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Large-scale mercury exposure due to a cream cosmetic: community-wide case series

大規模因使用美顏霜而接觸水銀的社區層面個案系列

Objective. To describe demographic characteristics, patterns of use, reported symptoms, and laboratory results associated with mercury exposure among people who used a beauty cream containing mercury.
Design. Descriptive study of a case series.
Setting. The Hong Kong community.
Participants. Users of a cream cosmetic who contacted the Department of Health following a public announcement.
Main outcome measures. Urine and blood mercury concentrations, cream mercury content, self-reported symptoms, duration of cream use, and duration since last cream use.
Results. We interviewed 314 cream users, 99% of whom were women. The mean urine and blood mercury concentrations of 286 users, who submitted a urine or blood sample, were 45.2 μg/L (reference level, <20 μg/L) and 17.1 μg/L (reference level, <10 μg/L), respectively; 65% of these participants had elevated mercury concentrations. The mercury content of the cream cosmetic ranged from 660 to 57 000 ppm. Seventy-eight percent of all cream users reported no symptoms, but absence of symptoms was not predictive of low urine and blood mercury concentrations. Urine mercury concentrations were significantly higher among people who last used the cream within 45 days. Blood mercury concentrations were elevated following cream use for as short as 2 days.
Conclusions. The majority of cream users had increased urine or blood mercury concentrations but remained asymptomatic, implying that the incidence of overt symptomatic mercury poisoning resulting from dermal application of creams with mercury content lower than 57 000 ppm is low. Doctors should take a history of the use of cosmetics if patients have clinical or laboratory evidence of mercury exposure; such cases should be reported to public health authorities.

目的：描述在一宗多人使用含水銀的美顏霜事件中，使用者的特徵、使用情況、所報告的病徵及化驗結果。
設計：個案系列的描述性研究。
安排：香港社區。
參與者：曾使用該美顏霜，並在衛生署公佈事件後接觸署方的人士。
主要結果測量：尿液及血液水銀濃度、該美顏霜的水銀含量、使用者自行報告的病徵、使用時間長短，及與最後一次使用該美顏霜的時間距離。
結果：訪問了314名曾使用該美顏霜的人士，當中99%為女性。其中286名提交尿液及血液樣本者，其平均尿液及血液的水銀濃度分別為45.2 μg/L(參考值: <20 μg/L)及 17.1 μg/L(參考值: <10 μg/L)；其中 65% 的人士體內水銀濃度過高。該美顏霜的水銀含量則為660-57 000 ppm。78%的美顏霜使用者表示沒有病徵，但病徵與尿液及血液水銀濃度的關係並不明顯。在45天內曾使用有關美顏霜的人士，其尿液水銀濃度明顯較高。在曾使用該美顏霜的人士中，血液的水銀濃度亦見上升，而他們最短的使用時間只為兩天。
結論：大部份曾使用該美顏霜者，其尿液或血液水銀濃度均有所上升，但他們並無病徵；顯示於皮膚接觸水銀含量低於57 000 ppm的美顏霜，而表現明顯水銀中毒病徵的機會不高。醫生當遇到臨床或化驗結果顯示曾接觸水銀的病人時，應查詢病人使用美容產品的資料，並將有關個案呈報公共衛生部門。

Key words:
Cosmetics/adverse effects;
Female;
Mercury poisoning

關鍵詞：
美容產品 / 副作用；
女性；
水銀中毒

Hong Kong Med J 2003;9:329-34

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Introduction

Historically, inorganic mercury compounds such as mercury chloride have been used in cosmetic preparations for their purported skin-lightening effect.[1,2] Mercury in such preparations can enter the human body by skin absorption.[3-5] Their use has been associated with renal,[6,7] neurological,[8,9] and dermal[8,10] toxicity. Inorganic mercury is partly cleared from the human body by renal excretion.[11] The reported half-life of mercury is approximately 4 days in the blood and 40 to 60 days in the urine.[12-16] Reports of large-scale mercury exposure associated with the use of cream cosmetics are uncommon in the medical literature,[5,9,17,18] and such exposure has not been documented previously in Hong Kong.

