ORIGINAL ARTICLE

Mercury exposure: the experience of the Hong Kong Poison Information Centre

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Objectives To review the characteristics of the consultation about the management of mercury exposure and identify the controversial issues on the clinical management of individuals with a history of mercury exposure.

Design Descriptive case series.

Setting Hong Kong Poison Information Centre, Hong Kong.

Participants Persons consulting the Hong Kong Poison Information Centre about individuals with possible or definitive mercury exposure.

Main outcome measures Characteristics of the consultations, including: the demographics of affected individuals, source and reason for the consultation, tissue mercury levels, the source of mercury exposure, specific intervention if any, and clinical outcomes.

Results Forty-one consultations were analysed. Most consultations were from the public sector. Reasons of the consultation were very variable. Individuals with abnormal tissue mercury levels were uncommon. There was only one case of acute mercury poisoning. The majority of identified individuals were not subjected to specific interventions. Chelation therapy was given to three patients, but in one of them it was considered to be contra-indicated.

Conclusion The management of mercury exposure is highly variable. Recommendations were made on the approach to an individual with potential mercury exposure or poisoning.

New knowledge added by this study

- Although mercury exposure is ubiquitous, acute mercury poisoning is uncommon.
- Local clinical practice for managing individuals with mercury exposure is very variable. Some practices are not evidence-based.

Implications for clinical practice or policy

- Evidence-based reference guidelines on mercury exposure management should be made available to health professionals.
- Use of chelating agents in diagnosis of mercury poisoning is not recommended; their use in treatment requires balancing of risks and benefits.

Introduction

Mercury (Hg) exists in three forms: the metallic element, inorganic salts, and organic compounds. The source, biological properties, and toxicity between these three forms differ. Elemental Hg is in liquid state at room temperature. The common route of exposure is through inhalation of its vapour. Inorganic Hg occurs as mercurous (Hg^{+}) or mercuric (Hg^{2+}) salts, and can be absorbed through the gastro-intestinal tract or skin. Organic Hg may exist as aryl, long-chain or short-chain forms. Methylmercury is the most important as it is the prevalent form in the environment. Most organic Hg compounds can be absorbed through the gastro-intestinal tract, respiratory tract, or skin.

In Hong Kong, the general public is exposed to Hg in different ways. Important modes include the consumption of predatory fish, the application of Hg-containing cosmetic creams and the intake of contaminated herbs used in traditional Chinese medicine. In fact, Hg exposure is an important public health issue. In 2003, there was a report of 185 citizens with elevated Hg level in either blood, urine, or both after the topical application of a contaminated beauty cream.[1] Although no significant toxicity occurred in all but one those exposed, constant surveillance is essential to prevent further outbreaks. Since its establishment in 2005, the Hong Kong Poison Information Centre

Key words
Mercury poisoning; Metals, heavy

Hong Kong Med J 2011;17:292-6

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(HKPIC) has been responsible for providing poison information and management advice on poisoned patients to health professionals. From time to time, the HKPIC is consulted about the management of individuals with Hg exposure or suspected Hg poisoning. The objectives of this study were to review the characteristics of the consultations about the management of Hg exposure and identify the controversial issues about the clinical management of individuals with a history of Hg exposure.

汞暴露：香港中毒諮詢中心的經驗

目的 回顧汞暴露個案的特點，以及探討對於汞暴露人士一些具爭議性的臨床治療方案。

設計 描述性病例系列。

安排 香港中毒諮詢中心。

參與者 到香港中毒諮詢中心求診的懷疑及確診汞暴露人士。

主要結果測量 求診者的特徵，包括其人口學資料、求診原因及轉介者、組織汞水平、汞接觸史、具體的介入治療（如有的話）和臨床結果。

結果 本文共分析了41宗個案。大部分個案由公立醫院轉介，求診原因各有不同。求診者的組織汞水平出現異常的情況很罕見，只有一宗出現急性汞中毒。大部分個案都沒有具體的介入治療。有三名病人接受螯合療法，其中一名病人出現禁忌反應。

