Respiratory Failure and Death Following Acute Inhalation of Mercury Vapor*

A Clinical and Histologic Perspective

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A family of four was exposed to toxic levels of mercury vapor while attempting to extract silver from mercury amalgam. All four suffered respiratory failure and subsequent death despite chelation therapy with dimercaprol. Histologic findings at autopsy were similar in all four cases demonstrating a progression of acute lung injury that appeared related to postexposure day survival. There were no clinical signs of extrapulmonary manifestations despite toxic serum mercury levels. Although serum mercury levels decreased in response to the mercury chelating agent dimercaprol, serum levels remained in the toxic range and no clinical response was observed. Acute inhalational exposure to high concentrations of mercury vapor causes pneumonitis that can lead to respiratory failure and death. This continues to be a health hazard in both the workplace and the home environment. (Chest 1991; 99:185-90)

We describe four cases of mercury vapor inhalation with subsequent respiratory failure and death; these patients had attempted to extract silver from a mercury-containing amalgam. A 41-year-old man illegally obtained a silver amalgam preparation containing 50 percent mercury. He apparently stole the amalgam and heated the powder in a small smelter in an attempt to obtain pure silver metal. This process took place in the home of his father-in-law. Present during this event were his wife, her father, and grandmother. There were also two dogs within the home who subsequently died. All four patients denied this history when they first presented to local hospitals. All stated that they had been exposed to freon fumes while attempting to clean a refrigerator. The mercury vapor inhalation history was eventually obtained five days later when local public health officials, notified of the unexplained inhalation exposure, detected amalgam powder and the smelter in the basement of the home.

Case Reports

Case 1

A 41-year-old white man was transferred to Henry Ford Hospital, Detroit, for evaluation of progressive dyspnea and pulmonary insufficiency. He had presented to a local hospital four days earlier because of nausea, shortness of breath, and nonspecific chest pain. On original presentation, he was mildly febrile, but results of his physical examination were otherwise unremarkable. Results of routine laboratory testing were also unremarkable with the exception of room air arterial blood gases that revealed a PaO₂ of 64 mm Hg, a PaCO₂ of 31 mm Hg, and a pH of 7.46. His initial chest roentgenogram was normal (Fig 1); however, on transfer, it revealed bilateral diffuse pulmonary infiltrates (Fig 2). His arterial blood gases, now obtained on a 50 percent oxygen concentration, revealed a PaO₂ of 69 mm Hg, a PaCO₂ of 39 mm Hg, and a pH of 7.40. The patient claimed to have been exposed to freon fumes while cleaning an old refrigerator, but Public Health officials evaluating the reported unexplained inhalation informed the physician staff of evidence found in the home implicating mercury vapor. When notified of such, serum and urine mercury levels were obtained and dimercaprol (BAL) therapy was started at 5 mg/kg intramuscularly every 4 h. The initial serum mercury concentration was 16.1 μg/dl with

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FIGURE 1. Chest roentgenogram on presentation shows no evidence of parenchymal disease.
Acute methylprednisolone therapy was started at the same time as mechanical ventilation was initiated. Despite ventilatory support, pulmonary compliance fell and oxygenation became difficult to achieve. Peak airway pressures rose to 90 cm H2O. On the 15th hospital day, a spontaneous right tension pneumothorax developed, requiring thoracotomy. On the 21st hospital day, a left-sided pneumothorax developed. Despite decompression, the patient suffered a cardiac arrest and died.

**CASE 2**

A 40-year-old white woman was transferred to Henry Ford Hospital because of respiratory insufficiency. She had been hospitalized at a community hospital for one day with a history of dyspnea, nausea, vomiting, and diarrhea. Other than a temperature of 37.2°C and mild tachypnea, results of her physical examination were normal. Room air arterial blood gases revealed a P02 of 71 mm Hg, a Paco2 of 36 mm Hg, and a pH of 7.44. Her initial chest roentgenogram demonstrated unchanged diffuse reticular nodular infiltrates consistent with her known diagnosis of sarcoidosis, but with superimposed bilateral alveolar disease also present. Findings from routine laboratory assessment were otherwise within normal limits. Over the first 24 hours of hospitalization, the patient's arterial blood gas values deteriorated, revealing a room air P02 of 25 mm Hg, Paco2 of 32 mm Hg, and a pH of 7.43. She was intubated and supported with mechanical ventilation and transferred at that time.

