

**Case Report**

# Blood, Urine, and Hair Kinetic Analysis Following an Acute Lead Intoxication

G. Ho<sup>1,\*</sup>, A. Keutgens<sup>1,\*</sup>, R. Schoofs<sup>2</sup>, S. Kotolenko<sup>2</sup>, R. Denooz<sup>1</sup>, and C. Charlier<sup>1,†</sup>

<sup>1</sup>Service de Toxicologie Clinique, Médicolégale, Environnementale et en Entreprise, Centre Interfacultaire de Recherche du Médicament, ULg, Centre Hospitalier Universitaire Sart-Tilman B35, B-4000 Liège, Belgium and <sup>2</sup>Centre Hospitalier Régional de la Citadelle, B-4000 Liège, Belgium

**Abstract**

A case of lead exposure resulting from the accidental ingestion of a lead-containing solution is reported. Because of clinical management rapidly performed through chelation therapy by 2,3-dimercaptopropane sulfonate sodium and meso-2,3-dimercaptosuccinic acid, blood lead levels of this 51-year-old patient were moderate (412.9 µg/L) and no clinical symptoms were observed. Numerous blood and urine samples were collected for kinetic analysis of lead elimination. However, we report the first case in which hair samples were analyzed to determine the excretion level of lead after acute intoxication.

**Introduction**

Lead is a natural, soft, blue-gray metal. Intoxication with this compound is a great public health problem. Nowadays, lead poisoning can be due to environmental (pollution and industries), occupational, or accidental exposure. Indeed, lead-based industry, fuel, paints, drinking water, food, handmade pottery used as food or beverage storage, cosmetics, or traditional medicine (Mexican or Asian remedies) are potential sources of contamination by ingestion or inhalation (1).

Toxic levels of lead affect the nervous, hematopoietic, and renal systems. The classical symptoms of acute intoxication are very general and nonspecific and include nausea, vomiting, gastrointestinal pain, renal dysfunction (with proteinuria, glycosuria, and hyperphosphaturia), and convulsions. After chronic exposure, in addition to those gastrointestinal and renal symptoms, cardiovascular effects (hypertension), endocrine effects (fertility, pregnancy outcomes), developmental effects (congenital abnormalities), neurological symptoms es-

pecially important for children even with lower blood lead levels (concentration deficiency, decreased verbal ability, irritability, changes in consciousness, encephalopathy), and hematological effects (anemia through inhibition of three enzymes involved in heme synthesis) can occur. Paresis, paralysis (wrist drop), and formation of a bluish line along the gums (Burton's line) can also be observed. All these signs of lead intoxication are commonly referred to as "Saturnism symptoms". Lethal poisoning from the ingestion of lead is rare but not impossible (2–4).

In this case report, we describe the case of an asymptomatic 51-year-old woman who had accidentally ingested a lead-containing solution.

**Case History**

A 51-year-old woman was working in the family garage. She told us that she was thirsty, and she picked up a bottle of water in a corner and drank 100 mL of the content at 12:00 a.m. Because of the bitter taste, she realized after a few gulps that the transparent liquid was not drinking water but a lead acetate-containing solution used to treat dermatological affections of horses. She then was transported by emergency services to the local hospital. A preliminary examination of the patient revealed no signs of lead intoxication; she was totally asymptomatic. X-rays of the abdomen did not reveal any opacity. A venous blood sample was taken at 1:37 p.m. on that day (day 0) and submitted to the laboratory for lead analysis. Eight supplementary blood samples were drawn at 9:30 p.m. (day 0), 5:30 a.m. (day 1), 1:30 p.m. (day 1), 1:30 p.m. (day 2), 1:30 p.m. (day 3), 1:30 p.m. (day 4), 1:30 p.m. (day 6), and 1:00 p.m. (day 7). Moreover, urine samples were collected at 9:30 p.m. (day 0), 5:30 a.m. (day 1), 1:30 p.m. (day 1), 1:30 p.m. (day 2), 1:30 p.m. (day 3), 1:30 p.m. (day 4), 1:30 p.m. (day 5), 2:52 p.m. (day 6), and 1:00 p.m. (day 7). At 6:00 p.m. (day 0), chelation therapy

\* These authors contributed equally to this work.

