ABSTRACT. Two children in the same household with symptomatic arterial hypertension simulating pheochromocytoma were found to be intoxicated with elemental mercury. The first child was a 4-year-old boy who presented with new-onset seizures, rash, and painful extremities, who was found to have a blood pressure of 171/123 mm Hg. An extensive investigation ensued. Elevated catecholamines were demonstrated in plasma and urine; studies did not confirm pheochromocytoma. Mercury levels were elevated. These findings prompted an evaluation of the family. A foster sister had similar findings of rash and hypertension. Both had been exposed to elemental mercury in the home. The family was temporarily relocated and chelation therapy was started.

A Medline search for mercury intoxication with hypertension found 6 reports of patients ranging from 11 months to 17 years old. All patients showed symptoms of acrodynia. Because of the clinical presentation and the finding of elevated catecholamines, most of the patients were first studied for possible pheochromocytoma. Subsequently, elevated levels of mercury were found. Three children had contact with elemental mercury from a broken thermometer, 2 had played with metallic mercury and 1 had poorly protected occupational exposure. All responded to chelation therapy.

Severe systemic arterial hypertension in infants and children is usually secondary to an underlying disease process. The most frequent causes of hypertension in this group include renal parenchymal disease, obstructive uropathy, and chronic pyelonephritis associated with reflux and renal artery stenosis. Less frequent causes include adrenal tumors, pheochromocytomas, neurofibromas, and an increasing number of familial forms of hypertension. Other causes are medications and drugs of ingestion or abuse, especially cocaine and sympathomimetics. Heavy metal intoxication is also implicated. We present 2 patients with an infrequent cause of hypertension.

CASE REPORTS

Patient 1
A 4-year-old boy was seen at the emergency department because of new-onset seizures. History revealed headache for 1 week and no history of heavy metal exposure or toxin ingestion. He was found to have a blood pressure of 171/123 mm Hg, heart rate of 164/min, temperature of 96°F, and respirations of 28/min. He was anxious, irritable, diaphoretic, tremulous, and seemed to be in pain. His lips were dry, lungs clear to auscultation, and his abdomen revealed no masses or bruits. The skin was dry and rough with a scaly eczematous rash on his arms and legs, without palmar or plantar erythema. Two months before, during a physical examination for foster home placement, his blood pressure was 92/65 mm Hg. The family history was negative for chronic renal disease or hypertension. Initial evaluation revealed hemoglobin of 14.9, albumin of 5.5 g/dL. Basic metabolic studies, urinalysis, computed tomography scan of the head, and lumbar puncture all were unremarkable. A renal ultrasound was normal. Plasma renin activity was 20 ng/mL/hour, supine, (normal reference value [n]: <2.5), plasma aldosterone level 23 ng/dL (n: 3–35 supine), and urinary norepinephrine 72.1 μg/24 hours (n: 8–45). Vanillylmandelic acid was 13.6 mg/g of creatinine (n: 0–8.3). Magnetic resonance image of the head, chest, abdomen, and pelvis revealed no tumor or abnormalities. The blood lead level was <5 μg/dL (class I). The blood mercury level was 24 ng/mL (n: <3.9), and urinary mercury excretion 324 μg/24 hours (n: <10). During his inpatient stay, sodium concentration ranged from 128 to 136 mEq/L, associated with elevated fractional excretion of sodium between 1.4% and 2.5%. Plasma creatinine was 4 mg/dL and his creatinine clearance was 79 mL/minute/1.73 m². His hypertension was difficult to treat, requiring 4 antihypertensive medications, including prazosin up to 1.4 mg/kg/day, isradipine up to 1.07 mg/kg/day, captopril up to 7 mg/kg/day, and labetalol up to 70 mg/kg/day.

