Mercury Contamination of Skin-whitening Creams in Phnom Penh, Cambodia

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Background. In Cambodia, there is widespread use of skin-whitening creams containing levels of mercury that exceed Association of Southeast Asian Nations (ASEAN) guidelines by up to 35,000 times. Mercury in skin-whitening creams threatens to compromise the health of Cambodians.

Objectives. It is important to provide essential information on sources of mercury so that Cambodians can avoid exposure to elevated levels of mercury and to support informed management of consumer goods.

Methods. Students were directed to buy selected skin-whitening creams that were then sampled with replication in 2011 and 2015 and processed with X-ray fluorescence (XRF) at the University of Health Science (UHS), Phnom Penh, Cambodia.

Discussion. The analysis of skin-whitening creams in Phnom Penh in 2015 was compared to analyses in 2008 and 2011 and showed that several creams produced in Asia no longer contain mercury. However, skin creams produced in Phnom Penh continue to use mercury and counterfeit products also are contaminated with mercury. Vendors occasionally identified Vietnam as a source of counterfeit products, but often the source was unknown. Mercury continues to be the metal of greatest concern in skin creams. Creams with more than 1,000 μg/g of mercury are a common cause of dermatitis (27% of cases). A new XRF analyzer was also able to detect more lead and arsenic than that used in analyses performed in 2011, and these two metals also exceeded ASEAN guidelines. Arsenic contamination also reflected the presence of bismuth in creams.

Conclusion. Some producers of skin-whitening creams in Thailand, China and Taiwan appear to be aware of the risks of mercury contamination and have modified their products. However, other producers of skin-whitening creams continue to use mercury. XRF analysis allows for rapid screening of mercury in cosmetics and should be used to gather additional information on mercury content in cosmetics in support of public health efforts to stem the import, export and sales of skin creams containing mercury.

Competing Interests. The authors declare no competing financial interests.

Keywords. Toxicity, mercury, skin-whitening cream, Cambodia

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Introduction

An analysis in 2011 indicated that mercury was added to about 16% of skin-whitening creams in Cambodia to block the formation of melanin.1 The maximum concentration of mercury found in a cream in Cambodia was 35,000 μg/g. None of the product labels indicated the addition of mercury. The half-life of inorganic mercury in the body is approximately 30–60 days, and mercury levels in the body increase with daily application of a mercury cream.2 Inorganic mercury commonly causes kidney damage and also results in neurological toxicity and skin disorders.3-6 Although chelation therapy has health risks, at times it has been used to expedite recovery from the use of skin creams with mercury.7-9 Usually the body recovers once use of such creams is stopped; however at times, neurological and kidney damage can be long term or even permanent.10,11

Unfortunately, use of mercury in skin creams is common.12-14 Social pressure to appear pale is centuries old and persists today. Reducing the use of mercury requires both education of users of cosmetics and rapid detection of mercury to facilitate enforcement and suppression of sales. This paper reviews the use of educational clinics in Cambodia and X-ray fluorescence (XRF) analysis to detect and discourage the use of mercury-containing creams. The Minamata Convention has addressed the issue of mercury in skin-whitening creams in order to reduce the use and availability of mercury (http://www.mercuryconvention.org/).
This paper reports previously unreported aspects of our educational clinics conducted in 2011. The collection of creams focused on strong replication in 2011 and 2015 to allow for analysis of changes in mercury use in creams. The main objectives were to: 1) determine if the mercury content of creams with a history of high levels of mercury in 2008 and 2011 has changed and 2) evaluate the presence of other metals in creams.

Methods

Educational Clinics
Sampling protocols were approved by the Ethical Review Committee of the Cambodian Ministry of Health. Students from the University of Health Sciences and two Don Bosco Institutes in Phnom Penh, garment factory workers and women in the service industry, were invited to bring skin creams that they were currently using for evaluation of their mercury content. Don Bosco Institutes are training schools run by the Catholic Church. More than 90% of the study participants were women between 18 and 22 years old. The analysis was preceded by short lectures in Khmer on the risks of mercury and were augmented whenever a toxic cream was discovered. The students asked questions and some returned later for more discussion. Students were given interview forms and direction prior to measurement of the creams (Table 1). An important aspect of the clinics was having students see the measurements directly using a Niton XL3t handheld x-ray XRF analyzer (Thermo Fisher Scientific, Waltham, MA).