At transfer, results of her physical examination were unrevealing, her chest roentgenogram was unchanged, and arterial blood gases while receiving an oxygen concentration of 50 percent revealed a P02 of 76 mm Hg, Paco2 of 35 mm Hg, and a pH of 7.43. When the history of mercury vapor exposure became apparent, dimercaprol (BAL) therapy at 5 mg/kg intramuscularly every 4 h was instituted along with intravenous corticosteroids. Serum and urine mercury levels obtained prior to chelation therapy were 12.7 μg/dl and 135 μg/L, respectively. Despite increase in urinary excretion with therapy, serum mercury levels remained elevated throughout her hospitalization.

Progressive respiratory insufficiency developed with peak airway pressures in excess of 90 cm H2O. Progressive roentgenogram changes consistent with the adult respiratory distress syndrome were recognized, with pulmonary artery catheterization confirming the presence of noncardiogenic pulmonary edema. On the 19th hospital day, a left-sided tension pneumothorax developed requiring tube thoracotomy. Two days later, she suffered a cardiac arrest and could not be resuscitated.

**CASE 3**

An 88-year-old white woman was transferred to Harper Hospital following a 36-hour hospitalization at a community hospital for dyspnea, nausea, vomiting, and diarrhea. Her respiratory status had rapidly deteriorated requiring endotracheal intubation and mechanical ventilatory support. Findings from the physical examination, both on presentation to the community hospital and on transfer to the tertiary care institution, were described as unremarkable. Arterial blood gases on transfer while receiving an oxygen concentration of 80 percent and 8 cm3 H2O of positive end-expiratory pressure revealed a P02 of 77 mm Hg, a Paco2 of 28 mm Hg, and a pH of 7.45. The chest roentgenogram revealed diffuse bilateral parenchymal infiltrates. The temperature was 38.3°C, but all other vital signs were stable. Routine laboratory studies at the time of hospital admission revealed a white blood cell count of 36,500/cu mm, hemoglobin of 10.8 g/dl, a serum urea nitrogen of 39 mg/dl, and a creatinine of 1.7 mg/dl. Because of concerns of community-acquired pneumonia, intravenous erythromycin therapy was started at a dose of 1 g every 6 h. Decreasing urine output together with a low cardiac output believed to be secondary to ventilatory support was treated with dobutamine and dopamine,
and normalization of urinary output, serum urea nitrogen, and serum creatinine was subsequently noted. On the fifth hospital day, the history of mercury exposure was obtained and chelation therapy with dimercaprol commenced. Serum levels of mercury were not obtained before her death, but urinary levels with chelation therapy rose from 94 to 230 \( \mu \text{g/L} \).

Progressive respiratory insufficiency with roentgenographic features compatible with adult respiratory distress syndrome continued until the ninth hospital day when a right-sided tension pneumothorax and subsequent cardiac arrest developed. Despite successful resuscitation, postanoxic seizures developed two days later with EEG changes consistent with severe cerebral dysfunction. Her respiratory and hemodynamic condition continued to deteriorate and she died on the 14th hospital day. The postmortem serum mercury level was 21.2 \( \mu \text{g/dl} \).

**Case 4**

A 69-year-old white man was transferred to Harper Hospital following a 36-hour hospitalization for progressive respiratory insufficiency that necessitated endotracheal intubation and mechanical ventilatory support. The patient had complained of nausea, vomiting, and diarrhea for one day prior to his admission to a local hospital. Other than a temperature of 38.5\(^\circ\)C, the patient's vital signs were normal. Arterial blood gases on 90 percent oxygen and 14 cm \( \text{H}_2\text{O} \) of positive end-expiratory pressure demonstrated a \( \text{Po}_\text{2} \) of 139 mm Hg, \( \text{PCO}_\text{2} \) of 36 mm Hg, and a pH of 7.38 on transfer to Harper Hospital. The chest roentgenogram on transfer revealed diffuse bilateral pulmonary infiltrates. Results of screening laboratory studies were normal except for serum urea nitrogen of 47 mg/dl and a serum creatinine of 1.7 mg/dl.

