Thailand (29%) and the United States (30%)^{7,16} when compared with European capitals (4%–18%), suggesting an effect of regulation.⁵¹

Cobalt release was identified from only 0.5% of belts purchased in China and 0.9% of belts purchased in the United States. The cobalt spot test becomes positive when cobalt is released in concentrations that may result in allergic cobalt dermatitis in already sensitized individuals (approximately 8 ppm).^{17,58} The low numbers of cobalt test-positive belts are in line with results from similar studies performed on other metallic items—less than 1% of more than 600 earrings purchased in Denmark, China, and Thailand; 0 of 50 mobile phones; and 0 of 200 work tools released cobalt when tested with cobalt spot test.^{16,59,60} Despite a relatively high cobalt allergy prevalence in dermatitis patients, significant sources of cobalt exposure have not yet been identified.⁶¹ Cobalt allergy is often concomitantly observed with nickel allergy; however, it is widely accepted that cross-reactivity between nickel and cobalt does not exist.⁶² Nevertheless, a Swedish study showed that when nickel-allergic individuals were orally exposed to nickel, previous cobalt patch test reactions also flared.⁶³ Possible explanations for the high prevalence of cobalt allergy in dermatitis patients include the following:

- (1) Concomitant exposure and sensitization to nickel and cobalt simultaneously released from metallic items. Although this might have been seen in the past when the market prices of cobalt were low and cobalt was not extracted from mined nickel, recent research suggests that this cannot explain the majority of concomitant nickel and cobalt sensitization today.⁶⁴
- (2) Sensitization to cobalt released from dental and orthopedic alloys inserted in the oral cavity and body. This could be an overlooked source of cobalt sensitization as shown in a recent study where high proportions of orthopedic and dental alloys gave positive cobalt spot test reactions.⁶⁰ However, because cobalt allergy is also prevalent in young patients,⁶⁰ this cannot fully explain the persistent, high prevalence of cobalt allergy.
- (3) Occupational cobalt exposure can explain the high prevalence of cobalt allergy, but in Denmark, for example, we see few metal industry workers in our clinic. In conclusion, there is a lack of data to appropriately determine sources of cobalt exposure that can explain the high prevalence of cobalt allergy.

We showed that dark metallic belts were more likely to release cobalt than metals with a silver, copper, or gold appearance. This finding is in line with results from previous studies on earrings where cobalt release was also mainly identified in dark metallic earrings. Also, a case report from Sweden found allergic cobalt dermatitis in a patient who had worn a dark metallic necklace that released high amounts of cobalt.⁶⁵ However, patients and clini-

cians should be aware that metal alloys with other appearances also may release cobalt (Fig. 4).¹⁶

REFERENCES

1. Thyssen JP, Linneberg A, Menné T, et al. The epidemiology of contact allergy in the general population—prevalence and main findings. *Contact Dermatitis* 2007;57:287–299.
2. Agner T, Andersen KE, Brandao FM, et al. Hand eczema severity and quality of life: a cross-sectional, multicentre study of hand eczema patients. *Contact Dermatitis* 2008;59:43–47.
3. Hamann CR, Hamann DJ, Hamann QJ, et al. Assessment of nickel release from earrings randomly purchased in China and Thailand using the dimethylglyoxime test. *Contact Dermatitis* 2010;62:232–240.
4. Warshaw EM, Belsito DV, DeLeo VA, et al. North American Contact Dermatitis Group patch-test results, 2003–2004 study period. *Dermatitis* 2008;19:129–136.
5. Zug KA, Warshaw EM, Fowler JF, et al. Patch-test results of the North American Contact Dermatitis Group 2005–2006. *Dermatitis* 2009;20:149–160.
6. Lee PW, Elsaie ML, Jacob SE. Allergic contact dermatitis in children: common allergens and treatment: a review. *Curr Opin Pediatr* 2009;21:491–498.
7. Thyssen JP, Maibach HI. Nickel release from earrings purchased in the United States: the San Francisco earring study. *J Am Acad Dermatol* 2008;58:1000–1005.
8. Heim KE, McKean BA. Children's clothing fasteners as a potential source of exposure to releasable nickel ions. *Contact Dermatitis* 2009;60:100–105.
9. Suneja T, Flanagan KH, Glaser DA. Blue-jean button nickel: prevalence and prevention of its release from buttons. *Dermatitis* 2007;18:208–211.
10. Byer TT, Morrell DS. Periumbilical allergic contact dermatitis: blue jeans or belt buckles? *Pediatr Dermatol* 2004;21:223–226.
11. McLean L, Yewchuk L, Israel DM, et al. Acute onset of generalized pruritic rash in a toddler. Diagnosis: systemic allergic (contact) dermatitis to nickel from ingestion of metal coins. *Pediatr Dermatol* 2011;28:53–54.
12. Corazza M, Baldo F, Pagnoni A, et al. Measurement of nickel, cobalt and chromium in toy make-up by atomic absorption spectroscopy. *Acta Dermatol Venereol* 2009;89:130–133.
13. Bercovitch L, Luo J. Cellphone contact dermatitis with nickel allergy. *Can Med Assoc J* 2008;178:23.
14. Hsu JW, Matiz C, Jacob SE. Nickel allergy: localized, id, and systemic manifestations in children. *Pediatr Dermatol* 2011;28:276–280.
15. Thyssen JP, Jellesen MS, Menné T, et al. Cobalt release from inexpensive jewellery: has the use of cobalt replaced nickel following regulatory intervention? *Contact Dermatitis* 2010;63:70–76.
16. Hamann C, Hamann D, Hamann KK, et al. Cobalt release from inexpensive earrings from Thailand and China. *Contact Dermatitis* 2011;64:238–240.
17. Thyssen JP, Menné T, Johansen JD, et al. A spot test for detection of cobalt release - early experience and findings. *Contact Dermatitis* 2010;63:63–69.
18. Yin R, Huang XY, Zhou XF, et al. A retrospective study of patch tests in Chongqing, China from 2004 to 2009. *Contact Dermatitis* 2011;65:28–33.
19. Wetter DA, Davis MD, Yiannias JA, et al. Patch test results from the Mayo Clinic Contact Dermatitis Group, 1998–2000. *J Am Acad Dermatol* 2005;53:416–421.
20. Nguyen SH, Dang TP, MacPherson C, et al. Prevalence of patch test results from 1970 to 2002 in a multi-centre population in North America (NACD). *Contact Dermatitis* 2008;58:101–106.
21. Mao H. Analysis of patch test results in 116 patients with suspected allergic contact dermatitis. *Chin J Dermatol* 1999;32:198.