The sampling methods in 2011 were presented in Murphy et al. 2012. In 2014, eight products that had been kept from the collection in 2011 for displays were analyzed with a Niton XL3T970 handheld XRF analyzer with a sample holder. In 2015, sixty cosmetic samples from 21 products were purchased from April to May from six different local markets such as Oreusey market, Old market, Psar Thom Toul Sanke, Kilo4 market and Beong Keng Kong market and analyzed using a Niton XL3T970 handheld XRF analyzer with a sample holder.

In addition, examples of creams with mercury were displayed as part of the clinic. Most students took pictures of the displays to show their friends and families. The results of the x-ray analysis of the creams were used to select students to donate samples urine or hair. Selection of samples included some without mercury exposure as controls, but most students had used a cream with high mercury levels. Analysis of urine was done at Central Laboratories, Bangkok using inductively coupled plasma mass spectrometry (ICPMS) and wet digestion. Hair samples were as long as 70 cm and as short as 20 cm. They were cut into segments of no less...
dimethyl sulfoxide, which assists in the mixing of mercury and reduced sampling errors, but for safety, was conducted only in the laboratory, not with students.

We had previously confirmed the skin cream analysis method with independent laboratories using inductively coupled plasma optical emission spectroscopy (ICP-OES) and spiking.

The analyses of other metals in the present study should be considered preliminary and require verification. Our study using XRF analysis of sediments found that XRF results deviated from certified reference materials as follows: iron (Fe) 3%, arsenic (As) 4%, copper (Cu) 6%, zinc (Zn) 32% and lead (Pb) 57%.

In 2015, the XRF mercury (Hg) results were within 1% of a certified reference material supplied by Thermo Fisher Inc.

Statistical analysis
Microsoft Excel 2013 was used for the basic statistical analysis. To determine the significance of \( r^2 \) values in linear regression the following website was used for Pearson's correlation coefficient: http://www.gifted.uconn.edu/siegel/research/correlation/corrchrt.htm. To compare the means of creams collected in 2011 to the same products in 2015, we used the Mann-Whitney U test calculator at the Vassar University website http://vassarstats.net/utest.html. To compare the three Thai cream products that were measured in 2008 to the analyses in 2011 and 2015 we combined the three products into a Thai data set and compared the years using the Mann-Whitney U test. For a Cambodian producer of skin creams (pseudonym Khmer1) we also combined creams in groups by year. To compare the significance of the proportion of rashes produced by skin creams, we used the Vassar University calculator.

Results
The thin film method allowed the educational clinics to proceed quickly so that the students' attention was maintained. Students were very concerned to see if their cream contained mercury. Most were worried about their health and planned to avoid using any creams with mercury. For screening purposes, the thin layer method is much faster than the sample cup method. In Figure 1, the relative standard deviation for the thin films in triplicate analysis was 3.98%, whereas with the sample cups it was 2.48%. The samples in Figure 1 were all fluid-type creams with some water (Vaseline). By comparison with more viscous creams (counterfeit Lemon Herbal Cream from Vietnam) the relative standard deviation was 1.69% with thin film and 9.24% for the sample cups. For viscous creams, which are common, the sample cups produced more variable than 10 cm.

Hair analysis was done at the University of California, Davis using cold vapor-atomic absorption spectrophotometry (CVAAS), following digestion under pressure at 95°C in a mixture of concentrated nitric and sulfuric acids with potassium permanganate.

XRF Calibration
For most of the analyses presented in this paper, about 0.3 g of cream was placed on Mylar film which was then folded over the cream and placed in front of the XRF analyzer in a sample stand. For a subset of samples, 5 g of cream was placed into sample cups. Calibration of the XRF unit was done by adding mercuric chloride to sample creams for both the sample cup and the thin film method. Calibration used dimethyl sulfoxide, which assists in the mixing of mercury and reduced sampling errors, but for safety, was conducted only in the laboratory, not with students. We had previously confirmed the skin cream analysis method with independent laboratories using inductively coupled plasma optical emission spectroscopy (ICP-OES) and spiking. The analyses of other metals in the present study should be considered preliminary and require verification. Our study using XRF analysis of sediments found that XRF results deviated from certified reference materials as follows: iron (Fe) 3%, arsenic (As) 4%, copper (Cu) 6%, zinc (Zn) 32% and lead (Pb) 57%. In 2015, the XRF mercury (Hg) results were within 1% of a certified reference material supplied by Thermo Fisher Inc.