結論 處理汞暴露有多種不同的方法。應對每個不同的汞暴露或汞中毒的懷疑個案按個別需要提出相應的建議。

Methods

This study was retrospective. Consultations made to HKPIC between 2005 and 2009 about Hg exposure or poisoning were reviewed. The HKPIC records, supplemented by records retrieved from the clinical management system of the Hospital Authority where applicable, were traced. Data on patients' age, gender, reasons for initiating measurement of Hg levels or consultations, the source of the consultation (private or public sector), available tissue Hg levels, the possible source of Hg exposure, as well as specific interventions and patient outcomes were collected. A blood level greater than 77 nmol/L was considered abnormal. This was based on the reference range set by the laboratory of the Prince of Wales Hospital, Hong Kong, which had actually been adopted from studies of the local population without industrial exposure. A urine level greater than 50 nmol/day was considered abnormal, which was based on studies of unexposed individuals.[2] Descriptive statistics were used for data analysis.

Results

From 2005 to 2009, the HKPIC received 41 consultations on the management of Hg exposure. Of these, 19 subjects were male and 22 female, their mean age was 37 (range, 2-77) years. Regarding these consultations, 39% were from the private sector. Blood levels were obtained in 31 subjects, while urine levels were checked in 17. Among those who had Hg levels measured, 11 (35%) had abnormal blood levels and four (24%) had abnormal urine levels. Among the 20 subjects with 'normal' blood Hg levels, the levels ranged from <5 to 75 nmol/L. Chelation therapy was given to three patients. In one of them, the attending physician had initiated such treatment contrary to the advice of the HKPIC. For the remaining subjects, no specific treatment, besides advice on reducing exposure, was implemented. In 12 subjects (10 from the private sector), outcomes were unknown. The remaining two patients refused further care from Hospital Authority clinics. As for outcomes in the other 29 patients, 11 had symptoms judged not to be related to Hg poisoning or exposure, 17 had Hg exposure but were either asymptomatic or had unrelated symptoms. One patient, who ingested mercurochrome, presented with acute Hg poisoning. One patient died of an unrelated cause (Table 1).

The reasons for initiating Hg measurements or consultations were variable (Table 2). Neurological

TABLE 1. Characteristics of the 41 consultations

Characteristic	Data
Age (years)	
Mean	37
Range	2-77
Gender	
Male	19 (46%)
Female	22 (54%)
Source of consultation	
Private sector	16 (39%)
Public sector	25 (61%)
Mercury (Hg) measurement	
Subjects with blood level determined	31 (76%)
Range of blood Hg levels (nmol/L)	5-395
Subjects with urinary level determined	17 (41%)
Range of urine Hg levels (nmol/day)	0-609
Subjects with abnormal blood levels	11 (35%)
Range (mean) of abnormal blood Hg levels (nmol/L)	78-395 (137.7)
Subjects with abnormal urine excretion	4 (24%)
Range (mean) of abnormal urinary Hg excretion (nmol/day)	383-609 (509.8)
Outcome	
Unknown	12 (29%)
Non-exposure with alternative diagnosis	11 (27%)
Hg exposure without symptoms or with unrelated symptoms	17 (42%)
Hg poisoning	1 (2%)
Fatality (unrelated to mercury)	1 (2%)
Chelation therapy	3 (7%)

symptoms accounted for the majority. Not all had an identifiable source of Hg exposure. A broken thermometer was identified as the source in eight subjects (Table 3).