† Author to whom correspondence should be addressed. Email: c.charlier@chu.ulg.ac.be.

was performed. On day 7, because she was still asymptomatic with stabilized blood and urine lead levels, the patient was allowed to go home with oral chelators. A follow-up was performed on two last blood and urine samples taken on day 24 and 2 months (day 55) after the intoxication.

Furthermore, two hair samples were collected, the first at the time of the intoxication, and the second three months after the ingestion of the lead-containing solution.

## Materials and Methods

The analysis was performed on an Agilent 7500a ICP-MS (Agilent Technologies, Santa Clara, CA) equipped with an autosampler (CETAC Technologies, Omaha, NE). Optimization of the instrument's operating parameters was effected by means of a tuning solution containing the elements cerium, cobalt, lithium, thallium, and yttrium (Agilent Technologies).

### Reagents

Injectable water was obtained from Baxter (Lessines, Belgium); HNO<sub>3</sub> 65%, *n*-butanol dichloromethane, and Triton X-100 were purchased from VWR (West Chester, PA). Solutions of germanium (1000 mg/L), rhodium (1000 mg/L), and scandium (1000 mg/L) used as internal standards were from VWR, as were the Lead ICP Standard CertiPur and the Multielement Standard Solution IV CertiPur used for the calibration curves.

### Patient samples

Urine samples were collected in plastic bottles. Total volume excreted was measured and recorded for each urine specimen. All whole blood samples were collected in Vacutainer tubes containing sodium heparin anticoagulant (Vacurette, Greiner Bio-One, Kremsmünster, Austria). Specimens were stored at 4°C. Both urine and whole blood samples were mixed thoroughly before taking aliquots.

Hair samples were collected from the nape of the neck the day of the contamination (5-cm length) and three months later (8-cm length). Hair was decontaminated with dichloromethane under ultrasonication (2 × 5 min). Before

analysis, each individual hair sample was cut into approximately 1-cm pieces, weighted (10 mg), and mineralized in polypropylene tubes with 250 µL of 65% HNO<sub>3</sub> at 70°C for 60 min. Before testing, the residue was diluted to 8 mL with 0.1% HNO<sub>3</sub> (5,6).

### Certified controls

Quality control materials were purchased from Seronorm (Trace Elements whole blood control, SERO, Billingstad, Norway) and Bio-Rad (Lyphochek urine metals control, Bio-Rad Laboratories, Diagnostic Group, Hercules, CA).

### Calibrator and sample preparation

Calibrators for blood analysis were prepared at Pb concentrations of 0, 25, 50, 100, 250, 500, and 1000 µg/L by spiking into whole blood from a nonexposed subject. Calibrators for urine analysis were prepared at Pb concentrations of 0, 12.5, 25, 50, 100, and 200 µg/L by fortifying urine from a nonexposed subject. Calibrators for hair analysis were prepared at Pb concentrations of 0, 0.5, 1, 10, 25, 50, 100, 200, and 500 ng/mg of hair in 0.5% HNO<sub>3</sub>.

Five-hundred microliters of blood, urine, or mineralized hair sample, control, or calibration standard was mixed with 100 µL of internal standard (mix of equal proportions of Ge, Rh, and Sc solutions at 500 µg/L) and diluted in 4500 µL of 0.5% HNO<sub>3</sub>, 0.2% *n*-butanol, and 0.1% triton (blood determination) or in 4500 µL 0.5% HNO<sub>3</sub> (urine and hair determination). The final mix was then ready for Pb determination.

## Results

The blood and urine lead levels were assessed by ICP-MS, and the data are shown in Table I. Figures 1 and 2 demonstrate the graphical display of lead concentration in blood and urine samples, respectively.