Table 1 — Interview Questions

| Date | Name | Age | Phone number | Email | Approval to send results by email | Signature |
|------|------|-----|--------------|-------|-----------------------------------|-----------|
| Weight (used to estimate skin surface and thus assimilation of mercury) | Skin cream product name | Bought where | Cost | Size | How long does it last the user? | How long have you been using it? | Do you mix the product with anything else and if yes what? | Times a day used? | Face only, or % of rest of body covered? | Does it lighten your skin as desired? | Have you noticed any changes other than lighter skin? | Did you know that some skin whiteners contain mercury? |

Table 1 — Interview Questions
data. For screening purposes, this degree of variability was not a concern.

The response with the sample cups was more curvilinear than was seen in the thin film layer in Figure 1, but by itself, this was not a significant concern. With higher concentrations of mercury, the response was more curvilinear (data not shown). Because of the greater adsorption of fluorescent x-rays by mercury at high concentrations, XRF analysis is fundamentally curvilinear. Likely this self-adsorption of mercury at higher concentrations is also greater in thicker samples. For screening purposes, this small deviation causing a curvilinear response is not a concern.

In Figure 1, the detection of mercury was virtually 1:1. Recoveries of mercury were close to 100% and never more than 110% or less than 98%. The cream used in Figure 1 contained about 6.5% titanium, but this had no apparent effect on the mercury analysis. However, the mercury greatly impeded the measurement of titanium. The degree of suppression varied with the mercury concentration: 5,000 μg/g Hg suppressed titanium measurement by 90%. The variability of the XRF analysis of titanium (Ti) was much greater than for other metals. For example, in a set of 6 products analyzed in triplicate, the average coefficients of variation for titanium and mercury were 33.9% and 7.4%, respectively. Each of the tested products had more than 1000 μg Ti/g or 600 μg Hg/g. The subsampling of viscous creams is awkward, but even with a fluid sunblock and use of a Vortex stirrer immediately before subsampling, the variability in Ti analysis was high with both the thin film and cup methods.

Effect of Sample Depth on XRF Analysis
The Thermo Niton manual suggests using deep samples, which is not optimal for screening skin creams. When the depth of cream (or plastic) varies, the depth of the samples should be recorded in the analyzer. The algorithm is then able to make accommodations for depth. If the sample cups were used, another variable was added to the analysis because the volume of cream was often less than 5 ml and an attempt should be made to measure the height of the sample. Without correction for height, the error could be as much as 40%. With the thin film method, all triplicates had coefficients of variation less than 9%. As can be seen in Figure 2, the curve appears to be the flattest (least variable) with cream sample thicknesses of 0.2 to 0.7 mm. Verified by testing on multiple days, spiked samples within this range of depths produced an average of 99% recovery. Note that in Figure 2, we kept the sample thickness setting on the analyzer at 0.3 mm. This was done to evaluate whether sample thickness had an important effect on the thickness used for the thin sample method. It is easy to work within the desired thickness of 0.2 to 0.7 mm. For routine analysis it is unnecessary to measure the sample thickness.

Mercury Analysis with a Thin Film Method
The procedure recommended in the Thermo manual uses sample cups, but this is awkward for screening of skin creams. The manual is mainly written to guide the preparation of geological powders and soil samples. Many skin creams are too viscous to fill the sample cups well. For viscous creams it is difficult to avoid having air bubbles at the bottom of the sample cup, which reduces the apparent concentration of mercury. Moreover, the Thermo manual’s suggestion of samples of at least 5 g is impossible for many of
the creams which are often sold in 3 ml jars. For screening purposes, it is not necessary to have a 5 g sample. Students did not mind donating 0.3 g of their cream, but may have had an issue with donating the entire cream. Creams could be removed from the sample cups, but this would take time, and handling of these products should be kept to a minimum or be done in a fume hood, which is not conducive to a live demonstration. Our demonstrations were typically done in simple classrooms with over 30 students.

**Advantages of Thin Film vs Sample Cup Method**
1) No need for cups, which reduces costs and amount of toxic wastes.
2) Much smaller mass of sample needed (~0.3 g vs >5 g).
3) Much faster, which is important when screening many samples in front of students.
4) With viscous creams there is better reproducibility due to fewer air bubbles produced by sample transfer to the sample and which are resistant to release by Vortex agitation.