Chelation was initiated with British antilewisite and changed to dimercaptosuccinic acid after consultation with a toxicologist. With chelation and control of his hypertension, his symptoms improved in 3 weeks. After 4 months of treatment, his urine mercury excretion decreased to 30 μg/24 hours, his plasma renin activity returned to normal, and his blood pressure normalized. His plasma sodium was 138 mEq/L and he gained 2 kg of weight. There was no neurologic sequela and his skin was normal at a 4-month recheck.

Investigation by Agency for Toxic Substances and Disease Reg-
<table>
<thead>
<tr>
<th>Reference</th>
<th>Author</th>
<th>Patient’s Age/Sex</th>
<th>Urine Mercury nmol/L</th>
<th>Source of Mercury</th>
<th>Symptoms and Blood Pressure (mm Hg)</th>
<th>Catecholamine Level</th>
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<tbody>
<tr>
<td>2</td>
<td>McNeil et al</td>
<td>14-y-old girl</td>
<td>2600</td>
<td>Elemental mercury spillage</td>
<td>122/98</td>
<td>Not available</td>
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<td></td>
<td></td>
<td></td>
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<td>Weight loss, anxiety, rash, pain</td>
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<td>Plasm (nmol/L)</td>
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<td>3</td>
<td>Henningsson et al</td>
<td>14-y-old boy</td>
<td>400</td>
<td>Playing with elemental mercury, mercury poured into an electrical coil heater</td>
<td>160/120</td>
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<td>Irritability, tachycardia, sweating, tremors, rash, back pain</td>
<td></td>
<td>Plasm (nmol/L)</td>
</tr>
<tr>
<td>4</td>
<td>Cloarec et al</td>
<td>32-mo-old girl</td>
<td>273</td>
<td>Broken thermometer</td>
<td>150/100</td>
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<td>5</td>
<td>Oliveira and Silva</td>
<td>17-y-old boy</td>
<td>1045</td>
<td>Manual handling of elemental Hg for extraction of gold without appropriate protection</td>
<td>200/130</td>
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<td>6</td>
<td>Boudouin et al</td>
<td>28-mo-old girl</td>
<td>98</td>
<td>Broken thermometer</td>
<td>150/100</td>
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<td></td>
<td>Tachycardia, irritability, anorexia, insomnia, rash of hands and feet</td>
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<td>Norepi 206 μg/24 h</td>
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<td>7</td>
<td>Velzeboer et al</td>
<td>11-mo-old girl</td>
<td>62.7</td>
<td>Broken thermometer</td>
<td>130/90</td>
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<td>Tachycardia, drowsiness, malaise, anorexia, sweating, pruritis, swollen extremities</td>
<td></td>
<td>Norepi 14.1 (n: 1.1–1.6) Epi 1.2 (n: .15–4) Urine (mmol/mmol creatinine) (Over 3 d)</td>
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<td>Dopamine 1173–1761 (n: 70–470)</td>
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<td>4-y-old boy</td>
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<td>Spilled elemental mercury from a pressure gauge</td>
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<td>Tachycardia, seizures, diaphoresis, irritability, anorexia, pain, weight loss</td>
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<td>VMA: 10.1 mg/g of creatinine (n: 0–8.3)</td>
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<td>Epi 18 (n: 2.1–10)</td>
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<td>Velzeboer et al</td>
<td>6-y-old girl</td>
<td>6773.8</td>
<td>Spilled elemental mercury from a pressure gauge</td>
<td>148/78</td>
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<td>Desquamating rash of hands and palms, erythema, tachycardia</td>
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<td>Plasm (mg/mL)</td>
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<td>Dopamine 212.1 (n: 65–400) VMA 10.1 mg/g of creatinine (n: 0–8.3)</td>
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<td>Dopamine 183.5 (n: 65–400) VMA: 10.1 mg/g of creatinine (n: 0–8.3)</td>
</tr>
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</table>