One and one-half hours after lead ingestion, the subject's blood lead concentration was 244.7 µg/L and doubled 9 h 30 min later. The chelation therapy was started approximately 6 h after ingestion. During the first 24 h of chelation, 2,3-dimer-

**Table I. Values of Blood and Urine Lead Concentrations in Relation to the Time after Ingestion\***

	Day 0		Day 1		Day 2 49.5 h	Day 3 73.5 h	Day 4 97.5 h	Day 5 121.5 h	Day 6 145.5 h	Day 7 169 h	Day 24 600 h	Day 55 1344 h
	1.6 h	9.5 h	17.5 h	25.5 h								
PbB (µg/L)	244.7	412.9	347.7	278.6	254	240.6	208.8		142.2	155.2	31.93	38.34
PbU (µg/L)		642	271	980	378	143	91	85	86	73	21	
PbU (µg/g creatinine)		878.9	166.3	1440.9	858.6	366.9	240.1	235.6	330.8	236.7	26.4	
PbU (µg/24 h)		1926	813	2940	378	143	91	85	81.4	79.1		
Creatinine (g/L)		0.73	1.63	0.68	0.44	0.39	0.38	0.36	0.26	0.31	0.81	
Diuresis (mL)		650	200	750	2950	3250	3000	3250	3600	3600		

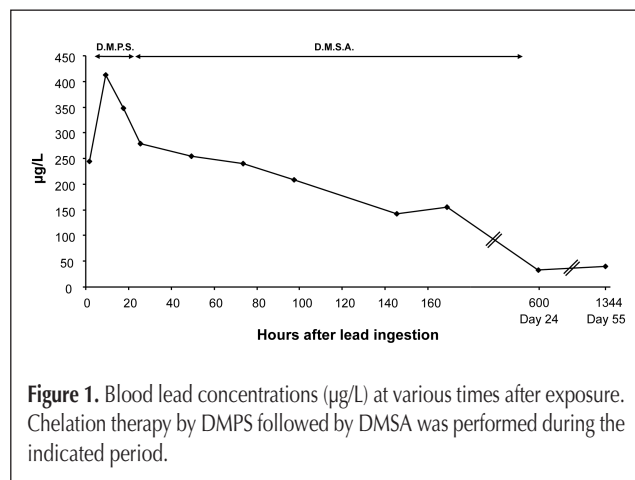
\* Normal range of lead concentration in blood: < 100 µg/L and in urine: < 25 µg/g creatinine.

captrop propane sulfonate sodium (DMPS) was administered intravenously (250 mg every 4 h). On the following day, the patient was given 600 mg of succimer (meso-2,3-dimercaptosuccinic acid, DMSA) orally. At this moment, the blood lead concentration was 278.6  $\mu\text{g/L}$ . The chelation therapy by succimer was carried on (600 mg every 8 h orally) during the rest of the hospitalization and blood lead levels continued to decrease progressively. After 7 days, the patient was allowed to go home, but the chelation treatment by DMSA (600 mg orally twice per day) was carried on at home for 16 days. Blood and urine samples taken on this day (day 24) were at a lead concentration usually found in the general population justifying thereby the cessation of the chelation therapy, such as the blood and urine samples taken two months after the intoxication.

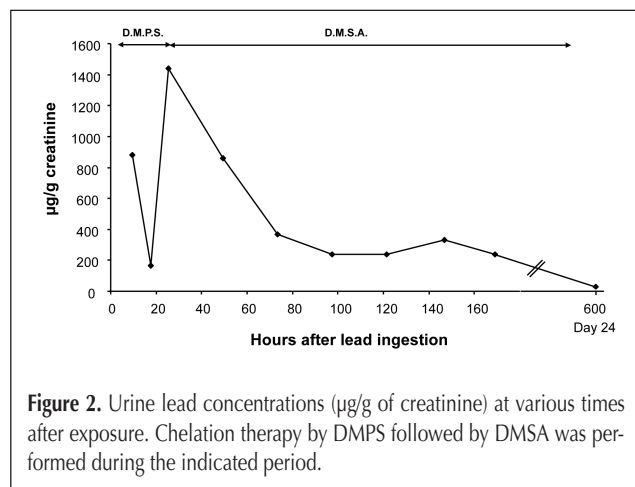
The hair lead concentrations were also assessed by ICP-MS. Interestingly, no significant differences were observed within the various 1-cm pieces with lead values included between 2 and 5 ng/mg of hair (Table II). These concentrations are typical for the general population (5).

