

Volume 107 • No. 2 • November 2005 • ISSN 0163-4984

Biological Trace Element Research

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Profiles of Trace Elements in Toenails of Arab-Americans in the Detroit Area, Michigan

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Received August 9, 2004; Revised November 2, 2004;
Accepted November 30, 2004

ABSTRACT

Exposure to environmental contaminants is complicated by factors related to socioeconomic status, diet, and other culturally conditioned risk behaviors. Determination of a trace element profile in toenails can be used as a tool in biomonitoring the exposure history or assessing the deficiency of a particular element in a study population, which can lead to a better understanding of environmental and disease risks. Toenail clippings from 259 Arab Americans (163 adults, 96 children) residing in a highly industrialized area were analyzed for Al, V, Cr, Mn, Co, Ni, Cu, As, Se, Mo, Cd, Ba, Tl, and Pb using an inductively coupled plasma-mass spectrometer. Mean concentrations were compared with published values, and the influence of age, gender, and other demographic factors were explored. Elevated levels of Ni in this population warrant further investigation. Significant differences in the mean concentration of Al, V, Cr, Mn, Cd, Pb, and Se exist between toenails of adults and children. Pearson correlation coefficients reveal strong significant associations among Cd, Cr, and Tl ($p < 0.05$), in addition to other elements. These investigations provide insight into exposures and factors influencing exposures in this population while adding to the growing fund of knowledge surrounding use of toenails as a marker of exposure.

Index Entries: Toenails; biomarkers; ICP-MS; Arab-Americans; multielement analysis.

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INTRODUCTION

Dearborn, in the southeastern part of the Detroit metropolitan area, was the birthplace of the automotive industry and attracted immigrants from all over the world, including a large number from the Middle East (1). The Arab community continued to grow over the years in this area, and Dearborn now represents the highest concentration of the Arab population in North America. In particular, communities around the Ford Motor Rouge Plant, the largest industrial presence in the area, have become predominantly Arab-American, with one neighborhood, known as the "South End," serving as an important reception area for recent immigrants from the Middle East. Income, educational status, and employment levels are generally low in the South End Arab-American community (1).

Other industries, subsidiary to the Ford Motor Rouge Plant, have arisen in the area, many of them related to automobile, steel, and trucking service sectors (1). Releases of large quantities of pollutants into local ecosystems have thereby been sustained for nearly 100 years. Most Arab-Americans in the South End live and work in close proximity to the Rouge Plant and are constantly being exposed to dangerously high levels of air pollution and associated dusts (1). According to the US Environmental Protection Agency's (EPA's) Toxic Release Inventory (TRI) database, toxic chemicals released into the environment by the local industry include arsenic compounds, barium compounds, cadmium, chromium compounds, copper compounds, lead and lead compounds, manganese and manganese compounds, and nickel and nickel compounds (2). The low socioeconomic status, low educational attainment, and residence in one of the most polluted areas of Michigan combine to make the Arab-American communities in the South End, a high-risk population for environmental exposures.

Toenails are often used as a biomarker of exposure, as many elements bind to keratin, the fibrous proteins present in nails (3). An advantage of using toenails as a biomonitoring tool is that the collection of toenail clippings is noninvasive, allows for easy storage, and, as opposed to hair or fingernail samples, reduces the likelihood of external contamination (4). Toenails have advantages over other biological materials that have been used in human biomonitoring studies. They reflect exposures that have occurred over the past 6–12 mo, compared to an order of hours or days for blood, saliva, or urine (5–7). Furthermore, elements in toenails are removed from metabolic processes after nail formation and, thus, might be more stable markers of exposure (3). It has been shown that levels of trace elements in nails are significantly correlated over time, suggesting that a one-time measurement might be reflective of long-term exposure because of low intraindividual variability (4).

