# CASE REPORT

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# Fatal Acute Selenium Toxicity

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**ABSTRACT:** Selenium is used widely in industry and as a dietary supplement. Reports of acute selenium toxicity are infrequent, however, and the relationship of toxicity to selenium concentrations in blood and tissues has not been established. We describe a patient who died eight days after ingesting selenious acid in the form of gun blueing. The patient's clinical course demonstrated many of the features of inorganic selenium toxicity described in animals; hypotension as a result of both vasodilation and decreased cardiac output, adult respiratory distress syndrome, severe myopathy which contributed to respiratory failure, and a garlicky odor to the breath. Four days after ingestion the serum selenium concentration was twenty times normal and urinary excretion seventy times normal. Postmortem tissue selenium concentrations were up to 40 times normal.

**KEYWORDS:** pathology and biology, selenium, death

Selenium is an essential trace element used widely in the electronics, steel, glass, and ceramics industries. It is estimated that approximately one million pounds of selenium are used in the United States annually. Over the past several years selenium has also been heavily promoted as a dietary supplement because of data suggesting that it may act as an inhibitor of chemical carcinogenesis [*1*]. Thus, exposure of humans to selenium is common.

Most reports of selenium toxicity in humans involve *chronic* exposure to organic selenium compounds in seleniferous plants or to inorganic selenium (sodium selenate, sodium selenite, selenious acid, and hydrogen selenide) in the workplace. Adverse effects from such exposure, with the exception of an increased incidence of dental caries, are poorly documented [*2,3*]. Experience with *acute* selenium toxicity is primarily limited to the inhalation of selenium dusts or fumes, which are respiratory tract irritants. The consequences of acute selenium ingestion in humans are largely unknown. Doses of inorganic selenium as low as 1 to 2 mg/kg, however, can be rapidly fatal in animals [*4-6*]. We describe a patient who died eight days after ingestion of selenious acid, whose clinical course demonstrated features of acute inorganic selenium toxicity similar to those reported in animals.

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**Case Report**

A 52-year-old female ingested between 30 and 60 mL of liquid gun blueing containing 2% selenious acid, 2% copper sulfate, and 10% methanol (estimated selenious acid dose 10 to 20 mg/kg), and possibly also unknown amounts of typewriter cleaner (perchloroethylene) and three preparations containing petroleum distillates (gun oil, sewing machine oil, and Liquid Wrench®). One hour later at a local hospital she was alert and without complaint but with blood pressure not palpable, heart rate 80 to 120 with a sinus rhythm, respirations 30, and temperature 36.5°C. She had several nonbloody emeses. Metabolic acidosis was noted (pH 7.27, $pCO_2$ 24, $HCO_3$ 12) and ethanol 1.0 gm/kg was administered orally for presumed methanol toxicity. After receiving 4 L of lactated Ringer's solution and 200 meq of sodium bicarbonate, the patient was trasferred to Hennepin County Medical Center. On arrival approximately 12 h after the ingestion, she was alert with systolic blood pressure 55, sinus tachycardia, and frequent ventricular premature beats. The chest was clear to auscultation, neck veins not elevated, and the cardiac examination normal. A garlicky odor was noted on the patient's breath as well as from the stool and emesis. Initial treatment included the intravenous administration of dopamine, lidocaine, normal saline, and sodium bicarbonate. Blood methanol concentration was less than 10 mg/dL, and no other drugs were identified in blood or urine by thin-layer chromatography (Toxi-lab A and B).

Over the next 24 h the patient's blood pressure stabilized at 110/70 without dopamine and the metabolic acidosis resolved. Because of the possibility of copper sulfate toxicity causing hypotension, the patient was given two doses of dimercaprol (BAL). Serum and urine copper concentrations were subsequently found to be only minimally elevated (Table 1) and dimercaprol was discontinued. Attempts to administer oral activated charcoal were limited by poor bowel motility.