## Discussion

Lead intoxication in humans can have environmental, oc-



**Figure 1.** Blood lead concentrations ( $\mu\text{g/L}$ ) at various times after exposure. Chelation therapy by DMPS followed by DMSA was performed during the indicated period.



**Figure 2.** Urine lead concentrations ( $\mu\text{g/g}$  of creatinine) at various times after exposure. Chelation therapy by DMPS followed by DMSA was performed during the indicated period.

cupational, or accidental origins. The first cause of lead contamination in the general population is ingestion of contaminated food, water, or alcohol for adults and via hand-to-mouth activity for children. The second major pathway of exposure is inhalation, especially for workers in lead-based industries or adults involved in home renovation activities. Injured skin absorption or parenteral injection with rifle pellets are also potential ways of poisoning (1). Lead absorption is more problematic for two groups: pregnant women, because of the potential for neurological problems in the fetus, and young children, because neurological symptoms occur at lower exposure levels.

Generally, approximately 20% of the inorganic ingested lead is absorbed in the adult human body and is distributed into three compartments (7): blood (2%), soft (3%), and mineralizing tissues (95%). In blood, lead is principally found in erythrocytes (99%), with the remainder (1%) being in blood plasma; consequently, blood lead level analysis must be carried out on whole blood. Soft tissues like liver, lungs, brain, spleen, muscles, heart, and predominantly kidneys are targeted with a maximal concentration reached after 1 h of intoxication. Mineralizing tissues (bones and teeth) contain the lead body burden. The release of lead from bones to blood, soft tissues, and hair is slow. The rate of excretion of lead is low. Urinary excretion accounts for 76% of daily losses, whereas gastrointestinal secretions account for 16%, and hair, nails, sweat, and other routes account for 8% (1).

In our case, lead analysis confirmed the accidental ingestion of the toxic element. The first sample, taken only 1 h 30 min after intoxication, showed a blood lead level of 244.7  $\mu\text{g/L}$ . In this concentration range (200–440  $\mu\text{g/L}$ ), the Belgian Poison Control Center recommends a second blood lead level analysis (8). The second sample, drawn 9 h 30 min after the lead ingestion, revealed a significantly higher lead level of 412.9  $\mu\text{g/L}$

**Table II. Values of Hair Lead Concentrations in Various 1-cm Pieces of Hair on the Day of Intoxication and Three Months Later\***

	1-cm Pieces	Lead Concentration (ng/mg hair)
Day 0	Piece 1	2.80
	Piece 2	3.14
	Piece 3	3.75
Day 90	Piece 1	1.16
	Piece 2	2.09
	Piece 3 <sup>†</sup>	2.51
	Piece 4	3.08
	Piece 5	3.37
	Piece 6	3.41
	Piece 7	3.76
	Piece 8	5.02

\* Values in the general population: 0.15–6.13 ng/mg of hair (5).

<sup>†</sup> The section corresponding to the time of intoxication.

justifying the chelation therapy started a few hours previously. Actually, at this early time, lead resides mainly in the blood compartment where it can be easily chelated and removed before distribution to bones where it becomes a chronic source of exposure for the patient. Other acute lead intoxications were previously reported, but the blood levels described were higher, and clinical symptoms were reported: 560 µg/L (9); 570 µg/L (10); 1124 µg/L (11); 850, 1090, and 2590 µg/L (4); 1230 µg/L (12); 1290 µg/L (13); and 4227 µg/L (14). However, the analysis of blood lead kinetics is rare and usually determined only on a few samples during a limited period of chelation.