Little attempt has been made thus far to ascertain exposure of the Arab-American population in Dearborn to contaminants in the environment. The goal of this study is to explore the use of toenails in biomoni-

toring toxic metal exposures in this population and to assess the effect of gender, age, and demographic variables on metal concentrations. A secondary objective of this study is to assess the use of toenails to ascertain the deficiency level of some of the essential microelements in the population; this application has not been extensively explored in the scientific literature. Multielement analysis of toenails for this population allows for construction of an element profile. An extensive compilation of previously published data, presented also with subpopulations such as children or high-exposure groups, is reported for comparison and lends insight into interpretation of the element profile. Furthermore, correlations between elements are investigated and reported, and intrapopulation differences in trace element status are explored, adding to the growing fund of knowledge surrounding use of toenails in biomonitoring exposures.

METHODS

The study population was selected from four neighborhoods in the Detroit area with high densities of Arab-Americans. Toenail samples were provided by 259 participants (163 adults, 96 children), and demographic data were obtained from a questionnaire completed for a different study (8). Toenail samples were collected using precleaned stainless-steel clipper by either participants themselves or by study team members. Clippings were provided from all 10 toes when possible, placed in a plastic vial, and stored in a plastic bag until analysis.

All plasticware was acid-washed for trace metals determination following modification of a previously described protocol (9). All materials contacting the samples were washed with 0.5% trace-metal-grade HNO_3 and Milli-Q water between samples to prevent cross-sample contamination. Prior to digestion, toenails were washed to minimize external contamination. Visible exogenous material was manually removed using a Teflon policeman and Teflon forceps. Samples were sonicated for 5 min in acetone, rinsed with Milli-Q water, rinsed with acetone, sonicated for 10 min in Milli-Q water, and rinsed twice with more Milli-Q water. Following washing, samples were dried overnight in a 60°C oven and weighed. Samples were digested in 1 mL trace-metal-grade HNO_3 for 5 min before transferring to a digital heating block. Samples were gradually heated to 100°C, after which the temperature was maintained for approx 30 min. When samples turned from brown to a light yellow, 1 mL of ACS-grade H_2O_2 was added, and samples were maintained at 100°C until the volume was reduced by half. Blanks were included from the washing through digestion procedures for 10% of the samples.

Simultaneous analysis of many elements in a sample was done using an Agilent 7500c inductively coupled plasma-mass spectrometer (ICP-MS). Operating conditions are listed in Table 1; additionally, the torch and lenses were adjusted for maximum sensitivity. The Agilent 7500c is

Table 1
Agilent 7500c Operating Conditions

ICP-MS Operating Conditions	
RF Power	1500 W
Sample uptake	0.1 ml min ⁻¹
Argon gas flow	1.15 ml min ⁻¹
Nebulizer	Babington
Torch and spray chamber	Quartz
Sample depth	8 mm
Dwell time per point	0.1-0.5 s
Points per peak	3
Sensitivity	10,000 CPS ppb ⁻¹
Number of replicates	3
Isotopes used for analyses	²⁷ Al, ⁵¹ V, ⁵² Cr, ⁵⁵ Mn, ⁵⁹ Co, ⁶⁰ Ni, ⁶³ Cu, ⁷⁵ As, ⁸⁰ Se, ⁹⁸ Mo, ¹¹⁴ Cd, ¹³⁷ Ba, ²⁰⁵ Tl, Average (²⁰⁶ Pb, ²⁰⁷ Pb, ²⁰⁸ Pb)

equipped with a collision cell, and hydrogen and helium gases were used to minimize matrix interference for different elements. Calibration standards were prepared immediately prior to each analysis by dilution of the Agilent Multi-Element Calibration Standard in 5% trace-metal-grade HNO₃. The calibration was validated using NIST SRM 1640, Trace Elements in Natural Water. For quality control purposes, sample batches included reagent blanks and certified reference materials (NIST 1577b Bovine Liver and SRM 1568a Rice Flour). The instrument detection limit was calculated as being three times the standard deviation of reagent blanks. Concentrations below the instrument detection limit were designated as below detection limit (BDL) and were excluded from statistical analyses. The remaining values were converted to micrograms per gram dry weight. Results for the blank samples were averaged for each washing and digestion batch. For each batch and element with an average blank value greater than zero, that value was subtracted from the result to obtain the concentration used for analysis.