Hypotension recurred on Day 2 with pulmonary artery wedge pressure 12 mmHg (normal 1 to 10), cardiac output index 2.0 L/min/$m^2$ (normal 2.5 to 4.2) and peripheral vascular resistance 0.0068 N/s-$cm^{-5}$ (680 dynes/s-$cm^{-5}$) (normal 0.0077 to 0.015 [770 to 1500]). Blood pressure was supported with dopamine. The patient was intubated 24 h after admission during an exacerbation of hypotension, and required assisted ventilation thereafter because of the development of adult respiratory distress syndrome. Cephazolin and tobramycin were administered when she became febrile. Sputum cultures grew mixed flora and blood cultures were negative. Pulmonary function was subsequently stable with the $pO_2$ between 50 and 70 mm Hg. Diffuse weakness and hyporeflexia were noted after one day, with nontender muscles and a normal sensory examination. The serum creatine kinase increased to a maximum of 11 200 IU/L on Day 4. Progressive thrombocytopenia was noted starting on Day 2 with platelets decreasing to 19 000/$mm^3$, white blood cells 5 500/$mm^3$ with a normal differential count, and hemoglobin 8.9 gm/dL with normal red blood cell morphology. The prothrombin time, partial thromboplastin time, and serum fibrinogen and haptoglobin concentrations were normal. A bone marrow biopsy was also normal, with adequate megakaryocytes. Shortened platelet survival was demonstrated by a decrease in platelet count from 65 000 to 33 000/$mm^3$ over 12 h after platelet transfusion. On Day 2, the patient developed mild abdominal discomfort with decreased bowel sounds and minimal tenderness. Mild renal insufficiency was noted with a maximum serum creatinine of 2.9 on Day 4. Urine output was normal. Forced diuresis could not be attempted because of the patient's pulmonary edema and hypotension. The serum aspartate aminotransferase concentration was increased but the alkaline phosphatase and bilirubin concentrations were normal.

On Day 8, the patient's abdomen became markedly distended. Exploratory laparotomy revealed extensive infarction of the entire small bowel. The abdomen was closed and the patient expired several hours later.

Postmortem examination confirmed acute small bowel infarction extending from the proximal duodenum to the distal ileum. Microscopically this showed a coagulative necrosis with minimal inflammatory reaction. The lungs were diffusely consolidated. Microscopic examina-

TABLE 1—*Laboratory values.*

| | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 | Day 7 | Day 8 | (Normal) |
|---|---|---|---|---|---|---|---|---|---|
| Hemoglobin, g/dL | 15.5 | 14.4 | 12.4 | 11.15 | 10.3 | 9.3 | 11.0 | 10.1 | (12-14) |
| White blood cells/mm$^3$ | 30 000 | 21 700 | ... | ... | 9 000 | 5 500 | 5 200 | 5 500 | (4 500-12 500) |
| Platelets/mm$^3$ | adequate | ... | 127 000 | ... | 29 000 | 19 000 | 18 000 | 33 000 | (150 000-350 000) |
| Prothrombin time, s | 13.9 | ... | 13.8 | 12.4 | 11.3 | 11.1 | 11.2 | 12.6 | (10.5-13.5) |
| Partial thromboplastin time, s | 35.7 | ... | 42.0 | 36.2 | 32.0 | 35.0 | 33.2 | 33.2 | (25-38) |
| Fibrinogen, mg/dL | ... | ... | ... | ... | 650 | 580 | 650 | ... | (150-320) |
| Haptoglobin, mg/dL | ... | ... | 122 | 176 | 234 | ... | ... | ... | (27-140) |
| Blood urea nitrogen, mg/dL | 26 | 29 | 29 | 36 | 31 | 39 | 48 | 54 | (8-24) |
| Creatinine, mg/dL | ... | 2.0 | 2.9 | 2.6 | 2.2 | 2.5 | 1.7 | 1.8 | (0.5-1.2) |
| Aspartate amino-transferase, IU/L | 66 | ... | 151 | 252 | ... | 123 | ... | 29 | (11-22) |
| Creatine kinase, IU/L | ... | 753 | 4 660 | 11 200 | 6 300 | ... | 1 530 | ... | (16-84) |
| %MB isoenzyme | ... | 2-5 | ... | 2-5 | 2 | ... | 2 | ... | (2) |
| Lactate dehydrogenase, IU/L | ... | 248 | 568 | 884 | ... | ... | ... | ... | (50-110) |
| Fraction 1, % | ... | 11 | 13 | 18 | ... | ... | ... | ... | (14-29) |
| Fraction 5, % | ... | 18 | 29 | 28 | ... | ... | ... | ... | (3-16) |
| Copper | | | | | | | | | |
| serum $\mu$g/dL | ... | 72 | 78 | 98 | 110 | 106 | ... | ... | (<60) |
| urine $\mu$g/24 h | ... | ... | 250 | ... | ... | ... | ... | ... | (70-140) |