**Comparison of Samples from 2015 to Earlier Sampling in 2008 and 2011**
In 2015, mercury was detected in 41% of samples. In 2011, 16% of 581 creams collected in non-biased clinics contained detectable mercury. For simplicity, the same detection level of 20 μg/g as was determined in 2011 was used for both, i.e. results lower than 20 μg/g in 2015 were considered non-detects. In this case, the differences in sample processing and smaller sample size in 2015 (n=60) did not warrant discussion of the significance of the apparent increase in the proportion of samples in which mercury was detected. The highest mercury concentration found in 2015 was 6,305 μg/g, whereas it was 35,000 μg/g in 2011. Table 2 illustrates that in 2015, mercury was found at much higher concentrations than arsenic or lead, the only other toxic metals above the Association of Southeast Asian Nations (ASEAN) guidelines.

**Other Metals**
In 2015, the XRF analysis was done with a newer model and appeared to detect more arsenic and lead. These results should be considered preliminary and qualitative, but could guide future sampling. Lead is able to suppress detection of arsenic in XRF analysis and these results might mask the significance of arsenic in skin creams. In 2011, the XRF analyzer results of As and Pb in soils were...
confirmed with certified reference materials and detection levels were about 9 μg/g for Pb and 13 μg/g for As. In 2015, the detection levels were about 5 μg/g for both Pb and As. By ignoring detected values lower than the 2011 detection level, the increases in arsenic and lead in skin creams were significant (α = 0.05) in a Mann-Whitney analysis. No lead was observed in creams in 2011, whereas it was detected in 22% of creams in 2015. Only 6% of creams in 2011 appeared to contain arsenic, whereas in 2015, 22% of creams appeared to contain arsenic. In 2015, two samples of Rojzy Jiali appeared to exceed the ASEAN guideline for arsenic by a factor of about 9 times. In 2015, Qian Mei exceeded the ASEAN guideline for arsenic by up to three-fold. The Chinese cream Qian Mei contained bismuth that was contaminated with arsenic. Figure 3 illustrates a highly significant relationship between bismuth and arsenic (r^2 = 0.858, p < 0.01, four of the 17 points were superimposed). A set of 8 samples from the 2011 collection were kept for display and analyzed in 2014. The relationship between bismuth (Bi) and arsenic was y = 0.0144x - 8.0129, r^2 = 0.99, n = 8. The relationship

Table 2 — Metals in Skin Whitening Creams 2008, 2011 and 2015

| Country/year | Sample Guideline | Pb ± SD (n) | As ± SD (n) | Hg ± SD (n) | Comments |
|--------------|------------------|------------|------------|------------|----------|
| Thailand 2008| 3 products       | ND (3)     | ND (3)     | 4600 ± 3608(3) | Significant p <0.01 |
| Thailand 2011| 3 products       | ND (9)     | ND (9)     | ND (3)     | Significant p <0.1 |
| Thailand 2015| 3 products       | ND (9)     | ND (9)     | ND (3)     | Significant p <0.1 |
| Taiwan 2011  | Rojzy Jiali      | ND (6)     | ND (6)     | 4333 ± 4791(6) | Significant p <0.01 |
| Taiwan 2015  | Rojzy Jiali      | ND (9)     | 32 ± 28 (4) | 28 ± 30 (4) | Significant p <0.01 |
| China 2011   | Hua Thu Li       | ND (10)    | ND (10)    | 6401 ± 7397(10) | Significant p < 0.01 |
| China 2015   | Hua Thu Li       | ND (5)     | ND (5)     | 0 ± 0 (5)   | Significant p < 0.01 |
| China 2011   | Qian Mei         | ND (10)    | ND (10)    | 3779 ± 1926(10) | Significant p < 0.01 |
| China 2015   | Qian Mei         | ND (12)    | 9 ± 4 (12) | 17 ± 31 (12) | Significant p < 0.01 |
| Cambodia 2011| 3 products*      | ND (4)     | ND (4)     | 2599 ± 2320(4) | Not Significant |
| Cambodia 2015| 13 products      | 9 ± 31 (13)| ND (13)    | 2022 ± 2232(13) | Not Significant |
| USA 2011     | “Enjoy”          | ND (6)     | ND (6)     | 12947 ± 826 (6) | Significant p < 0.01 |
| USA 2015     | “Enjoy”          | 52 ± 9 (6) | ND (6)     | 5989 ± 252 (6) | Significant p < 0.01 |
| Vietnam 2015 | “Lemon”          | 5 ± 5 (6)  | ND (6)     | 3649 ± 229 (6) | Reported bootleg |
between Bi (x) and As (y) in 2011 and 2014 was similar (2011: y = 0.0093 x -0.1884), but any statistical analysis of limited data is inappropriate. The one extreme sample of Rojzy Jiali analyzed in 2014 exceeded ASEAN guidelines for arsenic by 86 times. The trend in the 2014 data was dominated by one sample of Rojzy Jiali that contained 433 μg/g of arsenic, and 30,270 μg/g of bismuth. Of the eight samples reprocessed in 2014, five contained more than 39 μg/g of arsenic, which confirms that the newer analyzer was more sensitive for arsenic analysis. Some other creams such as fake Lemon Herbal contained similar concentrations of bismuth, but had undetectable levels of arsenic. Clearly if one producer can find a supply of bismuth without arsenic, all could.

