

# Thallium intoxication

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## Abstract

We report a rare case of serious voluntary intoxication by laboratory thallium monobromate combined with alcohol intake by a 24-years old man. The diagnosis of thallium intoxication was based on history, nonspecific but typical clinical symptoms including gastrointestinal complaints, painful polyneuropathy, alopecia, and confirmed by the finding of increased thallium concentration in the urine. The treatment, performed at the due time, consisted of decontamination of the stomach by irrigation, administration of active charcoal and Prussian blue, correction of water and mineral dysbalance, symptomatic treatment, and led to complete recovery.

## INTRODUCTION

Thallium intoxication occurred frequently as a complex clinical injury caused by contact with rodenticides and the use of rodenticides containing thallium have been abandoned in many countries. Thus, in Slovakia, the thallium intoxication has not occurred since 30 years (personal communication, data from National toxicological information centre, Slovakia).

Thallium is a heavy metal. Together with indium, gallium, aluminium and boron it constitutes the 13<sup>th</sup> group of the periodic table. In the past, thallium was used first of all as a rodenticide. Presently, its usage for this purpose is banned in many countries because of numerous unintentional accidental intoxications. The element also ceased to be used in the treatment of syphilis,

gonorrhoea, tuberculosis and trichophytosis infection. Thallium is further used in the production of optical lenses, in institutions for gamma radiation, as part of tungsten filaments in light bulbs and as a component of artistic paints. It is also added to gildings because of its anticorrosive effect. In medicine, it is used in the perfusion scintigraphy of myocardium and in the detection of some malignant tumours (Mercurio-Zappala 2007; Blain & Kazantzis 2014).

The normal physiological function of thallium in humans and animals is unknown. Intoxication with thallium can occur in melting plants, when cleaning and maintaining pipes and air chimneys during inhalation or skin contact, and by ingestion when using cocaine, heroin or herbal products which are contaminated with thallium. Even in the present day, cases of criminal and also uninten-

tional poisonings with rodenticides (especially in developing countries) (Mercurio-Zappala 2007) are known. After every type of exposure to thallium, its quick and almost total absorption occurs. Over the course of several hours, the element gathers first of all in organs well perfused with blood, particularly in the kidneys, liver and brain (Smith & Doherty 1964).

In biological pairing, thallium imitates potassium. In lower concentrations, it has stimulation effects on enzymes depending on potassium. However, higher concentrations of thallium cause its inhibition. The key mechanisms of the toxic effect of thallium seem to be inhibitions of pyruvate-kinase, succinate-dehydrogenase, Na/K-ATPases, disturbance of depolarization of muscle fibres and increased oxidation stress after disturbance of glutathione metabolism (Britten & Blank 1968; Villaverde & Verstraeted 2003; Galván-Arzate & Santamaria 1998). Elimination of thallium begins 24 hours after ingestion. The biological half-life of thallium in humans is 30 days (Gastel 1978). Due to the long duration of the elimination phase, thallium is classified as a cumulative poison. The cause of slow elimination of thallium is its big distributive volume. The main methods of elimination are via stool and urine. Besides these, thallium is then excreted from the organism via saliva, tears, hairs and nails (Cvjetko *et al.* 2010).

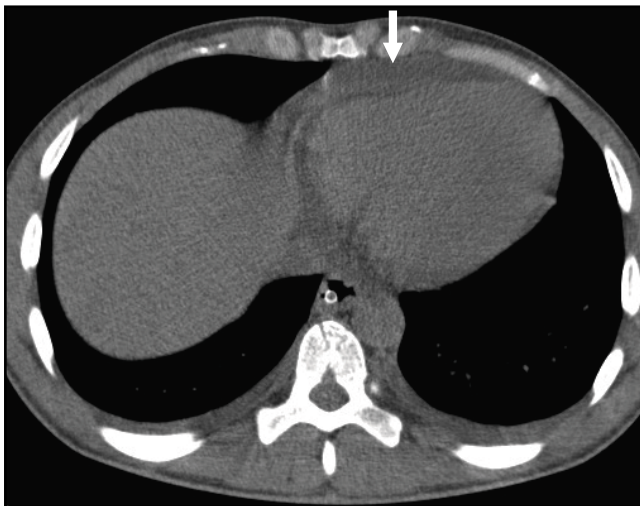
The initial clinical symptoms of acute intoxication are gastrointestinal complaints. Later, symptoms and signs of alteration of the nervous system, cardiovascular system, respiratory system, kidney and skin appear (Mercurio-Zappala 2007). After chronic exposure, the gastrointestinal symptoms are missing and signs of damage of the peripheral nervous system are predominant (Cvjetko *et al.* 2010).