Progressive deterioration in arterial oxygenation together with chest roentgenogram and pulmonary artery catheter data consistent with the adult respiratory distress syndrome were noted. With hemodynamic support, the serum urea nitrogen and serum creatinine values normalized. On obtaining the history of mercury vapor exposure, dimercaprol therapy was commenced. On the fifth hospital day, a tension pneumothorax and hypotension developed requiring the addition of significant vasopressor therapy and thoracostomy to maintain an adequate blood pressure. On the seventh hospital day, clinical deterioration with computed tomographic evidence of diffuse cerebral edema and subfalcine herniation developed. Clinical protocols for cerebral silence were commenced and the patient was declared dead three days later. The postmortem serum mercury level was 36.8 \( \mu \text{g/dl} \).

**Pathology**

**Lungs**

The combined lung weights ranged from 2,100 to 3,100 g. All cases were similar grossly: airless, firm, and expanded with small amounts of hemorrhagic mucus present. The histologic picture varied in accordance to how long each patient survived after insult. Case 4, who died 11 days after insult, had pulmonary changes of early acute lung injury characterized by slight pneumocyte hyperplasia, hyaline membrane formation, and foci of fibrosis (Fig 4). The fibrotic areas were predominantly arranged in edematous interstitium. A mild interstitial mononuclear infiltrate was also present. Case 3, who died 15 days after insult, revealed a similar picture; however, there were fewer hyaline membranes and the fibrous areas were increased in size and appeared more mature and less edematous. Additionally, emphysema was present.

**Figure 4.** Histologic section of lung demonstrating mild interstitial fibrosis, hyaline membranes, and congestion (hematoxylin-eosin, original magnification \( \times 6.6 \)).

Case 2, who died 22 days after insult, had pulmonary changes consistent with a late stage of acute lung injury. There was marked pneumocyte hyperplasia and a significant decrease in the air spaces that were replaced with extensive fibrosis. Congestion and alveolar hemorrhage were prominent. Mild emphysematous changes were also present. Case 1, who died 24 days after insult, had changes of end stage acute lung injury (Fig 5). There was almost total obliteration of the alveolar spaces with extensive mature interstitial fibrosis. The remaining alveolar spaces were filled with inflammatory cells, hyperplastic pneumocytes, and hemosiderophages. Congestion was prominent.

**Kidneys**

Combined kidney weight ranged from 240 to 460 g. They were grossly edematous with poor corticomedullary demarcation. Histologically all were similar, revealing acute tubular necrosis of the proximal tubules. The distal tubules and glomeruli were without abnormalities. Transmission electron microscopic examination of case 3 revealed only degenerative tubular changes. Mercury deposits and glomerular damage were not identified.

**Figure 5.** Histologic section of lung demonstrating marked interstitial fibrosis and obliteration of alveolar airspace (hematoxylin-eosin, original magnification \( \times 10 \)).
Acute mercury inhalation exposure tends to occur in three settings: industrial accidents, accidents within the home, and in association with novice attempts to extract precious metals from mercury amalgam. We reviewed 109 reported cases of acute mercury inhalation. We found that industrial accidents occurred most frequently (61 percent) followed by attempts to extract precious metals from amalgams (24 percent) and then home accidents (15 percent). There were nine reported deaths: five children and four adults. All deaths were related to respiratory failure following acute inhalation. We describe four family members exposed to toxic concentrations of mercury vapor in their home during attempts to extract silver from mercury amalgam. The threshold limit value of acceptable mercury vapor concentration is 0.05 mg/m³.¹ The first Environmental Protection Agency (EPA) mercury vapor concentration measurements were recorded 11 days after the inhalation. The maximal concentration in the home was 0.885 mg/m³. We cannot explain the delay in measuring the ambient mercury vapor concentrations within the home after powder samples analyzed six days earlier showed evidence implicating mercury. Measurements may have been made in the interim but they were not reported.