Another interesting relationship is the significant correlation between tin and mercury in Khmer1 cream products in 2015 ($R^2 = 0.7006$, n = 14 p<0.01, Figure 4). Mercury and tin are found together in geological deposits. Mercury in other products such as fake Lemon Herbal had no tin and presumably got their mercury from another source. The set of five samples of the fake cream “Enjoy” had two samples with high tin and high mercury, but three with high mercury and low tin, so there was no significant relationship in “Enjoy” creams between tin and mercury.

We commonly detected the following 15 elements: Arsenic (As), barium (Ba), Bismuth (Bi), bromine (Br), chlorine (Cl), chromium (Cr), copper (Cu), iron (Fe), mercury (Hg), nickel (Ni), lead (Pb), antimony (Sb), tin (Sn), titanium (Ti) and zinc (Zn). Moreover cadmium (Cd), selenium (Se), and vanadium (V) were occasionally detected. Analysis of these 18 elements might at times fingerprint producers of bootleg creams. However, this is likely done with a simpler analysis. Some bootleg products are obvious. Figure 5 shows “Enjoy” cream packaging that was purchased at markets. Note the obvious worn appearance of the packaging. The label claims that this Enjoy cream is produced in the USA. With “Lemon Herbal” and other creams a vendor said that they were produced in Vietnam and placed into packaging that was recycled. This vendor offered a discount for recycled cream containers and packaging. The labeling on the “Lemon Herbal” package said it was produced in Thailand. Not all use of mercury is hidden by bootlegging. Eight of 13 products of Khmer1 creams contained mercury. This producer in Phnom Penh operates outlet stores. In 2011, a third of such small companies including beauty shops produced whitening creams with mercury and there is no reason to believe that this has changed. We sampled Khmer1 creams only as an example, but believe mercury is as common now in beauty shops in Phnom Penh as it was in 2011.

**Dermatitis**

The improved sensitivity of the new XRF analyzer could better support more detailed assessment of dermatitis in relation to other ingredients contained within the creams. In interviews in 2011, students using creams with more than 1,000 μg/g mercury were significantly (P < 0.0002, two tailed) more likely to develop a skin rash. Of 30 students using a cream with more than 1,000 μg/g of mercury, eight reported having a rash. In the set of students (n = 274) using a cream with less than 1,000 μg/g of mercury, only five reported having a rash. These 5 creams did not contain mercury. There were 30 creams with less than 1,000 μg/g, but with detectible concentrations of mercury (20–100 μg/g, n = 12; 100-500 μg/g, n = 12; 500-1,000 μg/g, n = 6).

Two cases of allergic reaction were associated with commercial creams containing 8,000 μg/g and 13,000 μg/g of titanium, a common ingredient in...
sunblock. The three other reported cases of allergic reaction without mercury were from beauty shop creams, and they contained no major concentrations of metals. In 2011, one unique cream had 878 μg/g of cadmium, and three women in the service industry who had used this cream complained of dermatitis. That level is almost 300-fold the Canadian guideline of 3 μg Cd/g. Cadmium was undetected in 2015. ASEAN is apparently evaluating a guideline of 1-3 μg Cd/g in skin creams.

Two samples of fake Enjoy appeared to have 500 μg/g of antimony, which is 100-fold the Canadian guideline. Otherwise, it was rarely found and had no obvious relationship to other contaminants. The Canadian review states “Dermal absorption of antimony has not been well studied.” Antimony in skin creams is not currently regulated in ASEAN guidelines. We are uncertain of the validity of the XRF measurements of antimony, but any substance that exceeds a guideline by as much as a hundredfold warrants some concern and validation. The antimony and lead in fake Enjoy are of academic interest. Because of the extreme concentration of mercury (mean 5,989 ± 250 μg/g, n = 6), we recommend that this bootlegged version of Enjoy skin cream be taken off the market.