The diagnosis of thallium intoxication is based on proof of its increased concentration in urine (more than 7–10 µg/l) (Blain & Kazantzis 2014). Immediately after ingestion, the presence of thallium in the digestive tract can be proven by X-ray examination of the abdomen. Thallium intoxication can also be proven in hair tips, where a black pigment appears. (Gerdtz 1974)

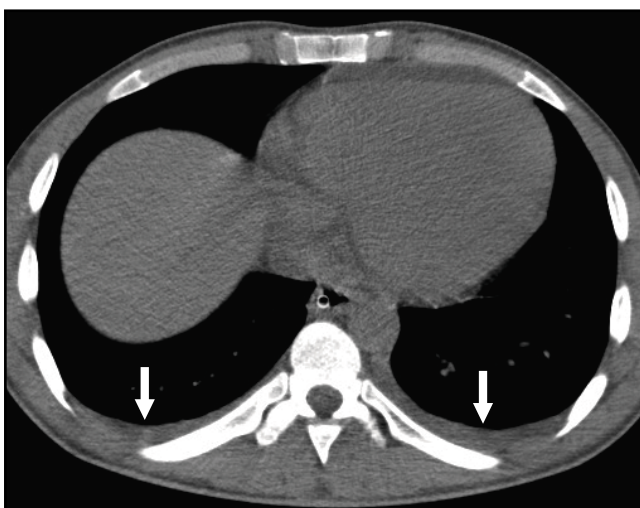
Treatment consists mainly of detoxication by gastric lavage, administration of activated charcoal and administration of Prussian blue (in doses of 250 mg/kg of body weight, 2–4 doses daily), which is presently considered the most effective chelating substance for thallium intoxications (Stevens 1974). Data on the effectiveness of other antidotes (penicillamine, diethyldithiocarbamate) are discrepant. Moreover, in cases of their administration, deteriorated brain functions were described (Alarcón-Segovia *et al.* 1989; Kamerbeek *et al.* 1971). Extracorporeal elimination methods, administered simultaneously with the medical treatment, can be effective in early stages, mainly in patients with renal failure and expected lethal intoxication (Riyaz *et al.* 2013; Ghannoum *et al.* 2012). Symptomatic treatment is important, especially in painful paraesthesia and obstipation.

## CASE REPORT

A 24 years old patient, a student of faculty of natural sciences, without history of somatic diseases was admitted to the 1<sup>st</sup> Department of Internal Medicine, Dérer Memorial Hospital, University Hospital of Bratislava, due to repeated short-time disturbances of consciousness after drinking 0.1 dcl of alcohol (spirits) in combination with approximately 100 mg of thallium monobromide. He evaluated his behaviour as being a rash action, and had not realized all the effects of the substance. His complaints were painful paraesthesia of the legs and deterioration of long-lasting depression, due to which he repeatedly took part in psychological sessions. The objective finding at the admission was boundary but with normal values of blood pressure (140/75 mm Hg). The values of blood count, biochemistry and haemocoagulation were also normal. Due to obvious toxicological anamnesis and painful paraesthesia of the legs, the specific therapy was started. It consisted of Prussian blue in total daily dose of 250 mg/kg of body weight, penicillamine in total daily dose of 1200 mg, in combination with non-specific elimination therapy (active charcoal in dose of 1 g/kg of body weight, lactulosis and forced diuresis) started within 8 hours after admission. After a worsening painful paraesthesia appeared, vitamins of the B group, analgesics and anticonvulsants were administered. The toxicological analysis of the urine showed a concentration of thallium 100 times higher than upper limit of normal value (Table 1). On the day 3, sinus tachycardia with a frequency of 130/min occurred. Echocardiographic examination showed the bicuspid aortic valve with medium aortic regurgitation and pericardial effusion of 150–200 ml, located mainly before the right ventricle. CT scan of the chest confirmed pericardial effusion and revealed pleural effusion (Figures 1 and 2). The effusions receded over the course of the next 10 days. From the day 4 on, the patient suffered from stubborn obstipation up to paralytic ileus (Figure 3), treated by administration of synthostigmine (subcutaneously 0.5 mg 3× daily), 20% of mannitol solution (i.v. 100 ml twice a day) and lactulosis clysmata (3 times a day). A nasogastric probe was introduced. Normalization of intestinal peristalsis appeared on the 10<sup>th</sup> day. The neuropsychiatric symptomatology consisted in delirium, paleocerebellar syndrome and symptoms of the frontal lobes damage which required psychiatric drugs and antidepressants to be administered. The CT examination of brain was normal. In the course of 9 days, delirium and paleocerebellar symptomatology subsided, but anxious depression and affective irritability together with psychomotor unrest and insomnia increased. A clinically unapparent partial atrophy of the optical nerve was found by ophthalmoscopy. Further, skin alterations appeared: acute cheilitis at week two, diffuse alopecia at week three, and, at week four, seborrheic dermatitis of the face and microbial eczema of the hands (Figures 4 and 5).



**Fig. 1.** Computer tomography. Pericardial effusion.



**Fig. 2.** Computer tomography. Pleural effusion.



**Fig. 3.** Computer tomography. Marked meteorism of transverse colon.

After 30 days of hospitalization and stabilization of the somatic status, the treatment with Prussian blue and penicillamine was terminated. Due to persisting mixed



**Fig. 4.** Diffuse alopecia.



**Fig. 5.** Microbial eczema of the hands.

anxious depression, we transferred the patient to the Psychiatric Clinic. Follow-up examinations should take place after six months. However, the relatives refused the contact with the patient because of the harrowing experience, and confirmed that he had no serious persistent problems except alopecia.