All data analyses were carried out using SAS statistical software. To satisfy the normality assumption of the statistical methods used, those parameters with log-normal distributions were log-transformed prior to analysis.

RESULTS

To determine accuracy of the data, Bovine Liver (SRM 1577b) and Rice Flour (SRM 1568a) certified reference materials were digested as described and included for 10% of the samples (Table 2). Recovery for Zn was low;

Table 2
Results for Certified Reference Materials ($\mu\text{g/g}$)

Element	Liver Observed Mean $\pm$ SD (n=14)	Liver Certified Value Mean $\pm$ SD	Rice Observed Value Mean $\pm$ SD (n=14)	Rice Certified Value Mean $\pm$ SD
Al			4.85 $\pm$ 0.88	4.4 $\pm$ 1.0
Mn	8.04 $\pm$ 1.77	10.5 $\pm$ 1.7	16.89 $\pm$ 3.50	20.0 $\pm$ 1.6
Cu	137.2 $\pm$ 16.01	160 $\pm$ 8	2.27 $\pm$ 0.43	2.4 $\pm$ 0.3
As	0.05 $\pm$ 0.01	0.05*	0.26 $\pm$ 0.03	0.29 $\pm$ 0.03
Se	0.80 $\pm$ 0.12	0.73 $\pm$ 0.06	0.34 $\pm$ 0.05	0.38 $\pm$ 0.04
Mo	3.36 $\pm$ 0.33	3.5 $\pm$ 0.3	1.30 $\pm$ 0.05	1.46 $\pm$ 0.08
Cd	0.49 $\pm$ 0.05	0.50 $\pm$ 0.03	0.08 $\pm$ 0.07	0.022 $\pm$ 0.002
Pb	0.15 $\pm$ 0.05	0.129 $\pm$ 0.004		

* Reported noncertified value for reference material.

Table 3
Trace Elements ($\mu\text{g/g}$) in Toenails of All Participants, Descriptive Statistics

Element	Mean	Standard Deviation	Minimum	Maximum	n
Al	32.72	27.10	2.40	187.85	263
V	0.06	0.06	0.01	0.54	261
Cr	2.19	1.79	0.45	14.76	263
Mn	0.71	1.09	0.08	14.00	263
Co	0.20	0.76	0.01	10.53	247
Ni	37.42	109.00	0.20	1160.34	263
Cu	5.28	4.85	1.22	50.32	263
As	0.11	0.22	0.01	2.47	252
Se	0.79	0.39	0.34	4.67	256
Mo	0.24	0.25	0.01	0.75	21
Cd	0.93	1.15	0.05	7.70	263
Ba	1.37	2.06	0.10	22.55	263
Tl	0.09	0.10	0.01	0.52	49
Pb	1.06	1.53	0.01	13.42	263

Note: Values below the detection level were removed from analysis.

therefore, Zn was not included in the results. All other values for SRM 1568a, except for Cd, were within 20% of the given values. The poor Cd recovery for SRM 1568a is the result of a low Cd concentration in SRM 1568a when compared with the blanks. However, the result for Cd was within the 95% confidence interval for SRM 1577b, which had a concentration similar to that observed in the study samples.

Descriptive statistics were generated for the entire study population (Table 3). To facilitate interpretation of the results, weighted means calculated from previous studies reporting levels of trace elements in human nails for each of the elements analyzed (10) are presented for comparison (Table 4).