Discussion

This study showed that individuals of any age could be affected by Hg, which is not surprising as it is ubiquitous in the environment. However, Hg exposure is not equivalent to Hg toxicity. To determine whether an individual is at risk of Hg toxicity, the clinician should take note of the presenting symptoms, exposure history, and Hg levels in the body. According to the findings listed in Table 2, the presenting symptoms of some of the subjects did not warrant an investigation for Hg toxicity. The typical toxic manifestations of the three forms of Hg are shown in Table 4.[3] Subjects with headache, non-specific dizziness, generalised discomfort, insomnia, anxiety or short stature were probably not suitable for Hg testing. Of particular note is the relationship of Hg with autism. A paper by Wakefield et al[4] published on *Lancet* in 1998 first postulated a possible link between autism and vaccines (containing thimerosal, ie ethylmercury). Other investigators have also hypothesised that autism was a form of Hg poisoning,[5] but this postulation was not supported by subsequent studies. For instance, a local study did not find any difference in blood Hg level in children with or without autism.[6] Indeed, the original paper by Wakefield et al[4] was retracted by the *Lancet* as several claims of authors' claims were found to be false. Thus, autism should not be considered an indication for Hg testing.

A detailed exposure history is essential to determine whether an alleged exposure is significant or a certain symptom is related to Hg. The common sources of exposure for the three forms of Hg are shown in Table 5.[3] In the 41 subjects we reviewed, eight were exposed from a broken thermometer. Thermometers contain small amounts of elemental Hg. If ingested, elemental Hg is poorly absorbed via the gastro-intestinal tract.[7] Therefore, patients who have ingested Hg from a broken thermometer are not at risk of Hg poisoning, but may be susceptible to gastro-intestinal tract injury from sharp fragments of broken glass. In six cases, seafood, especially fish, was believed to be the source of Hg exposure. Predatory fish, like sharks, swordfish and marlin, may accumulate high levels of methylmercury in their body tissues. Most of the fish available in Hong Kong contain low levels of methylmercury while certain types, eg alfonsino and tuna, may contain higher levels.[8] In an analysis of 280 samples of fish available in Hong Kong conducted by the Centre for Food Safety in 2007, the median total Hg and methylmercury levels were 63 μg/kg and 48 μg/kg, respectively. In three samples of alfonsino, however, the methylmercury level was over 500 μg/kg.[9] In general, while continuous and heavy consumption of predatory fish is not advised, a well-balanced diet and intake of moderate quantity of fish consistent with a healthy diet is recommended. In another eight cases, exposure was possibly through the use of cosmetic creams or herbs. Contaminated cosmetic creams may contain up to 40 000 times the allowed quantities of Hg designated by a national standards agency.[8] As for herbal medicines, not uncommonly they contain heavy metals, including Hg.[10] Their presence may be due to adulteration during manufacture or deliberately added to enhance their alleged therapeutic properties. For example, Hg is used in preparations with cinnabaris (mercury sulphide) or calomelas (mercury chloride). They may be used to treat nervousness, epilepsy, ulcers, or insomnia. Dental amalgam was a suspected source of Hg in three cases. Amalgam contains elemental Hg and other metals, and has been used in dentistry for over a century. Exposure is through inhalation of Hg vapour. Despite claims that it might lead to

TABLE 2. Reasons for initiating mercury measurement or consultation

Reason	No. (%)
Neurological symptoms including limb paraesthesia, memory loss, chronic vertigo, chronic headache, Guillain-Barré syndrome, non-specific dizziness, developmental delay, encephalopathy, and tremulousness	18 (44)
Psychiatric symptoms including insomnia, anxiety, personality change, autism, and depression	5 (12)
Renal problems including urinary frequency and nephrotic syndrome	4 (10)
Dermatological symptoms including skin rash and dermatitis	2 (5)
Gastro-intestinal symptoms including deranged liver function	1 (2)
Haematological problem including anaemia	1 (2)
Mercury exposure suggested by a history of: ingestion of mercurochrome, contact with mercury from broken thermometer, ingestion of inner coating of a vacuum flask, and post anti–tetanus toxoid injection	11 (27)
Miscellaneous including: heard from news about mercury toxicity, short stature, angioedema after chelation treatment by private doctor, generalised non-specific discomfort, and malaise	8 (20)