In December 2001, the Department of Health of the Hong Kong Special Administrative Region Government received a report of mercury poisoning from a local hospital. The patient was a 32-year-old female domestic helper with good past health. In November 2001, she had noticed bilateral ankle swelling. When she was admitted to hospital, her 24-hour urine sample contained 7.74 g of protein. Renal biopsy showed minimal-change glomerulopathy. No neurological deficit was evident. A blood test for heavy metals showed a mercury concentration of 48.6 μg/L (reference level for follow-up, <10 μg/L [<50 nmol/L]). Chelation therapy with penicillamine was given, and her blood mercury level returned to our reference level by December 2001.

The Department of Health investigated possible sources of mercury exposure in this patient. She reported eating fish three to four times a week and denied having been exposed to herbal medicines, insecticides, or broken mercury-thermometers or other mercury-containing devices. No mercury was detected in indoor air samples taken from her residence. However, she reported using a beauty cream that she had bought from a hawker for skin whitening. From August to November 2001, she had applied the cream to her face once daily. The bottle of cream that she had used was tested at the Government Laboratory and found to contain mercury at 34 292 parts per million (ppm) by weight. No mercury-containing compound was listed on the packaging.

The Department of Health referred the case to the Customs and Excise Department, which seized 14 bottles of the cream and traced them to a single supplier. All bottles of the seized cream were found to contain mercury ranging from 7000 to 21 000 ppm. A search of approximately 100 major cosmetic outlets did not find the cream on sale. According to the package insert, the product was manufactured in mainland China, but no additional information was available about whether the bottles of cream had come from the same batch. On 4 January 2002, the Department of Health held a press conference and warned the public not to use the cream cosmetic. A telephone hotline and free doctor consultations were set up; doctors in Hong Kong were also informed to refer possible cases to the Department of Health.

On the basis of interviews and laboratory test results of cream users, this report describes the extent and pattern of use of the particular brand of cream cosmetic, reported health effects, mercury content of cream samples and of blood and urine collected from users.

Methods

To determine the extent of use of the particular cream cosmetic in Hong Kong, we set up a telephone hotline between 4 and 19 January 2002 and publicised it through television, radio, and newspapers. The hotline was staffed daily between 9:00 am and 9:00 pm (including weekends), and message recording was available during the remaining 12 hours of the day. People who have left messages were called back by department staff for follow-up. We arranged free doctor consultations at the regional offices of the Department of Health for callers who reported having used the cream any time during the past 180 days before the public announcement, and also for cream users who were anxious about their health. To determine the pattern of cream use and possible health effects, we used a standard questionnaire to collect demographic data of cream users, periods of cream use, and current signs and symptoms that might be related to mercury poisoning. Nurses trained in public health performed the interviews before medical examination by Government doctors. We also sent letters to all doctors registered with the Medical Council of Hong Kong asking them to report to the Department of Health any patients they encountered who had used that cream.

During the doctor consultations, attendees were asked to give a urine sample. A blood sample was also collected from those who reported using the cream during the past 14 days. Twenty-one cream samples were selected randomly from the 117 samples collected and sent for laboratory testing. All urine, blood, and cream samples were analysed for mercury at the Government Laboratory using inductively coupled plasma mass spectrometry. We referred patients to hospital or specialist out-patient clinics if they were pregnant, showed signs of renal disease, or had an elevated mercury concentration in the blood or urine.

We used two-tailed independent-sample Student's *t* tests to compare the geometric mean levels of mercury in the blood and urine between different groups of cream users. We derived Pearson's correlation coefficients between logarithm-transformed mercury concentrations and duration of cream use, and duration since last cream use. The cut-off P value for statistical significance was taken as 0.05.

Results

We received 971 telephone calls during the phone-in period. Among the calls, 138 were received during the initial 3 days;

calls peaked on day 4 (208 calls), the first Monday after the public announcement. A total of 724 (75%) calls were received during the first week. One referral was received from hospital.

A total of 332 callers fulfilled the criteria for doctor consultations. The median age of the 314 people who attended the special consultations was 35 years (range, 15-76 years). All but one were female. Unskilled or semi-skilled workers (including domestic helpers) and homemakers accounted for 193 (61%) and 78 (25%) of the attendees, respectively.