Moreover, urinary lead excretion is a good marker for recent lead exposure and for patients who underwent chelation therapy. In this case report, we had the opportunity to analyze on many urine samples, more than in other case reports (4,14). Furthermore, δ-aminolevulinic acid (ALA) excretion and δ-aminolevulinic acid dehydratase (ALA-D) enzymatic activity are also good markers for recent exposition but may fluctuate and are less reliable. Hair analysis could also reflect a lead intoxication (15,16), but no one has yet evaluated the hair excretion three months after exposition. In our case, the lead levels were between 2 and 5 ng/mg of hair at the moment of intoxication. These concentrations are usual in the general population and demonstrate that the patient was non-exposed to lead before. Three months later, no peak of lead excretion was observed in the different 1-cm pieces of hair, especially in the section corresponding to the moment of intoxication and the lead values were also included between 2 and 5 ng/mg of hair. The chelation therapy performed early after the intoxication can therefore explain these results.

Chelation therapy should be considered in cases with blood lead levels > 450 µg/L in symptomatic patients and > 800 µg/L in asymptomatic patients. Nevertheless, blood levels between 250 and 450 µg/L could also lead to chelator treatment (17). According to the recent guidelines, intravenous chelation therapy with a single CaNa<sub>2</sub>EDTA or in combination with dimercaprol should be applied in acute phase of lead intoxication (18) followed by orally administered succimer if needed (12). Intensive intravenous chelation therapy in early phase of acute intoxication is crucial for the patient's outcome and for the prevention of organ dysfunction. Because the blood lead concentration was unknown 6 h after ingestion and the patient presented a chronic vitamin D deficiency, which can dramatically increase the absorption of ingested lead (up to 50%), she was chelated by intravenous DMPS, a derivative from dimercaprol used for serious intoxication, in prevention of a massive intoxication during the first 24 h. The chelation therapy was followed by oral succimer during 23 days. Succimer is usually administered to patients with moderate blood lead level and is also used in serious lead intoxication following a first treatment with dimercaprol or edetate disodium calcium. The third blood sample, taken approximately 17 h after the accidental ingestion, showed a slight decrease of the lead level (347.7 µg/L), and 24 h after the admission, the blood lead level was reduced to 278.6 µg/L, a relatively moderate level, which showed that the chelation treatment was effective. After seven days, the blood and urine lead levels were well decreased, and patient was discharged home with oral succimer. A follow-up analysis was

performed at day 24 and 2 months after intoxication and revealed blood lead levels at concentrations usually found in the general population.

Moreover, the urine lead concentration, 24 h after the patient admission, revealed a high peak of lead excretion (1440.9 µg/g creatinine) demonstrating the efficiency of the chelation therapy to eliminate the absorbed lead.

In conclusion, with more than 10 blood as well as urine samples taken from the patient, this is the first paper reporting such a long kinetic profile both for blood and urine lead levels. These results demonstrate also the high efficiency of a chelation therapy started early after the ingestion of toxic metals.

Moreover, we can assume that chelation treatment is very important since lead dispersion into skeletal compartment seems to be avoided, as suggested by hair results three months after acute ingestion.

The primary management to lead poisoning is identification of the source and cessation of further exposure. In this case report, the patient had ingested accidentally a lead-containing solution. The current European standard, established in December 2003, for lead content in drinking water is < 25 µg/L, and this parametric value will be reduced to < 10 µg/L in December 2013 (19). Belgium adopted the lead parametric value of < 10 µg/L in 2002 (20). In the past, food contamination (fruits, vegetables, wine, milk, etc.) occurred mainly through contaminated soils with the use of lead in gasoline. Effectively, at the beginning of the 1980s, an adult ingested 56 µg of lead per day through alimentation; however, because lead is now banned from use in gasoline, this ingestion has been progressively reduced.

Finally, it is important to insist and to encourage the general population not to store toxics and poisons in vessels usually used for food or beverages and principally to avoid drinking or eating unknown liquids or substances.