TABLE 2—*Reports of acute selenium toxicity in humans.*

| Patient Age | Selenium Ingested | Clinical Course | Selenium Concentrations | Comment |
|---|---|---|---|---|
| 54-year-old female (current report) | selenious acid, 10 to 20 mg/kg in gun blueing | hypotension, pulmonary edema, myopathy, thrombocytopenia, death on Day 6 | serum (Day 4) 2435 ng/mL (normal 85 to 125 ng/mL)<br>(Day 5) 2765 ng/mL<br>urine (Day 4) 2435 μg/24 h (normal < 35 μg/24 h)<br>heart 3.36 μg (normal 0.004 to 0.083 μg/g) [2]<br>muscle 0.14 μg/g (normal 0.02 to 0.22 μg/g) [2]<br>liver 0.79 μg/g (normal 0.01 to 0.79 μg/g) [2] | also ingested copper sulfate, hydrocarbonds |
| 3-year-old male [8] | selenious acid, unknown amount, in gun blueing | stupor, respiratory depression, hypotension, death within several hours | gastric aspirate "high concentration" | |
| 15-year-old female [9] | sodium selenate, 22mg/kg | asymptomatic except nausea, flattened T waves on electrocardiogram, mildly elevated hepatic enzymes, resolved in 2 weeks | serum (Day 1) 3100 ng/mL<br>(Day 2) 200 ng/mL<br>(Day 3) 480 ng/mL<br>urine (Day 2) 680 ng/mL (total volume not stated)<br>(Day 4) 92 ng/mL<br>(Day 8) 108 ng/mL | emesis induced, amount retained may be less than amount ingested; treated with forced diuresis and dimercaprol |
| 17-year-old female with cystic fibrosis [10] | selenium yeast complex tablets 400 μg/day for 2 weeks | vomiting, decreased appetite, weight loss | urine 100 μg/24 h | |
| 5 adults ages 20 to 35 [14] | sodium selenite, 1 to 5 mg/kg | nausea, vomiting, mild abdominal pain, tremor, resolved in 24 h | serum (Day 1) 49 to 89 ng/ml (normal 20 ng/mL)<br>(Day 4) 14 to 19 ng/ml<br>urine (Day 1) 1170 to 4370 μg/24 h (normal 125 μg/24 h)<br>(Day 4) 31 to 508 μg/24 h | |

tion revealed diffuse pulmonary edema with intra-alveolar fibrinoid material, hyaline membranes, and hemorrhage compatible with the adult respiratory distress syndrome. The coronary arteries showed mild atherosclerosis. Cardiac muscle and skeletal muscle were normal. The liver showed centrilobular congestion. The kidneys showed a single area of papillary necrosis with coagulative necrosis. The bone marrow was normal.

Serum and urine selenium concentrations were collected from Day 4 on and postmortem tissue selenium concentrations measured by atomic absorption were greatly elevated (Table 2).

## Discussion

Although this patient ingested multiple compounds, it is likely that selenium toxicity was the main cause of her multiple complications and death. Copper sulfate can cause hypotension, but the amount ingested (10 to 20 mg/kg) was small and the serum and urine copper concentrations were much lower than those associated with systemic copper toxicity [*7*]. This patient's serum copper concentration was first determined 24 h after ingestion, and the serum copper concentration can decrease rapidly after copper sulfate overdose. However, the urine copper concentration remains high for up to two weeks and this patient's value on Day 2 was only minimally elevated. It is therefore unlikely that copper toxicity was an important contributor to the patient's clinical course.

The several hydrocarbons that this patient ingested were likewise probably unimportant since there was no initial evidence of aspiration, and respiratory insufficiency did not develop until more than 24 h after the ingestion. Moreover, hydrocarbons do not typically produce the systemic toxicity (described below) experienced by this patient. Massive selenium ingestion was confirmed by a serum selenium concentration 3 days after ingestion more than 20 times normal, and urinary selenium excretion 70 times normal (Table 2). The myocardial selenium concentration postmortem was approximately 40 times normal [*2*], and comparable to tissue concentrations reported in neonatal calves 24 to 48 h after a fatal dose of inorganic selenium [*4*]. Postmortem liver and muscle concentrations, however, were not elevated. While this could be due to the eight-day interval between ingestion and death, the reason for the discrepancy between these tissues and myocardium is not clear. Tissue selenium concentration in humans with acute selenium toxicity have not previously been reported.

Reports of acute selenium toxicity in humans are scarce and involve different forms of selenium (Table 2). The only previously reported death from selenium was also due to ingestion of selenious acid in the form of gun blueing. This patient was moribund when found and no information is available regarding the mechanism of death [*8*]. Postmortem examination was entirely unremarkable. One patient who ingested a large amount of sodium selenate (22 mg/kg) showed very little toxicity despite greatly elevated concentrations of selenium in serum and urine [*9*]. The maximum serum selenium concentration was in fact higher than that of our patient, but was measured much sooner after selenium ingestion. We are aware of no reports of acute toxicity from organic selenium compounds in humans, but one patient is described who developed symptoms and mildly elevated urinary selenium excretion after taking selenium yeast complex tablets for two weeks [*10*].