The frequency, duration, and manner of cream application varied according to the preference of individual cream users. Of the 314 interviewees, 95 (30%) used the cream until they learned about our public announcement. Almost two thirds last used the cream within 90 days before the public announcement (Table 1). Four in 10 had been using the cream for 90 days or less, and more than one in 10 had been using it for about half a year or more. The main reason for cream use was to eliminate freckles.

Seventy-eight percent of the cream users reported no symptoms. Self-reported symptoms in descending order of prevalence were headache (12%), insomnia (9%), memory loss (5%), irritability (5%), abdominal discomfort (3%), nervousness (2%), joint pain (2%), weakness (2%), nausea (2%), and hand tremor (1%). No tingling and burning sensations or metallic taste were reported. No attendees had signs of renal disease or neurological deficit on physical examination.

A total of 282 urine samples and 183 blood samples from 286 cream users were sent for laboratory analysis (28 interviewees did not or refused to give samples). Among them, 154 (55%) urine samples and 119 (65%) blood samples had mercury concentrations that exceeded the upper limit of the reference range (<20 μg/L for urine and <10 μg/L for blood). One hundred and eighty-five (65%) of the 286 cream users who submitted clinical specimens showed elevated mercury levels in either blood or urine. The mercury content of the 21 selected cream samples ranged from 660 to 57 000 ppm (median, 22 000 ppm).

Table 1. Duration since last use of a mercury-containing cream cosmetic, duration of use, and indications among 314 users

	No. (%)
Duration since last use	
≤90 days	202 (64)
91-180 days	24 (8)
>180 days	20 (6)
Unsure/did not know	68 (22)
Duration of use	
≤90 days	127 (40)
91-180 days	65 (21)
>180 days	41 (13)
Unsure/did not know	81 (26)
Indications	
Freckles	189 (60)
Acne	39 (12)
Wrinkles	2 (1)
Others (including skin whitening)	84 (27)

The distributions of blood and urine mercury levels were right-skewed (Figs 1 and 2). However, after logarithmic transformation, the distribution was approximately normal. The mean and median urine mercury levels were 45.2 μg/L (standard deviation [SD], 71.7 μg/L) and 23.0 μg/L, respectively. The mean and median blood mercury levels were 17.1 μg/L (SD, 13.8 μg/L) and 13.0 μg/L, respectively. The highest recorded urine and blood concentrations were 720 μg/L and 82 μg/L, respectively.

Attendees whose duration since last cream use was 45 days or less (one half-life of inorganic mercury in urine) had significantly higher mercury levels in the urine than those whose duration since last cream use was at least 46 days (Table 2). Furthermore, attendees whose duration since last cream use was 4 days or less (one half-life of inorganic mercury in blood) had a significantly higher mercury level in the blood and urine than those whose duration since last

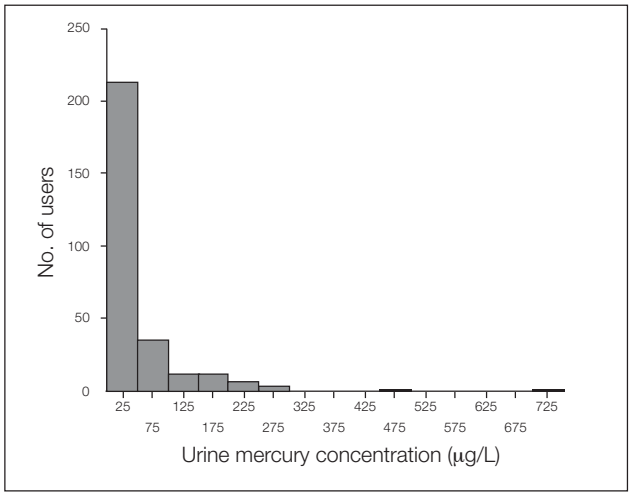

Fig 1. Distribution of urine mercury concentrations among 282 cream users who submitted urine samples

