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FAMILIAL OUTBREAK OF MERCURY POISONING

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ABSTRACT
Mercury poisoning is often misdiagnosed due to the rarity of this condition; sometimes initially mild clinical presentation can rapidly progress to respiratory failure leading to mechanical ventilation and death. There is no consensus about treatment of mercury vapor intoxication with chelating agents when the etiological role in the patient's illness is in question or when the therapy is to be initiated late in the clinical course. Cases of possible mercury exposure with symptoms and signs of intoxication, even without laboratory result, must be indicated aggressive treatment. Alarm symptoms, such as respiratory distress, suggest the need for chelation. A family of four started with a nonspecific illness that rapidly progressed to an aggressive pneumonia and acute respiratory distress syndrome (ARDS) of initially presumed infectious origin with 50% lethality. Mercury levels were measured in all four cases, and in the two survivors, chelation therapy with dimercaptopropanol (also called British Anti-Lewisite, BAL) was administered approximately a month after the start of illness. This resulted in no residual pulmonary disease in either case or obvious developmental delay in the child. When investigating a family outbreak with no additional cases among close contacts in shared environments outside the home, poisoning should be suspected and assessed, and the appropriate antidote located and administered promptly.

KEYWODS: Dimercaptopropanol, pneumonia and ARDS.

INTRODUCTION
June 25, 2013, the Public Health Department of Sonora State, Mexico (PHDS) notified the General Directorate of Epidemiology (DGE) of Mexico's Ministry of Health that four family members in Nacozari, Sonora State had severe pneumonia of unknown etiology. The youngest family member, a 4-year old girl, died in route to the hospital, and the other three family members were admitted to tertiary care hospitals. The familial outbreak was characterized by its clinical seriousness and unknown etiology. DGE and PHDS epidemiologists investigated the outbreak to identify the etiology, find additional cases, and recommend control measures. This outbreak highlights the importance of partnerships among public health officials from state and federal institutions in the same and neighboring countries to find the source of an outbreak and to improve access to medical and nonmedical countermeasures in health emergencies.

CASE REPORT
Four cases within a same family, two adults (case 1, male 40 years old, and case 2, female 38 years old) and two children (case 3, male 12 years old and case 4, female 4 years old), had symptoms from 06:00 to 20:00 hours on June 23, 2013 (figure 1). Their initial symptoms were diarrhea, abdominal pain, headache, myalgia, and arthralgia. In the morning of June 24, all of them had fever and were visited at their home by a private medical doctor (PMD). The PMD diagnosed acute diarrheal disease of unknown etiology and prescribed trimethoprim/sulfamethoxazole and fluid replenishment.

On the night of June 24, cases 1, 3 and 4 developed dyspnea and were transferred to the local health unit. The

patients were evaluated and referred to the community hospital, two hours away. Case 4 died while on route to this facility. The others three cases were evaluated and referred to the regional tertiary care hospitals, four hours away, due to the compromised respiratory function and the need for respiratory support.

On hospital admission (15:00 June 25, 2013), case 1 presented with signs of respiratory failure and was intubated 11 hours post-admission. Despite maximal supportive therapy, he developed acute respiratory distress syndrome (ARDS), sepsis, and multi-organ failure, and died on day 28 of hospitalization. On admission, case 2 presented a temperature of 99.1 F. She was admitted to the hospital for observation but developed respiratory symptoms that required sedation, but not mechanical ventilation, during her 41-day hospital admission. On admission, case 3 presented with signs of respiratory failure and was immediately intubated. The respiratory status gradually worsened and positive end expiratory pressure was necessary to maintain oxygen saturations >90%. He was successfully extubated on hospital day 29 and discharged on day 45 without any sign of residual pulmonary disease.

The admitting diagnosis of cases 1 and 3 was severe pneumonia of suspected infectious etiology, and the used treatment was with antibiotics and antifungal. Respiratory specimens from the upper and lower respiratory tract of case 3 were sent to a reference laboratory. All test results were negative for the ARDS diagnostic algorithm for known (i.e., Hantavirus) and novel agents (i.e., MERS-CoV) used at the reference laboratory.