Table 4
Weighted Means ($\mu\text{g/g}$) from Reviewed Literature, Mean
(Number of Pooled Studies)

Element	All Studies ¹	General Population ²	High Exposure Populations ³	U.S. Populations	This Study
Al	47.04 (10)	47.04 (10)	N/A (0)	19.24 (3)	32.72
V	0.12 (8)	0.12 (8)	N/A (0)	0.05 (2)	0.06
Cr	7.41 (16)	7.08 (14)	11.07 (3)	1.72 (6)	2.19
Mn	4.22 (16)	3.37 (14)	11.17 (2)	0.82 (5)	0.71
Co	2.63 (13)	0.14 (13)	19.67 (3)	0.04 (5)	0.20
Ni	7.96 (10)	2.62 (10)	37.63 (2)	7.17 (2)	37.42
Cu	12.08 (35)	12.76 (32)	4.39 (2)	15.06 (6)	5.28
As	4.88 (28)	0.54 (18)	6.32 (7)	0.13 (9)	0.11
Se	1.55 (31)	1.55 (30)	1.89 (1)	0.91 (15)	0.79
Cd	0.84 (17)	0.73 (14)	2.60 (2)	0.37 (4)	0.93
Ba	8.59 (3)	8.59 (3)	N/A (0)	7.51 (1)	1.37
Pb	8.96 (18)	8.97 (14)	8.90 (3)	5.30 (3)	1.06

* Study populations were classified into categories as defined by the study author(s). For example, if the age of the population was not specified or if it included both children and adults, it was not included in calculating the mean.

¹ Weighted means from all studies reporting levels of trace elements in nails.

² Weighted means from all studies not specifying elevated exposure in the population.

³ Weighted means from all studies specifying elevated exposure in the population.

Study populations were classified into categories as defined by the study author(s). Although different washing, digestion, and analysis procedures were followed for different studies, compilation of results from a large number of studies increases the likelihood of obtaining a representative sample for comparison. To date, no studies have included such an extensive review of the literature when comparing results to previously reported levels.

The *t*-tests for differences between two means in this study population were performed on the elemental data for adults and children (Table 5). The *t*-tests reveal that, with the exception of Mn, children have significantly higher levels of those nonessential elements with potential environmental sources (Al, Cd, Cr, Pb, and V) whereas adults have significantly higher levels of Se, an essential element (Table 5).

The *t*-tests and analysis of variance (ANOVA) were performed to assess the effect of gender and immigration status on trace element levels. Differences in concentrations of Co, Al, Ba, and V were observed for male and female participants (Table 6). Results indicate that children born in the United States have elevated levels of Cd compared with children born elsewhere (Table 6). ANOVA with multiple comparisons reveals that levels of Ni and Pb differ significantly by respondent's country of origin and city of residence, respectively (Table 7). Because these data were only available for adult respondents, children were not included in the ANOVA analysis for country of origin.

Table 5
Comparing Mean Concentration of Trace Elements in Nails ($\mu\text{g/g}$)
for Children and Adults

Element	Adults This study Mean($\pm$ SD)	Children This study Mean($\pm$ SD)	p-value*	Adults Pooled literature**	Children Pooled literature**
Al	26.91 (21.65)	42.68 (32.24)	<.0001	36.22 (7)	134.04 (4)
V	0.04 (0.04)	0.09 (0.08)	<.0001	0.10 (7)	0.11 (1)
Cr	1.91 (1.66)	2.65 (1.90)	0.0014	10.22 (9)	3.04 (2)
Mn	0.60 (1.15)	0.90 (0.943)	0.0259	6.26 (10)	3.57 (3)
Co	0.17 (0.86)	0.27 (0.55)		4.00 (9)	0.29 (2)
Ni	32.89 (68.97)	45.18 (155.41)		10.18 (7)	N/A (0)
Cu	5.05 (4.64)	5.66 (5.21)		9.61 (14)	14.61 (5)
As	0.10 (0.22)	0.14 (0.22)		0.23 (9)	0.10 (1)
Se	0.82 (0.46)	0.73 (0.21)	0.0415	0.73 (24)	0.65 (2)
Cd	0.64 (0.79)	1.44 (1.46)	<.0001	1.04 (5)	0.49 (2)
Ba	1.28 (2.40)	1.52 (1.28)		1.79 (2)	N/A (0)
Pb	0.74 (1.23)	1.60 (1.82)	<.0001	5.49 (7)	8.67 (2)

* The *p*-value is for testing the difference between means for results from this study. The *p*-value is reported if differences are significant at $\alpha=0.05$.