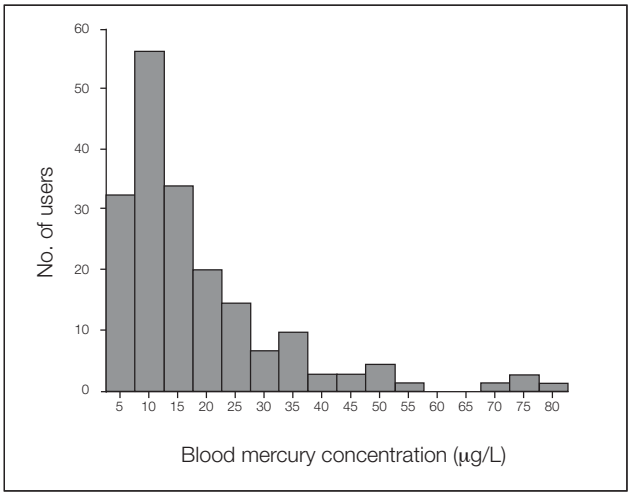

Fig 2. Distribution of blood mercury concentrations among 183 cream users who submitted blood samples

Table 2. Urine and blood mercury concentrations, by duration since last use, duration of use, cream mercury content, and presence of self-reported symptoms

	Geometric mean level in urine (μg/L)	Geometric mean level in blood (μg/L)
Duration since last use		
≤45 days	26.6	13.1
>45 days	9.7	11.3
t-statistic (P value)	4.91 (<0.01)	0.40 (0.69)
Duration since last use		
≤4 days	34.4	15.3
>4 days	18.0	12.0
t-statistic (P value)	3.08 (<0.01)	2.06 (0.04)
Duration of use (in recent users)		
≤90 days	21.1	13.4
>90 days	45.3	14.5
t-statistic (P value)	-2.99 (<0.01)	-0.54 (0.59)
Cream mercury content (ppm)		
≤10 000	13.7	7.2
>10 000	20.3	20.6
t-statistic (P value)	-0.56 (0.58)	-2.37 (0.03)
Any reported symptom		
Yes	15.8	12.1
No	19.7	13.4
t-statistic (P value)	-1.09 (0.28)	-0.77 (0.44)

cream use was at least 5 days. Among recent users whose duration since last cream use was a week or less, those who had used the cream for at least 91 days had a significantly higher mercury level in the urine than those who had used it for 90 days or less. Cream users whose cream mercury content exceeded 10 000 ppm had a significantly higher blood mercury level than those whose cream mercury content was 10 000 ppm or less. There was no significant difference in urine or blood mercury levels between cream users who reported any symptom and those who reported no symptoms. The blood mercury level was elevated in five patients who used the cream for less than 10 days, the shortest duration being 2 days. All these five patients last used the cream within 15 days.

Correlation between log values of the blood and urine mercury levels was significant (r=0.30; P<0.01) [Fig 3]. A significant negative correlation was found between the log of the urine mercury content and duration since last cream use (r= –0.29; P<0.01) [Fig 4]. Among recent users whose duration since last cream use was 1 week or less, the log of the urine mercury content was found to correlate positively with duration of cream use (r=0.28; P=0.01) [Fig 5]. However, no significant correlation existed between the log of the blood mercury concentration and the duration since last cream use (r= –0.08; P=0.322) or the duration of cream use among recent users (r=0.03; P=0.808).

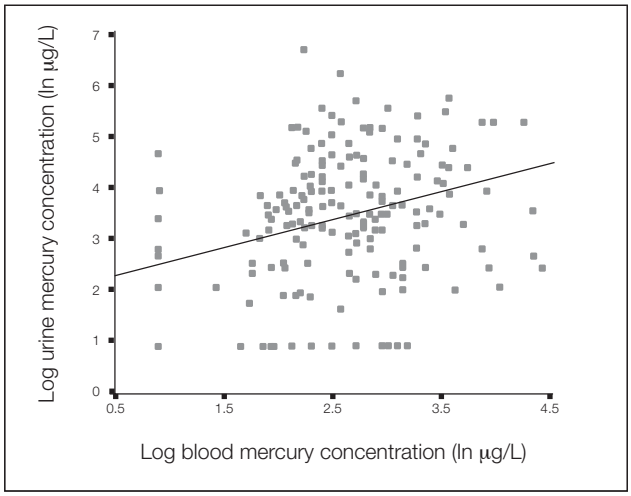

Fig 3. Scatter plot of the log urine mercury concentration versus log blood mercury concentration

Twenty-six cream users were referred to hospitals and another 155 to specialist clinics. Two of them were referred because of pregnancy, whereas the others were referred because of their high body mercury levels. All patients were discharged home uneventfully.