TABLE 3. Possible source of mercury exposure

Source of mercury exposure	No. (%)
Thermometer	8 (20)
Seafood	6 (15)
Herbs	4 (10)
Cosmetic creams	4 (10)
Occupation	3 (7)
Dental amalgam	3 (7)
Mercurochrome	1 (2)
Anti–tetanus toxoid	1 (2)
Unknown or no identifiable source	11 (27)

TABLE 4. Clinical manifestations of mercury toxicity[3]

	Acute exposure	Chronic or subacute exposure
Elemental mercury	Dyspnoea, cough or chest pain signifying pneumonitis, bronchiolitis, pulmonary oedema or frank respiratory failure, pruritic rash, conjunctivitis, gingivitis or stomatitis	Classic triad of tremor, gingivitis, and erethism
Inorganic mercury	Caustic gastroenteric symptoms like abdominal pain and bleeding; and renal impairment, if severe enough, acute renal failure	Kidneys (proteinuria or nephritic syndrome), nervous system (tremor, neurasthenia, erethism, neuropathy, ataxia, tunnel vision, anosmia), digestive tract (nausea, gingivostomatitis), skin (acrodynia)
Organic mercury (especially methylmercury)	Malaise, paraesthesia, ataxia and impaired visual, auditory, olfactory and gustatory senses	Peripheral neuropathy

cognitive changes like memory loss, there is no convincing evidence that dental amalgam can affect health.[11,12] Removal of existing amalgams without a good dental indication is also not advised, as this would temporarily raise blood Hg levels through inhaling more vapour. In one instance, the HKPIC was consulted for possibly Hg exposure after anti-tetanus toxoid (ATT). The subject was a Caucasian and attended the emergency department for a wound and ATT was given. He argued that he might be exposed to Hg because of ATT and demanded a second opinion. Thimerosal (ethylmercury) has been used as a preservative in vaccines for a long time, and the ATT used in Hong Kong was no exception. According to the World Health Organization, it is safe to use vaccines containing thimerosal[13]; the risk of not receiving the vaccines far outweighs the risk of Hg exposure from the vaccine. Another case involved an adolescent who ingested mercurochrome during a suicidal attempt. Mercurochrome has long been used as an antiseptic for its bacteriostatic effect conferred by mebromin, which is an organomercuric disodium salt that behaves like inorganic Hg. Ingestion of large amounts of mercurochrome can result in Hg poisoning.

If Hg poisoning or significant exposure is suspected, the level should be checked. In this series, the blood level was the most common measurement employed. For those who had undergone measurement of body Hg level, only a minority had abnormally high levels. For the remainder who had 'normal' levels, the presence of Hg in blood or urine reflects background exposure, presumably from eating fish. It is often recommended that abstinence of fish consumption 1 to 2 weeks before Hg measurements may reflect the extent of tissue Hg exposure more accurately. Mercury can be detected by analysis of hair, blood, or urine. However, because it is prone to contamination, hair analysis is not recommended for the diagnosis of Hg exposure,[14] whilst the validity of the test is also questionable. Instead, measuring blood or urine concentrations is preferred. For elemental or inorganic Hg, blood levels reflect acute exposure, as its half-life in blood is relatively short. In general, urine levels can be used as a reflection of recent or chronic exposure.