** Pooled literature values are weighted means (number of studies pooled).

Table 6
Effect of Gender and Birthplace on Trace Element Status: Significant Results
($p<0.05$) from *t*-Tests for Differences Between Means

Element	Factor	Group A	Group A Mean ($\mu\text{g g}^{-1}$)	Group B	Group B Mean ($\mu\text{g g}^{-1}$)	p-value
Cd	Birthplace	Children born in the USA	1.62	Children not born in the USA	0.89	0.02
Co	Gender	Boys	0.36	Girls	0.20	0.03
Al	Gender	Men	23.56	Women	29.33	0.04
Ba	Gender	Men	0.93	Women	1.51	0.04
V	Gender	Men	0.032	Women	0.05	0.0002

Table 7
Effect of County of Origin and City of Residence on Trace Element Status:
Significant Results from ANOVA and Pairwise Comparisons

Element	Factor	Group A	Group B	p-value
Ni	Country of Origin	Iraq (60.96)	Lebanon (16.62)	0.0222 ¹
Pb	City of Residence	Hamtramck (1.69)	Oak Park (0.652)	0.0062 ²

¹ *p*-Value for ANOVA. Differences are significant for Bonferroni's and Tukey's Studentized range methods for pairwise comparisons.

² *p*-Value for ANOVA. Differences are significant for Bonferroni's, Scheffe's, and Tukey's Studentized range methods for pairwise comparisons.

Table 8
Significant Pearson Correlation Coefficients ($p < 0.05$)
for All Samples Above Detection

	Al	V	Cr	Mn	Co	Ni	Cu	As	Se	Cd	Ba	Tl	Pb
Al	1.0	.564	.375	.465	.189		.201	.343		.274	.527	.304	.519
V		1.0	.596	.463	.335		.188	.441		.642	.463	.535	.398
Cr			1.0	.385	.476		.407	.407	.185	.708	.375	.809	.208
Mn				1.0	.554			.298	.156	.326	.412		.505
Co					1.0	.262		.226		.448	.175	.540	.273
Ni						1.0							
Cu							1.0	.177	.170	.271	.207		.316
As								1.0	.274	.242	.349		.397
Se									1.0		.178		
Cd										1.0	.178	.939	.250
Ba											1.0	.401	.553
Tl												1.0	
Pb													1.0

To assess potential interaction or coexistence of the trace elements analyzed, Pearson correlation coefficients were calculated (Table 8). The strongest significant ($\alpha=0.05$) correlations are apparent for the following nonessential element pairs: Cd and Cr, Tl and Cr, and Tl and Cd. However, a number of other significant correlations are reported. The significance of these and the above results are discussed next.

DISCUSSION

Human nails can accumulate both toxic and essential elements and, therefore, might provide insight into exposures from both environmental and dietary pathways (11,12). Essential elements are defined as those that are necessary for the human body to maintain normal physiological functioning (13). Elements measured in this study that are classified as essential include Cu, Se, Mn, Mb, and Co (14). Although these elements elicit an adverse response when the dose is too low, indicating deficiency, an excessive dose can result in toxicity. The elements measured in this study considered nonessential to humans include Al, As, Ba, Cd, Cr, Pb, Ni, Tl, and V (14,15).

When considering only essential elements, the study population has low mean values for Cu, Mn, and Se when compared with weighted means for all studies and, therefore, might be indicative of deficiencies in these elements. Although copper deficiency is considered rare in individuals consuming a variety of foods (14,16), deficiencies are present in some populations, particularly malnourished children (17). Mean Mn concentration for the study population is comparable to values observed in the

literature for US populations, but low when compared to other regions. Previous studies have not found Mn deficiency in North America, and dietary intake is considered to be adequate in US populations (13). It is possible that the comparatively low concentrations might be the result of regional dietary or environmental influences; however, difficulties in assessing Mn concentrations in biological media as a result of external contamination must also be considered (17).