Several aspects of this patient's course are similar to those noted with acute inorganic selenium toxicity in animals (Table 3). The garlicky odor of expired air is due to the volatile metabolite dimethylselenide, and is characteristic of inorganic selenium ingestion [*6*]. Pulmonary edema is a frequent finding in animals with fatal selenium intoxication. Whether pulmonary edema is due to direct pulmonary injury or to cardiac failure is not known. Our patient first developed pulmonary edema two days after selenium ingestion and after several episodes of hypotension. Her pulmonary findings may have been caused by hypotension-induced adult respiratory distress syndrome, but a contribution from direct selenium toxicity is also possible.

TABLE 3—*Features of acute inorganic selenium toxicity in animals* [4,6,11].

| Clinical | Histology |
|---|---|
| Vomiting | Pulmonary edema |
| Diarrhea | Hepatic necrosis |
| Labored breathing | Skeletal muscle degeneration |
| Weakness | Renal tubular hydropic degeneration |
| Unsteady gait | Swelling and disruption of myocardial mitochondria |
| Coma | |

The patient's severe hypotension was found to be due to both decreased cardiac contractility and inappropriately low peripheral vascular resistance. Available animal studies of acute selenium toxicity do not report blood pressure. Cardiac histology is usually normal in animals examined by light microscopy after fatal doses of inorganic selenium, but injury to myocardial mitochondria has been noted with electron microscopy [*11*]. Disruption of vascular integrity had also been noted [*4-6*] and could have contributed, together with cardiac injury, to hypotension in this patient.

A distinctive feature of this patient's course was profound muscular weakness severe enough to contribute to respiratory failure and associated with elevated serum creatine kinase concentrations. Postmortem examination of muscle, however, was entirely normal. Degenerative changes of skeletal muscle in animals with selenium toxicity have been described [*6*], but normal muscle histology has also been noted even in animals with marked weakness [*4*]. Thus, the clinical and histologic findings in our patient are consistent with selenium-induced myopathy. The possibility of rhabdomyolysis was also considered, but the degree of weakness observed was probably greater than would be expected for rhabdomyolysis producing a serum creatine kinase concentration of only 11 000 IU/L.

Thrombocytopenia has not been previously noted in either humans or animals with acute exposure to selenium. Bone marrow examination of this patient revealed normal numbers of megakaryocytes, and platelet survival following transfusion was shortened, suggesting that thrombocytopenia was due to platelet destruction or sequestration. Thrombocytopenia in this patient could have been secondary to the adult respiratory distress syndrome rather than selenium toxicity. Thrombocytopenia as a result of the adult respiratory distress syndrome, however, is usually less severe than was seen in this patient [*12*]. The only other previously reported hematologic abnormality associated with inorganic selenium toxicity in animals is a mild hemolytic anemia observed with chronic dosing [*13*].

Bowel infarction in this patient was probably a result of repeated episodes of hypotension. No evidence of caustic injury to the gut mucosa was found at postmortem examination. Renal insufficiency was most likely due to hypotension, since renal histology was normal.

Few data are available regarding the pharmacokinetics of inorganic selenium in humans. In animals given therapeutic doses, 50 to 60% of the administered dose is excreted within twelve days; 80% in urine, 15% in feces, and the remainder in expired air. With toxic doses, up to 50% may be excreted as dimethylselenide via the lungs [*2*]. No satisfactory treatment for selenium toxicity is available. The chelating agent calcium disodium edetate is useful in animals, but only if given within 15 min of the selenium dose [*5*]. Arsenic administration enhances selenium excretion but its toxicity precludes clinical use [*2*]. Forced diuresis to enhance urinary selenium excretion or the use of an oral sorbent to enhance fecal excretion and prevent reabsorption from the gastrointestinal tract have not been evaluated, but merit consideration. The potential value of these interventions will depend upon how much of an ingested dose is excreted unchanged and whether any selenium metabolites excreted by these routes contribute to its toxicity.

## Conclusion

In summary, we describe a patient who ingested a large amount of selenious acid and developed hypotension, pulmonary edema, weakness, and thrombocytopenia leading to death eight days later. These findings suggest that selenious acid has toxicity in humans similar to that seen with inorganic selenium salts in animals, and that toxicity may be fatal. Whether organic selenium, as is contained in most dietary selenium supplements, shares this potential for toxicity is not known.

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