TABLE 5. Some sources of mercury exposure[3]

Reason	Examples
Elemental mercury	Thermometers, barometers, sphygmomanometers, dental amalgams, gold-mining industry
Inorganic mercury	Antiseptics, whitening creams, Chinese herbs, mercury batteries, paint industries
Organic mercury	Fish, biocides, vaccines

Measurement of Hg in a 24-hour urine sample is better than obtaining the level in a spot urine sample, because the latter is affected by hydration status and the type of food taken. For organic Hg, the whole blood Hg level is the preferred measurement, as it is primarily excreted in the faeces and not through the kidneys. A high level in blood or urine may not correlate with clinical toxicity as Hg may be concentrated in various tissue compartments. Two subjects in our series underwent a post-chelation urine test for heavy metals. One was referred for raised urinary Hg post-chelation and another developed an allergic reaction to the chelating agent. This method of diagnosing Hg or other heavy metal toxicity is also open to misinterpretation and danger.[15] First, there is no scientifically validated reference range for this kind of test. Second, very often the analysis is performed soon after administration of the chelating agent, which often leads to erroneously high concentrations in urine. Serious reactions may ensue, as in one of our cases, and even fatality has been reported.[16] As a result, post-chelation or post-provocation urine testing is not recommended. One subject in our series had autism, and was referred with a suspicion of Hg toxicity because of an elevated urinary precoproporphyrin level detected in an overseas laboratory. The urine porphyrin profile has been used as a marker of Hg exposure in the conduct of population research and occupational monitoring. Its usefulness for individual patient management is doubtful, as the test is non-specific and a raised level can result from exposure to other metals. Also, there is no clinically useful reference range for Hg poisoning.

Acute Hg poisoning is rarely encountered. It was reported after inorganic Hg salt ingestion or elemental Hg vapour inhalation. Acute toxicity

requires standard resuscitative measures and if indicated, gut decontamination with activated charcoal administration or whole bowel irrigation. Mercury poisoning resulting from long-term Hg exposure is the commoner clinical presentation. Identification of the source of Hg exposure and its removal are the mainstay of treatment. The use of chelating agent should be considered on a case-to-case basis. There is no single set of symptoms and signs or single cut-off laboratory value that indicate chelation therapy. When in doubt, expert advice should be sought. Meso-2,3-dimercaptosuccinic acid (DMSA) and 2,3-dimercapto-1-propane sulphonic acid (DMPS) are the safer agents to use, although even these are not free from side-effects and there is inadequate evidence about their clinical efficacy.[17,18] Chelation therapy was given to three patients in our series. In the first case, DMSA was given to the patient who ingested mercurochrome, who presented with acute epigastric discomfort, nausea and vomiting but without neurological symptoms. His initial blood and urine Hg levels were 395 nmol/L and 449.2 nmol/day, respectively. Recovery was uneventful and the Hg level returned to normal after a course of DMSA treatment. The second patient was a 2-year-old child with carnitine-acylcarnitine translocase deficiency and developmental delay. The maximum blood Hg level encountered in him was 387 nmol/L (as detected by trace element monitoring). The source was believed to be dietary fish. After balancing the risk and benefits, and especially because of the difficulty in assessing Hg toxicity clinically in this child, a 19-day course of DMSA therapy was given and the Hg level normalised. The third patient was a 46-year-old female working in the airport. She presented with generalised discomfort and recurrent dizziness. The initial Hg blood level and urinary excretion values were 46 nmol/L and 36 nmol/day, respectively. The HKPIC was consulted in January 2009 and advised against the use of chelation. However, in July 2010 six courses of dimercaprol therapy were given by the attending physician, apparently for the 'benefit of doubt'. At her latest follow-up, her symptoms were about the same and the Hg blood level and urinary excretion values were 72 nmol/L and 36 nmol/day, respectively. The patient was told to 'come again when necessary'. On review, this patient's presentation was not compatible with Hg poisoning. The empirical use of chelating agents in patients without evidence of Hg exposure is not risk-free and is not recommended.

Conclusion

This study shows that there is much variation in the management of Hg exposure. The assessment should include evaluation of the presenting symptoms, a detailed exposure history, and blood Hg level and 24-hour urinary excretion measurement. Hair analysis is not recommended, neither is post-provocation urine test. Avoidance of seafood consumption 1 to 2 weeks before such measurements is preferred. Removal of the source of exposure is the mainstay of treatment. Use of chelation therapy should be considered individually and preferably after expert consultation.

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