22. L. Analysis of patch test results in 326 patients with suspected allergic contact dermatitis. *Lingnan Pi Fu Bing Xue Zai Zhi* 1999;6:1–3.
23. Wu Hu, Yu. Analysis of patch test results in 380 patients with suspected allergic contact dermatitis. *Zhejiang Yi Xue* 1999;21:235–236.
24. He Zeng. Analysis of patch test results in 153 patients with suspected allergic contact dermatitis. *J Hengyang Med Coll* 2000;28:175–176.
25. Chen J, Kuang X, Zhang J, et al. Analysis of patch test results in children with suspected allergic contact dermatitis. *Chin J Dermatol* 2001;34:441.
26. Han J, Zhang L. Analysis of patch test results in 348 patients with suspected allergic contact dermatitis in Haining, Qinhai, China. *Chin J Microb Immuno* 2001;21:99–100.
27. Zhang Y. Analysis of patch test results in 100 patients with suspected allergic contact dermatitis. *Liaoning Yao Wu Yu Lin Chuang* 2001;4:122–123.
28. Zhang G, Zhou Y, Wen H. Analysis of patch test results in 188 patients with suspected allergic contact dermatitis in Changsha, China. *Chin Clin Dermatol* 2002;31:357.
29. Zhang R, Zhang P, Yin C. Analysis of patch test results in 182 patients with suspected allergic contact dermatitis in Weihai, China. *Chin J Lepro Skin Dis* 2003;19:274–275.
30. Wang J, Wang Y, Liu J. Analysis of patch test results in 953 patients with suspected allergic contact dermatitis. *Chin J Lepro Skin Dis* 2003;19:502.
31. Su Y, Li Y, Xiao R. Analysis of patch test results in 235 patients with suspected allergic contact dermatitis. *China J Mod Med* 2003;13:65–66.
32. Luo P, Chen J, Zhang J. Analysis of patch test results in 716 children with suspected allergic contact dermatitis. *J Mod Clin Med Bioeng* 2003;9:435.
33. Lu D, Huang H, Hu X. Analysis of patch test results in patients with suspected allergic contact dermatitis in Zhuhai, Guangdong China. *Chin J Lepro Skin Dis* 2004;20:545–546.
34. Zhou S, Liu X, Zhao Z. Analysis of patch test results in 337 patients with suspected allergic contact dermatitis. *Chin J Lepro Skin Dis* 2004;27:551–553.
35. Zhang Y, Xu T, Zheng L. Analysis of patch test results in 108 patients with suspected allergic contact dermatitis. *Beijing Yi Xue* 2005;27:633.
36. Jin L, Zhao Y, Sun L. Analysis of patch test results in 100 patients with suspected allergic contact dermatitis in Dalian China. *Chin J Lepro Skin Dis* 2005;21:658.
37. Zhu X, Fu S. Analysis of patch test results in 121 patients with suspected allergic contact dermatitis in Linyi, China. *Chin J Dermatovenereol Integr Tradition West Med* 2006;5:114–115.
38. Fu L, Xie W, Yu M. Analysis of patch test results in 530 patients with suspected allergic contact dermatitis. *China Prev Med* 2006;7:412–414.
39. Liu Y. Analysis of patch test results in 200 patients with suspected allergic contact dermatitis in Linyi, China. *Med J Beijing Mil Reg* 2006;18:364.
40. Wang D, Zhang W, Yu B. Analysis of contact allergen in patients with suspected allergic contact dermatitis. *Chin J Dermatovenereol* 2006;20:608–609.
41. Zhao L, Wang L, Hong Y. Analysis of patch test results in 589 patients with chronic suspected allergic contact dermatitis. *Chin J Industrial Med* 2007;20:102–104.
42. Mi X, Ge P, Yuan X, et al. Analysis of patch test results in 1129 patients with suspected allergic contact dermatitis. *Acad J PLA Postgrad Med Sch* 2008;29:109–111.
43. Zhang J, Liu Y, Yang R. Analysis of patch test results in 400 patients with suspected allergic contact dermatitis. *Chin J Misdiagn* 2008;8:630–631.