**TABLE 1.** Two Children With Mercury Intoxication and Hypertension and Review of the Literature
decreased, and she clinically recovered. Her blood pressure was controlled with oral captopril and prazosin at normo-
mandelic acid of 10.1 mg/g of creatinine (n: 0 – 8.3). Her blood apathy, photophobia, polydypsia, excessive sweat-
rash of palms and soles, anorexia, fatigue, irritability, and weight loss were found in 50%. Other presenting
manifestations (purple hands and feet with or without desquamation). Excessive perspiration was
found to be apathetic and complaining of sore throat with ery-
thermia and desquamation of her palmar and plantar surfaces. Her blood pressure was 148/78 mm Hg and her heart rate was 114/
minute. Blood pressure levels were 42 mg/dl (n: <9.9), and urine
erine excretion was 885 µg/24 hours (n: <310). She had elevated
urine catecholamines levels: epinephrine of 12.4 µg/24 hours (n:
2–10), norepinephrine of 49 µg/24 hours (n: 8–45), and vanillyl-
mandelic acid of 10.1 mg/g of creatinine (n: 0–8.3). Her blood
pressure was controlled with oral captopril and prazosin at normal
doses. Chelation was started and after 3 months of therapy, her blood pressure normalized, her urinary mercury excretion
decreased, and she clinically recovered.

**Patient 2**

A 6-year-old girl, the foster sister of patient 1, was evaluated for mercury intoxication because of the findings in patient 1. She was
found to be apathetic and complaining of sore throat with ery-
thermia and desquamation of her palmar and plantar surfaces. Her blood pressure was 148/78 mm Hg and her heart rate was 114/
minute. Blood pressure levels were 42 mg/dl (n: <9.9), and urine
erine excretion was 885 µg/24 hours (n: <310). She had elevated
urine catecholamines levels: epinephrine of 12.4 µg/24 hours (n:
2–10), norepinephrine of 49 µg/24 hours (n: 8–45), and vanillyl-
mandelic acid of 10.1 mg/g of creatinine (n: 0–8.3). Her blood
pressure was controlled with oral captopril and prazosin at nor-

**LITERATURE REVIEW**

A search of Medline for mercury intoxication with hypertension produced 6 patients. Fifty percent were
young children (11, 28, and 32 months old) and 50% were adolescents (14, 14, and 17 years old). All were
hypertensive with pressures from 130/90 mm Hg in the 11-month-old to 200/130 mm Hg in the 17-year-
old young man. Irritability, apprehension, and anxiety were found in all cases, as were dermatologic
manifestations (purple hands and feet with or without desquamation). Excessive perspiration was
present in 83%. Sixty seven percent of the patients had tachycardia. Fatigue, pain in the feet, anorexia,
and weight loss were found in 50%. Other presenting complaints or findings in 1 or 2 patients included
insomnia, tremor, back pain, headache, palpitations, generalized flushes, polydipsia, pruritis, and opis-
thonos. Clinical presentations suggested pheochromocyto-
ma. This possibility was eliminated before mercury levels were found to be elevated.

**DISCUSSION**

A syndrome simulating pheochromocytoma secondary to elemental mercury intoxication has been
reported in 6 children since 1984. In this article, we report 2 new patients with similar findings. Our 2
patients and the 6 additional patients found in the search of Medline have acrodynia. These children,
from 11 months to 17 years old, have in common hypertension, tachycardia, mental status changes,
and dermatologic abnormalities. Elevated catecholamines in plasma and urine were demonstrated.
Although the diagnosis of pheochromocytoma was considered in most, it was never confirmed. There was environmental elemental mer-
cury exposure and elevated urinary mercury excre-
tion was demonstrated. Antihypertensive medica-
tions were required and the symptoms improved with chelation. Warkany and Hubbard,8 in their se-
ries of 26 pediatric patients published in 1953, estab-
lished the link between acrodynia (erythematous rash of palms and soles, anorexia, fatigue, irritability,
apathy, photophobia, polydipsia, excessive sweat-
ing, and pain in extremities) and inorganic mercury exposure. Of interest in this article is the lack of any
discussion regarding the well-documented hyperten-
sion and/or tachycardia demonstrated in 21 of the 28 patients reported.