In 2015 we detected four creams with more than 30 μg/g of nickel. Cobalt and chromium are also known to initiate allergic skin responses. We did not detect cobalt in skin creams. However, in 2015, two samples of creams appeared to contain more than 150 μg/g of chromium, a known essential micronutrient which is toxic at high concentrations.

Assessments of Mercury Bioaccumulation
Five of 15 samples of urine had higher...
levels than the warning level of 20 μg/L Hg required for physicians to report to the New York Department of Health (Table 3). However, one of the subjects with 25 μg/L Hg in urine claimed she was not using a cream with mercury. Interviews are not always accurate and the data on urine in the present study is not strong. The lab detection level of 18 μg/L is barely adequate. There was no significant relationship between the mercury in creams and mercury in urine. It would have been better to calculate the exposure of mercury via the interviews, but the experimental design did not anticipate the frequent inability of students to fill out the questionnaires. This area needs considerably more analysis, including blood analysis, to gather more information on mercury bioaccumulation and potential relationships between mercury and cases of infection and anemia.

The concentrations of mercury in hair in our study (Figure 6) were similar to what Agusa et al. observed in hair samples in Phnom Penh. The pattern of mercury in student hair samples in Figure 6 is quite strong. However, three of the subjects in Figure 6 had been using a cream with mercury for less than two months. No hair sample represented a growth period of less than 20 months. Since hair grows at approximately 1 cm a month, the longest hair sample represented growth of about 70 months and no subjects had used a cream for more than 24 months. The samples farthest from the scalp were all beyond the time frame that students had been using skin creams. The patterns observed in mercury concentration do not represent absorption of mercury through the skin and excretion into hair. Rather, it represents surface contamination that presumably takes place when the subjects are lying on their hair while sleeping.

**Student Interviews**

The most consistent data in the interviews was the reporting of the whitening of subjects’ skin, and presence of rashes or other skin irritations. We chose to ignore pimples because they are common and some organic whitening agents are used professionally to treat pimples. We also ignored reports of being tired and having itchy skin which might warrant specific questions in interviews. The new XRF is more sensitive and could produce a more detailed assessment of dermatitis. The biggest issues with interviews were inaccurate and incomplete data entry. These mistakes may possibly reflect the concentration of mercury in creams. In one subset (n = 72) of the best recorded interviews on use of the 16 creams with detectable mercury, 87.5% of respondents made mistakes in the questionnaire form responses. For those students using creams without mercury (n = 55), only 32.7% made mistakes on the questionnaire form responses. Any conclusion that this might reflect the effects of mercury toxicity might be compromised by students quickly learning from a display that their cream was toxic and having their attention disrupted or intentionally biasing their report.

**Discussion**

Producers of Me One, Ninatop, UCare, Rojzy Jiali, Hua Thu Li, and Qian Mei appear to have stopped using mercury in their skin-whitening creams. Interviews with students using the Thai creams in 2011 indicated that the creams without mercury still whitened skin. Likely a less toxic organic whitening agent had been added or whitening could have reflected use of one of the following white colouring agents: titanium dioxide, zinc oxide, barium oxide and bismuth-oxychloride which were detected (> 1,000 μg/g) in 75% of creams. Evaluation of organic whitening agents that block melanin production like hydroquinone, retinoic acid or betamethasone was not possible in this study. There are up to 50 such organic compounds that can suppress melanin production to whiten skin and full resolution is not practical for developing countries.
Mercury was the only metal in our study that was commonly associated with dermatitis. One Korean face cream with 878 μg/g of cadmium produced dermatitis in three Cambodian users of this cream. This cream was purchased in Korea by a tourist and does not represent most creams in Cambodia. The main concern with the counterfeit Enjoy product was the high concentration of mercury, but strangely two samples of Enjoy had 500 μg/g of Sb while the mean content of lead in Enjoy was 32 μg/g, which is 100-fold and five-fold, respectively, the Canadian guideline.24 The linkage with dermatitis was not assessed in 2015 as the data set was too small in 2015. A subset of individuals will be more sensitive and such responses cannot be assessed in small samples. For example, 10-20% of Americans are reported to be allergic to nickel.25 In general we found much higher levels of metals in creams than a recent study sponsored by the US Food and Drug Administration.29