The symptoms of mercury inhalation differ in regard to the duration and concentration of exposure. Acute exposure to high-level concentrations primarily involves the lung and results in symptoms of dyspnea, chest pain, and cough.² Long-term low-level exposure affects the neurologic system with resultant symptoms of tremor, neuropathy, and changes in personality referred to as mercurial erethism. All four of our patients had symptoms compatible with acute exposure at presentation. Our patients followed a similar clinical course of progressive respiratory failure and subsequent death. Their chest roentgenograms paralleled their clinical course and demonstrated progressive diffuse bilateral infiltrates consistent with the adult respiratory distress syndrome.

Chemical pneumonitis following acute exposure to mercury vapor is well described in recent literature.³,⁴ Prior to our series, only four adult deaths have been reported.³,⁵,⁶ Pulmonary toxicity appears related to local irritant effects created by oxidized mercury ions.⁸ There may be direct damage to bronchial and parenchymal cells with resultant acute lung injury. Mercury ions are also known to bind sulfhydryl groups and thus may disrupt sulfhydryl containing enzyme systems contributing to the injury cascade.

Respiratory absorption of mercury vapor is rapid and complete through the alveolar membrane. Studies by Berlin and Johansson⁹ reported that inhaled mercury ions were quickly transferred into the blood of guinea pigs. Jung and Aaronson¹ conclude that inhalation of mercury vapor can expose a person to very high toxic serum concentrations. The serum concentration in our patients are shown in Table 1. Case 1 had a serum level of 16.1 µg/dl and case 2 had a serum level of 12.7 µg/dl prior to the start of chelation therapy. The toxic serum concentration is greater than 1 µg/dl. Serum concentrations of case 3 and case 4 were obtained postmortem after receiving chelation therapy and were 21.2 and 36.8 µg/dl, respectively.

The question of serum concentration and extrapulmonary toxicity has been addressed throughout the literature. Matthes et al¹ reviewed the cases of four patients and noted the lack of correlation between pathologic findings and the concentration of mercury found in the tissues. Halle et al¹⁰ reported no correlation between the concentration of mercury found in urine and the condition of the patients. However, there have been two recent reports of extrapulmonary toxicity associated with acute mercury inhalation. Aguado et al¹¹ described the onset of acute renal failure following mercury inhalation, and Jaffe et al¹² reported renal, hepatic, and neurologic dysfunction in a child following inhalational exposure.

In our series, despite histologic evidence of acute tubular necrosis at autopsy in all four cases, only case 3 and case 4 showed transient laboratory evidence of renal insufficiency early in their hospital course. This was believed to be secondary to hemodynamic changes induced by ventilatory support, and responded to inotropic agents with resolution of the abnormal laboratory values. Case 4, after sustaining the subfalcine herniation and persistent hypotension, however, was noted to have an elevation of serum urea nitrogen and creatinine levels. This persisted until his death and was believed to be related to low renal blood flow and the persistent hypotension. There were no consistent abnormalities seen in the urine. Case 4 was noted to have two granular casts observed on hospital day 4. This appeared as an isolated finding as no other casts were seen during the rest of his hospital course. No

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*Therapy with dimercaprol initiated.
significant proteinuria, casts, or crystals were otherwise noted in any of the patients. Urine output remained greater than 1 ml/kg/h in all of the patients.

Gastrointestinal symptoms of nausea, vomiting, or diarrhea were noted in all four patients on presentation. These symptoms resolved quickly without signs of hepatic dysfunction. No hepatic abnormalities were seen at autopsy. We are unsure if these symptoms were related to the inhalation of mercury vapor; however, we believe that their transient nature and the lack of histologic abnormality indicate that they had no effect on hospital course or outcome.

Diffuse pulmonary infiltrates and respiratory failure developed in all four cases. Cases 2, 3, and 4 were intubated and placed on mechanical ventilation within 36 hours after exposure; case 1 was intubated and ventilated five days later. All progressed to the adult respiratory distress syndrome requiring high levels of positive end-expiratory pressure and high oxygen concentrations. Case 1 and case 2 survived the longest and developed extremely noncompliant lung function. Peak airway pressure exceeding 90 cm H₂O was required to deliver volumes necessary to maintain oxygenation. These clinical findings correlated with the finding of fibrosis on histologic sections of the lung. The severity of the adult respiratory distress syndrome following mercury vapor inhalation has been described previously.⁵,⁷

All four patients developed spontaneous tension pneumothorax as premonitory events. Tension pneumothorax has been observed in six of the nine reported deaths attributed to mercury inhalation. (In two patients, no mention was made of clinical course.) Barotrauma from prolonged high-pressure ventilation of noncompliant lungs was most likely responsible for these events.