The cause of increased catecholamines in plasma and
urine can be traced to the ability of mercury to interfere with the normal catabolic processing of catecholamines via the cytosolic enzyme catechol-
amine-O-methyltransferase.9,10 Catecholamine-O-
methyltransferase requires the use of the methyl
group provided by coenzyme S-adenosylmethionine (SAM). SAM is also essential in the conversion
of norepinephrine to epinephrine. Mercury inactivates
SAM; as a consequence, norepinephrine, dopamine,
and epinephrine accumulate in the urine in increased
amounts where they can be detected. This catechol-
amine excess is responsible for the pheochromocyto-
ma-like syndrome.

Mercury, a heavy metal, exists in the environment in 3 forms: organic, inorganic, and elemental. It is
toxic in any of these forms.13 Neurological manifes-
tations involving the central nervous system are seen with chronic mercury intoxication. The largest out-
breaks of mercury toxicity have occurred with the
ingestion of fish and seafood contaminated with methyl mercury by industrial pollution14 and by the
consumption of grain for seeds treated with methyl
mercury.15 Accidental exposure to dimethyl mer-
cury, a supertoxic chemical, has caused fatalities in
laboratory personnel.16 In the past, mercury was
used in many approved medical products, including
antisyphilitic agents, diuretics, cathartics, topical
salves, teething compounds, and diaper powders,
resulting in outbreaks of mercurialism in the 1940s
and 1950s. These products are no longer used in the
United States. Acrodynia is typically caused by inor-
ganic mercury poisoning; however, as demonstrated
in our work, new cases are being reported from
exposures to elemental mercury through broken
thermometers6 or other sources. Elemental mercury,
a liquid at room temperature, vaporizes easily and is
able to be inhaled and absorbed by the alveolar
membrane, causing pulmonary symptoms that in-
clude shortness of breath, cough, chills, fever, and
radiograph findings consistent with pneumonitis.17
Other symptoms include lethargy, confusion, stoma-
titis, vomiting, and colitis. These symptoms abate in
~1 week or may progress to pulmonary edema and
death. Early in the disease this illness may be con-
fused with a viral respiratory infection or flu.

In 3 of the 6 cases from the literature, the mercury
exposure resulted from spillage of mercury from a
broken thermometer and the younger patients were
affected. Parents had no symptoms. In 1 case from
Brazil, the 17-year-old patient was exposed to el-
mental mercury in an occupational activity. In the
other 4 cases, including the 2 described by us, mer-
cury was brought homes by individuals who were
unaware of the risk involved.

Of interest in our patient 1 was the observation of
hemoconcentration. This confirms a similar observa-
tion reported by Henningsson3 in the description of
his patient. It seems that these children have intra-

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vascular and extracellular volume depletion. The finding of elevated renin level with normal aldosterone secretion further reinforces these impressions. Also, our patient demonstrated relative hyponatremia associated with an elevated fractional excretion of sodium. These findings are consistent with pressure natriuresis, with stimulation of dopamine receptors in the kidney.\textsuperscript{11,12}

**CONCLUSION**

We conclude that in a child with severe hypertension, altered mental status, dermatological abnormalities, and elevated catecholamines, clinicians should consider pheochromocytoma as well as elemental mercury intoxication. The health hazards of heavy metal need to be reinforced to the medical profession and the public at large.

**ACKNOWLEDGMENTS**

We thank Dr Brooks for the review of this manuscript, and Mindy Mobley for her technical support.

**REFERENCES**

Mercury Intoxication and Arterial Hypertension: Report of Two Patients and Review of the Literature
Alfonso D. Torres, Ashok N. Rai and Melissa L. Hardiek

Pediatrics 2000;105;e34
DOI: 10.1542/peds.105.3.e34

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