## DISCUSSION

Thallium intoxication is a rare poisoning in developed countries. The most common cases are intentional or suicidal poisonings. They are more frequent in devel-

**Tab. 1.** Urinary excretion of thallium during first week of hospitalisation.

day of hospitalisation	urinary excretion of thallium
3 <sup>rd</sup>	1450 µg/l (4220 µg/24 hours)
6 <sup>th</sup>	1240 µg/l (4840 µg/24 hours)
7 <sup>th</sup>	601 µg/l (1440 µg/24 hours)

oping countries where rodenticides containing thallium are still in use (Blain & Kazantzis 2014). In Slovakia, a first case of intoxication by thallium was reported in 1949 (Hefka 1949). Later, a case of thallium intoxication in 8-years old girl by a meat from dead chicken and six cases of Romani children that eated scrambled eggs impregnated by a thallium sulfate, prepared for poisoning of hoodie crows, were reported (Némethová, 1953; Spišák *et al.* 1977). According to the data of the National toxicological information centre, only one additional case of thallium intoxication occurred in Slovakia (in 1985) (personal communication, data from National toxicological information centre, Slovakia).

Diagnosis of thallium intoxication may be difficult. In clinical suspicion, the diagnosis should be based on proof of increased concentration of thallium in the urine. In differential diagnosis, other causes of damage of the peripheral nervous system, i. e., arsenic, colchicine, or vinca alkaloids intoxication, botulism, thiamine deficiency, HIV infection and Guillain-Barré syndrome must be taken into consideration. The cause of alopecia, which is an important manifestation of thallium intoxication, may also be due to exposure to vincristine, chloroprene and mercaptopurine (Amato & Dumitru 2002). In our case, the diagnosis was easy due to obvious history, and an early therapy could be started.

The clinical symptoms of thallium intoxication depend on the type, intensity and duration of the exposure. The minimum amount of thallium ingested that causes signs of acute intoxication is 1.5–2.0 mg/kg of body weight. The minimum lethal dose is 8.0–15.0 mg/kg of body weight (Moeschlin 1980). Without treatment, death occurs within 10–12 days (Kemper 1979). Acute non-lethal intoxication usually appears early, several hours after consumption, with symptoms of gastroenteritis, vomiting and diarrhoea, abdominal pain or obstipation. The first signs of nervous system injury are delayed by a few days. They appear in the form of painful paraesthesia of the hands and legs (particularly the soles of the feet) accompanied by distal weakness, predominantly in the legs. This clinical picture of sensor-motor polyneuropathy can be accompanied by confusion, delirium, hallucinations and convulsions. After a week, headache, ataxia, tremor, muscle atrophy appear, with various symptoms and signs of damage of the cranial nerves: paralysis, oculomotor and facial nerves disturbances, retrobulbar neuritis. Tachycar-

dia and high blood pressure are common. Within two weeks after intoxication, damage of the kidney appears, as it is an organ with a high accumulation of thallium, with oliguria and albuminuria (Blain & Kazantzis 2014; Pelclová *et al.* 2009). The first skin symptoms are not specific, including skin desquamation on the palms and soles, and acne-like or pustular eruptions on the face. In the course of week 2 and week 3 after intoxication, hair loss and diffuse alopecia develop. At the same time, transverse white lines on nails (Mees' lines or Aldrich-Mees' lines) appear. Other skin and mucosa findings include: crusty eczema lesions, hypohidrosis, anhidrosis, palmar erythema, stomatitis and painful glossitis with tongue tip erubescence (Lu *et al.* 2007). Timely therapy can modify clinical thallium intoxication symptoms.

The clinical course of the symptomatology in our patient – paresthesia present at the admission, and subsequent gastrointestinal symptoms with strong paresthesia and neuropsychiatric symptomatology may rather imply a chronic thallium intoxication not confessed (or not known) by the patient, in combination with voluntary thallium bromide ingestion immediately before hospitalization. Possible inaccuracies in the patient's information about the time of consumption and about the amount of thallium bromide ingested might explain the severity of the clinical course, with rapid progression, and the relatively high values in the urine which occur, according to literature, in cases of heavy lethal poisoning (Riyaz *et al.* 2013).

## CONCLUSION

Thallium intoxication is presently scarce in developed countries, mainly due to the limited accessibility to rodenticides containing thallium, as they have been banned. Accidental, or intentional self-damage/suicidal poisoning may occur in laboratories that use the thallium bromide preparations. The intoxication should be taken into account especially in unclear acute polyneuropathies accompanied by gastrointestinal symptomatology and, later, by alopecia. A rapid and radical treatment is mandatory, and may lead to recovery even in cases of severe intoxications.

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