## References

1. Agency for Toxic Substances and Disease Registry. Case Studies in Environmental Medicine: Lead Toxicity Course WB 1105, <http://www.atsdr.cdc.gov> (accessed March 2010).
2. N. Forsby, B. Fristedt, and B. Kjellman. Acute, lethal poisoning after ingestion of metallic lead. *Acta Paediatr. Scand.* **Suppl. 177**: 107 (1967).
3. C.D. Hugelmeyer, J.C. Moorhead, L. Horenblas, and M.J. Bayer. Fatal lead encephalopathy following foreign body ingestion: case report. *J. Emerg. Med.* **6(5)**: 397–400 (1988).
4. R.J. Roberge, T.G. Martin, B.S. Dean, and R.W. Lasek. Ceramic lead glaze ingestions in nursing home residents with dementia. *Am. J. Emerg. Med.* **12(1)**: 77–81 (1994).
5. P. Kintz, M. Ginet, and V. Cirimele. Multi-element screening by ICP-MS of two specimens of Napoleon's hair. *J. Anal. Toxicol.* **30(8)**: 621–623 (2006).
6. A. Le Bouil, M. Avenel-Audran, A.-M. Bourgeois, J.-L. Verret, and P. Allain. Chronic arsenic poisoning. *Ann. Toxicol. Anal.* **13(3)**: 182–185 (2001) (in French).
7. M.B. Rabinowitz, G.W. Wetherill, and J.D. Kopple. Kinetic analysis of lead metabolism in healthy humans. *J. Clin. Invest.* **58(2)**: 260–270 (1976).
8. Centre Antipoisons. Intoxication au Plomb, <http://www.poisson-centre.be> (accessed March 2010).

9. R.G. Treble and T.S. Thompson. Elevated blood lead levels resulting from the ingestion of air rifle pellets. *J. Anal. Toxicol.* **26(6)**: 370–373 (2002).
10. P.E. McKinney. Acute elevation of blood lead levels within hours of ingestion of large quantities of lead shot. *J. Toxicol. Clin. Toxicol.* **38(4)**: 435–440 (2000).
11. S. Sabouraud, F. Testud, J. Descotes, M. Benevent, and G. Soglu. Lead poisoning following ingestion of pieces of lead roofing plates: pica-like behavior in an adult. *Clin. Toxicol. (Phila)*. **46(3)**: 267–269 (2008).
12. J.L. VanArsdale, R.D. Leiker, M. Kohn, T.A. Merritt, and B.Z. Horowitz. Lead poisoning from a toy necklace. *Pediatrics* **114(4)**: 1096–1099 (2004).
13. A. Patel and A.M. Athawale. Acute lead encephalopathy with optic neuropathy. *Indian Pediatr.* **42(2)**: 188–189 (2005).
14. J. Mikler, P. Banovcin, M. Jesenak, J. Hamzikova, and D. Statelova. Successful treatment of extreme acute lead intoxication. *Toxicol. Ind. Health* **25(2)**: 137–140 (2009).
15. H.I. Afridi, T.G. Kazi, N. Kazi, M.K. Jamali, M.B. Arain, N. Jalbani, J.A. Baig, and R.A. Sarfraz. Evaluation of status of toxic metals in biological samples of diabetes mellitus patients. *Diabetes Res. Clin. Pract.* **80(2)**: 280–288 (2008).
16. T.G. Kazi, N. Jalbani, N. Kazi, M.B. Arain, M.K. Jamali, H.I. Afridi, G.A. Kandhro, R.A. Sarfraz, A.Q. Shah, and R. Ansari. Estimation of toxic metals in scalp hair samples of chronic kidney patients. *Biol. Trace Elem. Res.* **127(1)**: 16–27 (2009).
17. L. Labat and M. Lhermitte. Sources, exploration and clinical management of lead intoxication. *Rev. Francophone Lab.* **2007(390)**: 45–49 (2007) (in French).
18. A.D. Woolf, R. Goldman, and D.C. Bellinger. Update on the clinical management of childhood lead poisoning. *Pediatr. Clin. North Am.* **54(2)**: 271–294, viii (2007).
19. Council Directive 98/83/CE on the Quality of Water Intended for Human Consumption. EU, 1998 (in French).
20. Royal Decree on the Quality of Water Intended for Human Consumption, Packaged, or Used in Food Establishments. Belgium, 2002 (in French).

Manuscript received April 2, 2010;  
revision received June 10, 2010.