PUBLIC HEALTH INVESTIGATION

On June 29, 2013, a DGE epidemiologist met with PHDS officials to discuss the field investigation and to interview the mother of the family. The mother (case 2) had two other children who were not ill: an adolescent daughter (14 years old) who was staying overnight at her grandparent's house on the night of the suspected exposure, and a married daughter who lived elsewhere. The family home (two rooms, one bath) had been occupied for just three weeks prior to the disease onset. On the evening of June 22, the mother and her two younger children (cases 3 and 4) were out of the house until 23:00 (approximately 7 hours before the start of the initial symptoms). The answers to questions about risk factors for the known and novel infectious and environmental causes of ARDS (e.g., Hantavirus infection, leptospirosis, legionellosis, influenza, coronavirus, ammonia intoxication, and carbon tetrachloride poisoning) were negative.

A case definition was developed, with a case being defined as a person who, from May 12, 2013 to June 30, 2013, had fever, headache, diarrhea, and one or more of the following: nausea, vomiting, abdominal pain, chest pain, cough and shortness of breath, muscle aches, abnormal state of consciousness, disorientation, or hypotension. The medical records of the five health units where the cases had any type of care or hospitalization were reviewed, and household members and close contacts of the current and previous homes of the affected family (n=74) were interviewed. No additional cases were found.

Interviews with family members and acquaintances elicited a history of suspected mercury vapor exposure. The suspected exposure occurred on June 22 when the father was alone at home and heated mercury with the belief that he could obtain gold. After the failed attempt the mercury was left in an uncovered container in the home. On July 2 an investigative team visited the family home and found an uncovered vessel (approximately 100 ml) with traces of mercury. Until further orders, the house was deemed unfit for human habitation and condemned by the Mexican Secretary of Environment and Natural Resources.

The Mexican health emergencies office contacted CDC for assistance with mercury levels testing on July 3, 2013. After phone consultations with CDC on July 5, 2013, blood samples from all cases and urine samples from cases 1, 2, and 3 were obtained following a modified protocol for investigating mercury poisoning. On July 6, samples travelled across the U.S.-Mexico land border and sent to the Arizona State Laboratory in Phoenix, which shipped them to CDC's Office of Non-communicable Diseases, Injury and Environmental Health, National Center for Environmental Health. The urine and blood mercury levels indicated mercury intoxication on July 9, 2013 (table 1).

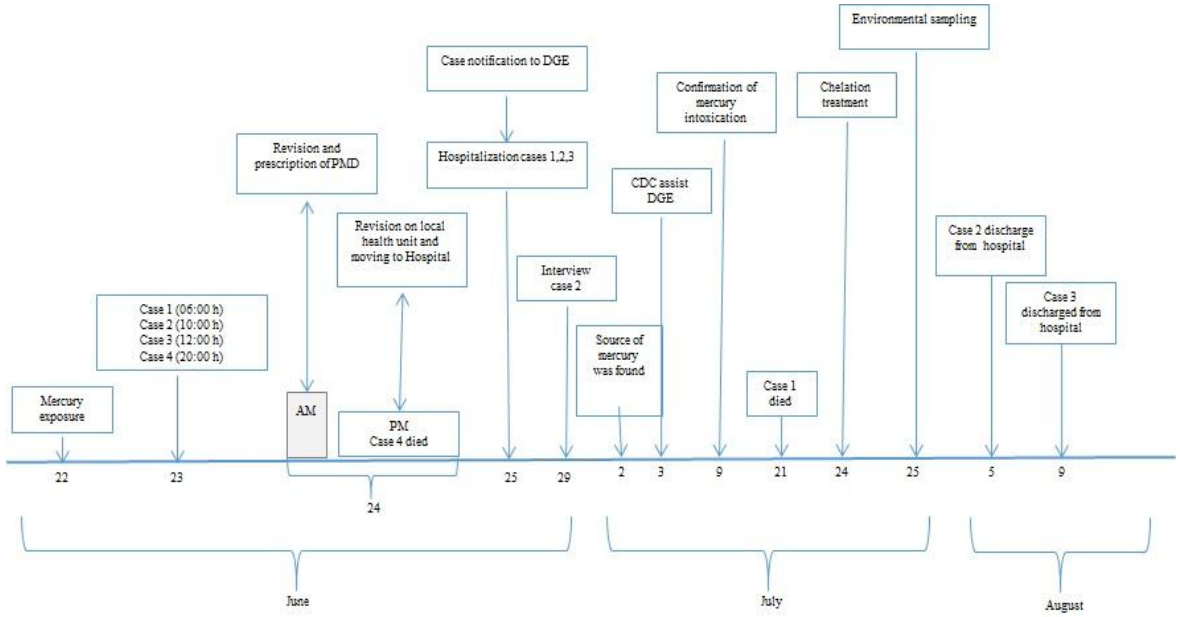
An expert committee including state and federal public health authorities, the treating clinicians, environmental and clinical toxicologists, and industrial hygienists from Mexico and the United States had a telephone conference call July 10, 2013 to discuss treatment and management options for the patients and mercury environmental evaluation and remediation recommendations. This committee recommended chelation treatment with dimercaptopropanol (also called British Anti-Lewisite, BAL). Due to BAL is not available in Mexico, the PHDS obtained it from Florida. On July 24, 2013 (32 days from presumed exposure day), cases 2 and 3 started chelation therapy for 10 doses.