Comparison of mean values for nonessential elements reveals slightly high concentrations of Al and Cd for the study population compared with other US populations and concentrations of Ni comparable to individuals experiencing occupational exposures (Table 4). Nickel in fingernails has been shown to increase as exposure increases, therefore supporting the use of human nails as a biomarker of Ni exposure (18,19). Because high concentrations are reported for children as well as adults, it is unlikely that the high levels observed in this population are the result of occupational exposures, leaving the possibility of a dietary or environmental source, or an analytical error.

Although Ni values were not reported in the liver and rice standard reference materials used, they were reported in NCSZC 81002, Trace Elements in Human Hair. This reference material was not available for use throughout the digestion procedure and, therefore, was not included to report overall data accuracy. However, inclusion of this value for Ni provides insight into the values obtained for Ni. Results from analysis of two samples of the human hair reference material in two of the digestion batches (observed mean = 2.33 $\mu\text{g/g}$; certified mean = 3.17 $\mu\text{g/g}$), and low blank values support the likelihood that the elevated observed values are not the result of the analysis procedures. The possibility of nickel contamination from the stainless-steel clippers, despite the described washing procedures, was also considered. This possibility is considered unlikely, although, as one would also then expect, elevated levels of Cr and Mn in the study population as a result of the composition of the stainless steel. Furthermore, previous studies used stainless-steel scissors or clippers to determine Ni concentrations in nails and reported average Ni levels of 2.34 ($n=48$), 1.19 ($n=95$), and 2.7 ($n=34$) $\mu\text{g/g}$, respectively, among nonoccupationally exposed populations (20–22). Finally, environmental exposure from surrounding industry could contribute to elevated levels of Ni in this population. Nickel compounds are commonly used in automotive-related industries, such as electroplating, battery production, machinery, and tool production (23). Further investigation into dietary and environmental sources for the study population must be conducted before conclusions can be drawn.

Children might be at higher risk of exposure to environmental contaminants, or nonessential elements, because of their physiological, physical, and behavioral characteristics. For example, children consume more food per body weight than adults and absorb heavy metals more efficiently in the gastrointestinal tract (24). Behaviors such as hand-to-mouth

activity or physical attributes, such as a high surface area-to-volume ratio, might also lead to increased risk of exposure to toxic metals (24,25). These factors could be influencing the elevated levels of Al, Cd, Cr, Pb, and V observed in children in this study population when compared to adults (Table 5). Previous studies have also found that both Al and V levels are higher in fingernails of younger individuals (26). When considering essential elements, children in this study have significantly higher concentrations of Mn when compared with adults, but significantly lower Se status (Table 5). The significantly lower Se levels observed in children might be related to the fact that children generally have lower plasma Se levels than adults (17).

These observed differences between adults versus children, however, are not completely consistent with the weighted means calculated from the literature (Table 5). Whereas differences in Al, V, Se, and Pb are in agreement with the literature when adults are compared with children, differences in Cr, Mn, Co, and Cd are not. When comparing the weighted literature means for adults and children, Cr, Mn, Co, and Cd are reportedly higher in adults than in children. Occupational exposures might be influencing these levels in adults. In addition, it is possible that the inconsistencies are the result of small population sizes for comparison, differences in analytical techniques, or variation in dietary or environmental exposures across the populations compared. For these reasons, comparison within the current study population, rather than with the reviewed literature, might be a more reliable indicator of differences in trace element exposure and metabolism between adults and children.

Assessment of the effect of gender on trace element status revealed a significant difference in mean Co concentration between boys and girls (Table 6). Although blood and serum Co levels have been reported to be higher in girls than in boys (27), no known studies report differences in toenail Co concentrations for boys and girls. Kanabrocki et al. did report higher thumbnail concentrations for women than for men, although this difference is not significant (28). Low Fe status is known to increase the uptake of Co (29); this interaction might help to explain the observed differences in mean toenail Co concentrations between boys and girls. In the present population, women have significantly higher mean concentrations of Al, Ba, and V (Table 6); no known studies have observed a gender influence on status of these elements in human nails. The source of elevated concentrations of these elements in toenails of women participants is difficult to determine. Although removed with acetone prior to analysis, it is possible that residual cosmetic applications, such as nail polish, might influence these concentrations. It is also possible that dietary intake and metabolism of these elements might differ between men and women. These findings warrant further investigation.