Discussion

This is the first documented case of large-scale mercury exposure due to a beauty cream sold in Hong Kong. A total of 185 cream users (65% of those tested) were found to have elevated mercury levels, with the highest urine and blood concentrations reaching 720 μg/L and 82 μg/L, respectively. Elevated blood mercury levels resulted from cream use for as short as 2 days. These data indicate that mercury can be readily absorbed through dermal application of a cream cosmetic.

In this investigation, we reached out to cream users through a wide variety of channels, including a press conference, the mass media, a telephone hotline, and letters to doctors. We prevented further mercury exposures in 95 current cream users who called the telephone hotline, and probably many more who heeded the public announcement but did not call. Sending letters to doctors seemed less effective in identifying cream users; nevertheless, this exercise may have been important in raising awareness in the medical community. We believe this combination of strategies provides a reasonably effective surveillance mechanism and protection against further exposure.

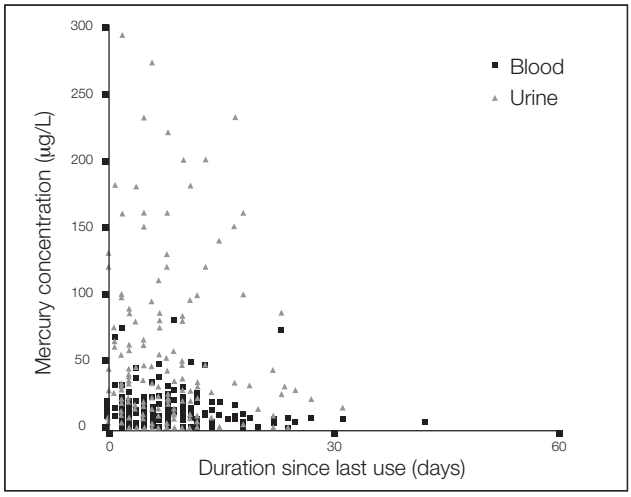

Fig 4. Scatter plot of urine and blood mercury concentrations versus duration since last cream use

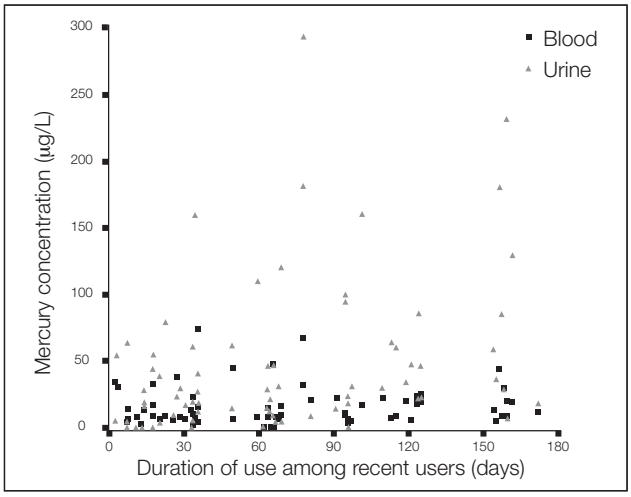

Fig 5. Scatter plot of urine and blood mercury concentrations versus duration of cream use among recent users

The prevalence of self-reported symptoms in this incident is substantially lower than an outbreak of mercury poisoning in the United States associated with the use of a Mexican beauty cream.[17] Among the 330 people who had used that cream, the prevalence of symptoms associated with mercury poisoning was high: fatigue (67%), nervousness or irritability (63%), severe headaches (61%), insomnia (51%), memory loss (44%), loss of leg strength (44%), tingling or burning sensations (39%), tremors or shaking of the hands (38%), depression (31%), and a metallic taste in the mouth (20%). The difference may be because of a lower level of mercury intoxication among our case series, as reflected by their lower mean urine mercury level (45.2 μg/L), compared with that in the United States report (146.7 μg/L)[17]; the cream mercury content in our series also appears to be lower (660-57 000 ppm versus 60 000-100 000 ppm).[17]