Environmental air sampling was performed on the home on July 25 (33 days after the date of suspected heating of mercury) and all samples were within normal levels for mercury (table 2).

Table 1. Levels of mercury in blood Hospitalized cases, Sonora, Mexico, July 2013

CASE	BLOOD MERCURY (µg/L)	UPPER NORMAL LIMITE (µg/L)
1	300	0.28
2	255	
3	130	

Source: Non-communicable Diseases, Injury and Environmental Health, National Center for Environmental Health. Centers for Disease Control and Prevention. USA.



Source: Sonora Department of Public Health and General Directorate of Epidemiology, Mexico.

Figure 1. Chronology of the family outbreak by mercury poisoning Sonora, Mexico, June-August 2013

Table 2. Levels of mercury in furniture of family house Sonora, Mexico, July 2013

SAMPLE	MERCURY CONCENTRATION (mg/m^3)	UPPER NORMAL LIMIT (mg/m^3)
Dinner table	<0.0003	0.05 mg/m^3
Refrigerator		
Sofa in living room		
Bathroom		
Bedroom		
Front window		

Source: Private laboratory analysis. Sonora Department of Public Health, Mexico

DISCUSION

When the cause or agent causing a disease outbreak is unknown, the cases themselves are the main sources for formulating causality hypotheses. The PHDS investigated a wide variety of agents, both infectious and noninfectious, and found no evidence implicating any of the etiologies considered at the early stages of the investigation. The break in this familial outbreak investigation occurred when a PMD called SDPH on June 30 to report that a woman living in the community developed signs and symptoms of an illness similar to the family under investigation (later determined to be drug withdrawal syndrome). During the medical history interview, this woman's housemate said that he was an acquaintance of the father of the ill family, and they had shared the idea that heating mercury was a process for obtaining gold (artisanal mining to extract gold of amalgam). Notifying local medical providers of a problem being investigated in their community encourages them to obtain information from people in the community to find the source of an outbreak.

In the artisanal mining to extract gold, the amalgam is heated whereby the mercury evaporate and gold is left behind.[1] To some extent, mercury can vaporize at room temperature but exposure to heat produces the most vapor which remains in the environment.[2,3] Mercury gases can be colorless and odorless,[4] and were presumably inhaled by family members sleeping in a poorly ventilated house. Mercury vapors dissipate after over time and were not measurable when the air was sampled in the home approximately one month after the

suspected mercury processing. Elemental mercury is not toxic if ingested because of its low gastrointestinal absorption; however, mercury vapors are significantly absorbed by the lung and can cause severe interstitial pneumonitis with compromised respiratory function.[5] The ARDS that develops after inhalation of elemental mercury is often fatal.[6] After mercury is absorbed, it travels through the bloodstream and is deposited primarily in the brain, kidneys, and liver. Acute exposure to mercury vapors include fever, weakness, chills, abdominal pain, nausea, vomiting, diarrhea, and dyspnea presenting within a few hours of exposure.[7]

The rapid clinical course resulting in the death of the 4-year-old child (case 4) was likely due to the amount of contaminated air she inhaled relative to her body weight, which was more than the adult and adolescent family members inhaled. The main autopsy finding in this child was fibrin in the cranial and thoracic cavities, which is compatible with the areas of predominant distribution for absorbed mercury.[6] The father (case 1), who is suspected to have heated the mercury, presumably had the largest exposure to mercury vapors and also presented with an aggressive course of illness and death. The case fatality rate in this mercury poisoning outbreak was 50% and exemplifies the danger of even short exposure to mercury vapors.

The risk to benefit ratio for chelation therapy has not been well defined in poisoning with heavy metals.[8] It is considered most useful when administered early but in this situation it was beneficial even days after the exposure and illness onset. The primary economic activity of the city where the outbreak occurred is mining, and the purchase of certain toxic materials, such as mercury, is commonplace.[5] In such places it is vital to make public the adverse effects of the metal[8] through prevention campaigns that encourage the proper handling and disposal of toxic and potentially lethal substances.

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