Further evaluations of dermatitis with respect to arsenic are warranted. Unfortunately, in the larger survey, the XRF analyser was less sensitive than the second XRF analyzer and exceedence of guidelines detected in the second smaller study of arsenic was not evaluated with respect to dermatitis. In 2015, three Thai products (UCare, Ninatop, Me One) and Qian Mei had arsenic levels that were twice the arsenic guidelines, while Rojzy Jiali had arsenic levels that were twice the arsenic guidelines (Table 2). Furthermore, one sample of Rojzy Jiali in 2014 had 86-times the guideline for arsenic. Arsenic can induce reactive oxygen species (ROS) and overproduction of ROS within tissues can damage DNA and promote cancer.30

With respect to ROS generation, two common major ingredients in skin creams, zinc oxide and titanium dioxide, likely have more potential to induce photo-oxidation than trace contaminants. Titanium dioxide and zinc oxides are added to creams to block ultraviolet (UV) rays by physical scattering. Some creams in our earlier analysis contained up to 100,000 μg/g of zinc and 165,000 μg/g of titanium. The guidelines in Canada for both zinc oxide and titanium dioxide are 250,000 μg/g.37,38 The European Union (EU) also allows titanium dioxide at 250,000 μg/g, but currently does not allow zinc oxide.35 At times both zinc oxide and titanium dioxide are also added without dispersants so that a whitening effect is achieved (white coloring, not suppression of melanin production). Titanium dioxide has been shown to induce production of ROS.39,40 Similarly, ROS production has been observed with zinc oxide.41 Recently, because of the fear associated with ROS and cancer, some products containing titanium dioxide were voluntarily removed from stores in California.42 Cosmetic producers have used various materials such as silicon dioxide to coat titanium dioxide, in part to reduce ROS.37,38 However, it is not clear if titanium dioxide in South East Asia is modified or if XRF analysis could detect this difference.

The production of ROS by titanium dioxide might have special relevance to the arsenic zone in Cambodia where more than 100,000 people are at risk of arsenic poisoning.39 The use of titanium dioxide should be evaluated with respect to potentially greater risks in people with added arsenic burden. The same situation with enhanced arsenic exposure and skin cream use exists in Vietnam, Bangladesh, India and other countries. The poorest people do not use skin creams, but some farmers have other jobs and in farming families with money, women may use such creams. Even though in the present study titanium dioxide was not a strong inducer of dermatitis, in the long-term it could have the potential to promote skin cancer in individuals who already have ROS production due to arsenic exposure. Any analysis of titanium dioxide in cosmetic creams in South East Asia should start with clarification of the apparent interference of titanium dioxide by mercury in XRF analysis, resolution of the high variability of titanium in XRF analysis, and assessment of the preparation of nanoparticles of titanium oxide.

**Current Situation**

In 2011, only 15% of Cambodians interviewed knew what mercury was. Informal interviews in 2015 suggest little has changed with regard to mercury awareness. Moreover, some of the potential health effects of mercury remain unresolved. Agusa et al. did not believe that mercury levels measured in Cambodian fish could be the source of the high levels in human hair and that there was an unknown source of mercury.26 If Agusa’s hair data reflected skin cream use, their hair data likely reflected surface contamination, but their blood analyses showed high levels of mercury must reflect bioaccumulation. The observation of estrone enhancement associated with mercury may also indicate a toxic response, i.e. endocrine disruption.26

New problems have also developed. Sampling via the Internet estimated that 6% of skin-lightening products globally contain more than 1,000 μg/g mercury.16 The ability to purchase products on the Internet opens up new opportunities for producers of toxic skin-whitening creams. The chances of buying a counterfeit item on the Internet is high. The situation in Cambodia is similar to that in many developing countries in that counterfeiting of products including face creams is common. A survey of 870 retail outlets found more than half...
had at least one counterfeited article. In 2006, 200 boxes of counterfeit Olay and Dove cosmetics were found in Indonesia. In 2010, seven tons of Cambodian-made fake cosmetics were discovered by the police in Phnom Penh. In 2014, Interpol raided a factory in China producing counterfeit cosmetics with high levels of mercury. Such formal confiscations of counterfeit consumer goods have become more common, but counterfeit products are still available. The potential for such products to be shipped overseas is high. It is simple for bootleggers to create new packaging and is not possible for the average citizen to detect a bootleg product. A website from Minnesota, USA shows “Lemon Herbal” in new packaging and with 10-times higher levels of mercury (33,000 μg/g) than found in the present study: http://www.health.state.mn.us/topics/skin/. Bootlegging of cosmetics is thus a global problem.