Despite the high number of cream users in our case series with elevated mercury levels in the body, none had clinical features clearly attributable to mercury poisoning, except the index patient who had nephrotic syndrome. Of the 314 cream users whom we interviewed, at least 106 had used the cream for 3 months or more—long enough for the effects of mercury poisoning to become visible.[19] Our study implies that the incidence of overt symptomatic mercury poisoning resulting from dermal application of creams containing less than 57 000 ppm of mercury is low—probably less than 1%. However, subtle symptoms such as insomnia or memory loss, especially when occurring in isolation, are more difficult to ascertain if they are due to mercury poisoning.

We find that urine and blood levels of mercury correlate poorly with self-reported symptoms among cream users. This result is consistent with those from previous reports showing that mercury levels in blood and urine generally do not relate well to clinical and neurological findings.[20,21] Thus, when doctors encounter patients with mercury exposures, absence of symptoms is not a reason for not taking urine or blood specimens for laboratory confirmation.

Our results conform to the known pharmacokinetics of inorganic mercury. Consistent relationships were shown between the urine level of mercury and the duration of cream use, and the duration since last cream use. Our findings indicate that the urine concentration of mercury is a better indicator of medium- to long-term exposure, whereas the level in the blood is useful to detect recent exposure.[11] Furthermore, in managing public health incidents of mercury exposure due to cosmetic creams, measuring the level of mercury in the urine may give better information than measuring the level in the blood, and the former is probably sufficient on its own.

The safety of consumer products sold in Hong Kong is governed by the Consumer Goods Safety Ordinance. It is the duty of manufacturers, importers, and suppliers to ensure that the consumer goods they supply are reasonably safe.[22] The Hygiene Standards for Cosmetics of the National Standard of the People's Republic of China prescribes an upper limit of 1 ppm for mercury in cosmetic products. In this incident, the supplier of the cream was prosecuted and fined HK$3000. In the year 2001, more than 300 checks on the safety of beauty products in the market were conducted by the Customs and Excise Department. However, such checks are not foolproof, especially when the product in question is not distributed through conventional channels. In this incident, the cream was not sold at major cosmetic outlets in Hong Kong; yet, hundreds of people still had access to it through hawkers. This study highlights the need to educate the public not to buy cosmetic products from questionable sources. There is currently no legislation requiring the labelling of contents of beauty products in Hong Kong. The usefulness of compulsory labelling would probably depend on the degree it could be effectively enforced.

Interpretation of data in this study should take into account some design limitations. It is possible that some interviewees who were anxious to be tested might have

overstated their extent and duration of cream use. The true prevalence of cream users with high urine or blood mercury levels may be lower than that observed in the study, because some people who had used the cream sparingly might not have called the telephone hotline. The effect of the cream in causing elevated levels of mercury in the body may also have been slightly overestimated, because we did not investigate exposure from other sources (eg fish, herbs, and occupational exposure). A control group would have been useful in better estimating the effect of the cream on body mercury concentrations. Owing to the emergency situation and practical difficulties, we collected only spot urine specimens rather than performing 24-hour urinalysis, and urine mercury was not adjusted for urine creatinine clearance. Nonetheless, measuring spot urine mercury concentrations has been found to correlate well with that of 24-hour urine,[23] and it is considered adequate for this kind of investigation.[24]

Doctors play an important role in a coordinated public health response involving a large number of people exposed to a mercury source. When encountering patients (especially young women) with clinical and laboratory evidence of mercury exposure, doctors should take a history of their use of cosmetics. Such cases should be referred to public health authorities immediately because of their public health implications. Doctors can also educate patients about harmful health effects from mercury-containing cosmetics. Effective management of such incidents requires a close working relationship between doctors in the hospital, primary care, and public health sectors.

Conclusion

This is the first documented large-scale mercury exposure related to a beauty cream sold in Hong Kong. The majority of cream users had increased urine or blood mercury levels but remained asymptomatic. A coordinated public health response is required to manage patients exposed to mercury from cosmetics and to stop further exposures. Doctors should consider a history of cosmetic use when seeing patients with clinical or laboratory evidence of mercury exposure. Such cases should be promptly reported to public health authorities.

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