Dimercaprol (BAL) is a chelating agent that functions by displacing heavy metal ions from sulfhydryl groups. The heavy metal dimercaprol complex is then excreted in the urine. Therapy with dimercaprol was started in all patients six days after exposure. Baseline urine and serum mercury concentrations were obtained in case 1 and case 2 prior to the initiation of therapy. A baseline urine concentration was obtained in case 3. These results and subsequent mercury concentration while receiving dimercaprol are shown in Table 1. Case 4 received dimercaprol but serum and urine levels were not obtained. Baseline serum mercury levels were 16.1 μg/dl in case 1 and 12.7 μg/dl in case 2. Baseline urine concentrations were 423 μg/L in case 1, 138 μg/L in case 2, and 94 μg/L in case 3. After three days of chelation therapy, the concentration of serum mercury in case 1 and case 2 had decreased to 10.1 and 9.8 μg/dl, respectively. The urine concentration of excreted mercury had increased to 438 μg/L in case 1, 167 μg/L in case 2, and 220 μg/L in case 3. This demonstrates that while chelation therapy was effective in decreasing serum mercury concentrations in our patients, the concentrations still remained in the toxic range.

Although chelation therapy has been shown to decrease serum mercury concentrations, review of the literature shows that this has no effect on progression of acute lung injury. Jaeger et al.⁸ postulated that lung tissue damage is complete and that the treatment of serum levels with chelating agents has no effect on the reversal of lung damage. Aguado et al.⁹ however, were able to effectively treat acute renal failure following inhalation of mercury vapor with chelation therapy. In our patients, despite reduction in serum mercury levels with dimercaprol, there was no reversal in the progression of lung injury and respiratory dysfunction.

Corticosteroids have been used sporadically, as reported in the literature. We saw no benefit in the two patients in our series started on corticosteroid therapy. It has been suggested that steroids may prevent progression to severe interstitial fibrosis if used in mildly affected patients.¹⁰ The acute lung injury in our patients may have been too severe for steroids to show any sparing effect. Alternatively, the response to corticosteroids described in other cases may have been coincidental given the absence of response now demonstrated in the adult respiratory distress syndrome.¹¹

There was a six-day delay after acute inhalation exposure with regard to the treatment with dimercaprol in all four patients and systemic corticosteroids in case 1 and case 2. Whether this delay in therapy played a role on outcomes is highly speculative. As discussed previously, there is no evidence in the literature to support a relationship between pulmonary toxicity and serum mercury concentration. Earlier therapy with dimercaprol and the resultant clearing of mercury ions would not necessarily have lessened lung damage or affected outcome. The evidence in the literature relating to the use of systemic corticosteroids in patients with acute lung injury is quite definitive.¹² There is no improvement in outcome of patients with acute lung injury when treated with corticosteroids. Thus, we believe that even if the patients had given an honest account of the events that precipitated the inhalation, the initiation of therapy earlier in their course would probably not have improved the outcome.

All four cases underwent autopsies and the findings were quite consistent with those described in the past.⁵ The histologic changes of acute lung injury seemed to correlate directly with survival time. Early changes of acute lung injury were seen in case 4 who died 11 days after exposure. The lungs of case 1, who survived 24 days after exposure, demonstrated end-
stage lung injury. The histologic changes seen in case 2 and case 3 were intermediate within this spectrum and related to survival days after exposure. These histologic changes are similar to changes described in the adult respiratory distress syndrome from other causes. The kidneys of all four patients demonstrated acute tubular necrosis of the proximal tubules, although only case 3 and case 4 demonstrated transient clinical signs of renal failure. These postmortem findings may be related to the immediate premorbid hypotensive and hypoxemic episodes they experienced prior to expiration.

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