Educational Clinic Benefits

The students were very keen to learn about this issue. They often came back with other creams from their family and friends, clearly demonstrating that they had discussed what they had learned with several people. Moreover, most students took pictures of creams with mercury to show their friends and family. With regard to security, operating in a university environment provides some isolation from producers and marketers of creams. Directly interfering with the cosmetic business in public markets might become confrontational. The intent of the present was to provide education, not enforcement. In addition, by processing products bought by students, we avoided the problem of vendors recognizing professional buyers and selling legal products instead of the counterfeit versions. We observed such awareness by vendors on a few occasions. Another benefit to holding the educational clinics at the Don Bosco institutes was it was very easy to get repeat interviews with students for follow-up. In our limited assessment of factory workers, it was very difficult to make follow-up appointments with clients.

Educational Clinic Limitations

There were several limitations to the present study. The students needed greater supervision on their written interviews. A greater number of staff or fewer students may have improved the output. Weak interviews limited interpretation of mercury exposure. Another limitation of the present study involves incomplete sampling of the population. It is possible women working in bars, massage shops and other occupations may be exposed to additional types of contaminated products. The present study was also limited in its ability to detect a number of potential toxins. Using any face cream to whiten skin includes risks from organic chemicals that cannot be rapidly screened using XRF metal analysis. In addition, medical and
laboratory services in Cambodia need further development. Ideally the mercury content of urine or blood would be analyzed shortly after collection. At the time of the present study, rapid analysis was not possible in Cambodia. The advantages of speed are to minimize storage problems and to facilitate data interpretation and health management.

As has been observed with mercury-containing soaps in Tanzania, the hair of users of skin-whitening creams is directly contaminated by surface contact of the cream with hair. Hair analysis is a very attractive technique in that samples can be easily shipped overseas. It is more difficult to ship blood or urine. Cambodia currently lacks the ability to measure metals in blood. In part this reflects political barriers and fears associated with HIV. In theory a few labs could measure metals in blood and urine, but that is not currently the case. In general, laboratories in Cambodia suffer from inadequate facilities, poor training and inadequate funding. For appropriate management of other potential sources of mercury, especially in the oil and gas industry, gold mining, and traditional Chinese medicines, Cambodia needs to improve its analytical capacity.

Cambodia has signed the Minamata Convention and is currently considering ratification of this agreement (http://www.mercuryconvention.org/). If it is ratified, Cambodia will be required to stop production of contaminated skin creams by 2020. Furthermore, the illegal importation of mercury would be halted. As illustrated by producers of Hua Thu Li, Ninatop, Me One, Qian Mei, Rojzy Jiali and Ucare skin-whitening creams, it is certainly possible to adapt manufacturing processes to avoid mercury. However, currently, some Cambodian producers of skin creams still use mercury and bootleggers continues to produce fake creams with mercury.

**Recommendations**

Based on the results of the present study, we recommend that future studies include specific questions in interviews on rashes, colored skin patches, itchy skin, headaches, and tiredness and that interviews be closely overseen. Data from groups that can be interviewed a second time are more useful for assessing relationships between mercury exposure and mercury bioaccumulation in urine and blood. Assessments of simple health indicators, such as hemoglobin/complete blood count (CBC) analysis would also be useful. Evaluations of mercury in skin creams should be conducted in as many regions of Cambodia as possible to develop a national database on mercury use in skin creams.

In addition, efforts should be made to provide education on the health risks of unnaturally whitening skin in pursuit of an artificial social construct of beauty. A lot of money is spent on cosmetics and the health risks of using contaminated products are very serious.

**Conclusions**

Although several cream producers in Asia appear to have removed mercury from their creams, mercury remains the metal of greatest concern in skin creams. Mercury remains a common problem in bootleg skin whitening creams and is commonly added to creams that are produced in Cambodia. Mercury is the metal most likely to induce a skin rash, and 27% of users of creams with high mercury content (> 1,000 μg/g) reported developing a rash. Use of XRF analysis allows for rapid screening of mercury in cosmetics and enables decisive police actions that could stop the import, export and sales of skin creams containing mercury.

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