44. Feng H, Hao Y, Liu G. Analysis of contact allergen in patients with suspected allergic contact dermatitis. *Inner Mongolia Med J* 2008;40:1456–1458.
45. Zhang Y, Wang X, Gao Y. Analysis of contact allergens in 300 patients with suspected allergic dermatitis. *J Bin Zhou Med Coll* 2008;31:65–66.
46. Wu P, Sun J, Yu T. Patch testing in 462 patients with chronic suspected allergic contact dermatitis. *Lab Med Clin* 2009;6:40–41.
47. Biesterbos J, Lidén C, van der Valk P. Nickel on the Dutch market: 10 years after entry into force of the EU Nickel Directive. *Contact Dermatitis* 2011;65:115–117.
48. Kim YY, Kim MY, Park YM, et al. Evaluating the nickel content in metal alloys and the threshold for nickel-induced allergic contact dermatitis. *J Korean Med Sci* 2008;23:315–319.
49. Menné T, Brandrup F, Thestrup-Pedersen K, et al. Patch test reactivity to nickel alloys. *Contact Dermatitis* 1987;16:255–259.
50. Thyssen JP, Skare L, Lundgren L, et al. Sensitivity and specificity of the nickel spot (dimethylglyoxime) test. *Contact Dermatitis* 2010;62:279–288.
51. Thyssen J, Menné T, Lidén C, et al. Excessive nickel release from earrings purchased from independent shops and street markets—a field study from Warsaw and London. *J Eur Acad Dermatol Venereol* 2010.
52. 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;407:5315–5318.
53. Jacob SE, Moennich JN, McKean BA, et al. Nickel allergy in the United States: a public health issue in need of a “nickel directive”. *J Am Acad Dermatol* 2009;60:1067–1069.
54. Thyssen JP, Johansen JD, Carlsen BC, et al. Prevalence of nickel and cobalt allergy among female patients with dermatitis before and after Danish government regulation: a 23-year retrospective study. *J Am Acad Dermatol* 2009;61:799–805.
55. Schnuch A, Wolter J, Geier J, et al. Nickel allergy is still frequent in young German females—probably because of insufficient protection from nickel-releasing objects. *Contact Dermatitis* 2011;64:142–150.
56. Biesterbos J, Yazar K, Lidén C. Nickel on the Swedish market: follow-up 10 years after entry into force of the EU Nickel Directive. *Contact Dermatitis* 2010;63:333–339.
57. Thyssen JP, Johansen JD, Menné T. Nickel allergy in Danish women before and after nickel regulation. *N Engl J Med* 2009;360:2259–2260.
58. Julander A, Hindsén M, Skare L, et al. Cobalt-containing alloys and their ability to release cobalt and cause dermatitis. *Contact Dermatitis* 2009;60:165–170.
59. Thyssen JP, Jensen P, Lidén C, et al. Assessment of nickel and cobalt release from 200 unused hand-held work tools for sale in Denmark—sources of occupational metal contact dermatitis? *Sci Total Environ* 2011;49:4663–4666.
60. Thyssen JP, Menné T, Lidén C, et al. Cobalt release from implants and consumer items and characteristics of cobalt sensitized patients with dermatitis. *Contact Dermatitis* 2011;66:113–122.
61. 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.
62. Wahlberg JE, Lidén C. Cross-reactivity patterns of cobalt and nickel studied with repeated open applications (ROATS) to the skin of guinea pigs. *Am J Contact Dermatitis* 2000;11:42–48.
63. Hindsén M, Spirén A, Bruze M. Cross-reactivity between nickel and palladium demonstrated by systemic administration of nickel. *Contact Dermatitis* 2005;53:2–8.
64. Thyssen JP. Nickel and cobalt allergy before and after nickel regulation—evaluation of a public health intervention. *Contact Dermatitis* 2011;(Suppl 1):1–75.
65. Hindsén M, Persson L, Gruvberger B. Allergic contact dermatitis from cobalt in jewellery. *Contact Dermatitis* 2005;53:350–351.