The *t*-tests conducted to investigate the role of birthplace reveal a significantly higher mean Cd concentration for children born in the United States (Table 6). Because Cd concentration in most tissues increases with

time (30), it is possible that levels observed in children born in the United States are reflective of cumulative exposures that might not be experienced by children who were recent immigrants. Therefore, this relationship might be suggestive of possible cumulative exposures to Cd in these highly industrialized communities.

To explore the role of industrialization on concentrations of elements in toenails, differences in mean concentrations were assessed for individuals living in the four different study areas of Detroit: Hamtramck, Oak Park, Detroit, and Dearborn. The analysis reveals a significantly higher concentration of Pb for individuals residing in the more industrialized Hamtramck when compared to Oak Park (Table 7). With respect to proximity to industries, these two areas show the most extreme differences in surrounding commercial and industrial land use. It is possible, therefore, that these differences are the result of the relative degree of industrialization in these neighborhoods as well as cultural or socioeconomic influences. Country of origin was also explored as an influencing factor on trace element status for adults. Results from ANOVA indicate a significant difference in mean concentration of Ni for respondents born in Iraq compared with respondents born in Lebanon (Table 7). Therefore, the possibility of a cultural or dietary influence on Ni exposure must not be ruled out; however, country of origin is highly correlated with city of residence in this population, making it difficult to tease apart these contributing factors.

Exposure to and health effects of chemical mixtures is an emerging area of interest in environmental health. Multielement analytical technologies allow for investigation of correlations between different elements, providing insight into potential metabolic interactions or sources of common exposures. Although evidence regarding metabolic interactions between these elements is still emerging, potential for interaction exists between Al and Mg, As and Se, and Al and Mn, for example (31,32). Many significant ($p < 0.05$) and positive correlations between elements analyzed were observed (Table 8). The strongest correlations observed in this study, those among Cd, Cr, and Tl, cannot be explained by known metabolic interactions; however, common sources of exposure are possible for these elements, particularly in a highly industrialized area. Associations reported in other studies between Cd and Cr concentrations in human nails are inconsistent with each other and are weak when compared to the current observations (33,34). To date, no known studies have reported correlations for Tl and Cd or Cr. A number of other positive and significant correlation coefficients were revealed in this analysis; several of these associations were also investigated in previous studies. For example, a strong significant correlation ($r = 0.70$) has also been observed between Al and V in toenails of a New Guinea population. A similar correlation, observed in the local staple food of this population, likely explains the relationship (35). Positive correlations between Co and Cr, Se and Cr, Cd and Cu, Cd and Pb, and Pb and Cu have also been observed in other studies (36,37). Future collection of both dietary

and environmental exposure data in this community, coupled with additional research on interelement interactions, might shed light on these intriguing interelement relationships.

Ease of collection and storage make use of toenails as a biomarker of exposure in community-based studies highly desirable. However, further steps must be taken to ensure validation of this tool for elements less commonly investigated. Although several elements have been highly correlated with environmental exposure in previous studies, further research is necessary to investigate such associations for other essential and nonessential elements. Knowledge of environmental and dietary exposures, as well as further investigation into metabolic interactions of trace elements, will improve the knowledge base surrounding use of this valuable biomarker. Finally, standardization of an analysis protocol will improve the ability to compare populations of interest, an important step that is necessary for interpretation of this wealth of data. Investigations such as this, through comparison with other studies and investigation of numerous factors affecting trace element status, take important steps toward improving interpretation of reported values and recognizing the potential use of this marker of exposure in future applications.

ACKNOWLEDGMENTS

This project was funded by a NIEHS grant under the Environmental Justice Program. The authors would like to thank Dr. Mary Suad and Dr. Farid Shamo for their assistance with data and toenail sample collection.

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