Thallium toxicity: A growing concern

Abstract
This review article deals with the growing concern of the toxicity of thallium. This article describes the characteristics of thallium, its potential sources of exposure, kinetics, and toxicity on human being and diagnosis of thallium poisoning. This article also describes some episodes of thallium poisoning arising from both occupational and nonoccupational exposure.

Key words: Acute poisoning, Chronic toxicity, Thallium

INTRODUCTION
Thallium is a toxic heavy metal, which was accidentally discovered by Sir William Crookes in 1861 by burning the dust from a sulfuric acid industrial plant. Since long back, thallium has been used extensively, and human exposure to thallium compounds has occurred naturally. Apart from thallium exposure in industrial set ups, poisoning of community people from thallium compounds has also taken place from time to time. Many cases of industrial and nonindustrial thallium poisoning have already been reported from different countries at regular intervals. Some incidents of such poisoning have resulted in fatalities. Cases of thallium poisoning from compounds already banned have also been reported. In India also, cases of thallium poisoning have been observed even in the recent past. In such a scenario, day-by-day, thallium poisoning is drawing more and more attention from the point of view of occupational health, as well as public health.

Thallium, a bluish white heavy elemental metal exists in two oxidative states, +3 (thallic), and the more common and stable +1 (thallous). It has an atomic weight of 203 and a melting point of 303.5°C. Thallium is present in the environment as a result of natural process and from man-made sources. It is ubiquitous in nature and occurs especially in sulfide ores of various heavy metals, but normally in low concentrations. Only a few areas contain a naturally very high-thallium concentration.

Use of thallium has been extensive and it has ranged from rodenticide to photoelectric cells, lamps, electronics, low-temperature thermometers, and semiconductors. Thallium has also been used in imaging procedures (Th-201 is widely used in myocardial imaging), scintillation counters, and optical lenses. It is also useful in the manufacture of imitation jewellery, pigments, and fireworks (green color).

Potential sources of exposure
Exposure occurs by oral, dermal, and inhalation routes. Water-soluble salts are more toxic than the less water-soluble salts (e.g., thallium sulfate is more toxic than sulfide). Dermal exposure may even occur through rubber gloves.

Industrial exposure
In most of the cases, thallium is emitted in the atmosphere as dust. Among the dusts of thallium compounds, thallium sulfate is the majority. This dust emitted from industrial outlets is either inhaled or settled down to contaminate surface water or soil. Thallium exposure occurs mainly from the following industrial emissions.

- Coal fired power plants.
- Smelting operations (mainly lead and zinc).
- Cement industries.
- Rodenticide manufacturing plants.
- Refinery (as a byproduct of cadmium production).

Nonindustrial exposure
- Consumption of fruits and vegetables grown in contaminated soil and the use of tobacco products.
- Acute and chronic poisoning cases where exposure has occurred directly from a thallium compound either self inflicted or induced (e.g., poisoning from rodenticides).
- Other exposure (rare atypical exposure)
- Thallium poisoning has occurred following nasal insufflations of a substance that was believed to be

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cocaine.[9]

· Poisoning from thallium has also occurred after ingestion of herbal medication/nutritional supplement.

Kinetics

Exposure to thallium is possible through oral, inhalation, dermal, eye, parenteral, and other routes. Water-soluble salts (sulfate, carbonate) are easily absorbed from the gut than the less water-soluble (sulfide, iodide) forms. Excretion occurs through urine, faeces, and salivary secretion. In an affected subject, considerable levels of thallium may be found in blood and hair also.

The toxicokinetics of thallium in human beings is explained by a three-compartment model.

· Central compartment consisting of blood, as well as well-perfused peripheral organs and tissues, is the fast exchange compartment.
· Brain, the target organ for neurotoxicity constitutes the slow exchange compartment.
· Intestine as well as the intestinal contents, where the absorption of thallium takes place.

In the first phase, lasting about 4 h, thallium is distributed through the entire central compartment. In the second phase (4 – 48 h), distribution occurs in the brain. Afterwards, thallium is distributed throughout the body tissues.

Effects of thallium poisoning

Initially, thallium was used as medicine, mainly as a depilatory agent. This use has resulted in many cases of intoxication. Because thallium is tasteless, odorless, colorless and highly toxic it was frequently used for suicide, homicide, and illegal abortion. Accidental exposure to thallium has also occurred after ingestion of contaminated food.[10]

Depending upon the mode and dose of exposure, thallium toxicity represents either as acute manifestation or as chronic manifestation.

Acute poisoning

Acute intoxication by thallium salts in humans, causing severe symptoms have been reported after ingestion of single or multiple oral doses of the order of 100 mg or more for adults. The main features of acute thallium toxicity in order of appearance are as follows (where intoxication is less severe):

· Anorexia, constipation, vomiting, retrosternal, and abdominal pain.
· Polyneuritis (sensory and motor), insomnia and darkening of hair roots.
· Alopecia, Mee’s lines (whitish lines in nails), alteration in blood pressure and ST, T changes in ECG.

In severe cases, where people die within 8–10 h, increasing tachycardia, progressive hypotension, early hyporeflexia, and peripheral cyanosis is observed.

The ingestion of lower lethal doses causes gastrointestinal hemorrhage, gastroenteritis, metallic taste, salivation, nausea, and vomiting. Afterwards, neurological disorders, hallucination, lethargy, delirium, convulsions, tingling pain in extremities, and muscular weaknesses are followed by coma. The cause of death is respiratory failure or cardiac arrest.

Chronic toxicity

The symptoms of chronic toxicity show strong variation and are in general milder than in cases of acute poisoning. A relatively long-latent period of even several weeks may be followed by just a few symptoms.

· Peripheral sensorial disturbances, mental aberrations, loss of weight, and sleeplessness have been the most common features.
· Disturbances of vision, pain without marked polyneuritis, loss of hair are reported. Later severe polyneuritis may develop.
· Cardiac disorders include hypertension, irregular pulse, and angina-like pain.
· Other symptoms include gastric antacidity, lack of appetite, loss of weight, albuminurea, haematuria, endocrine disorders, psychoses, and encephalitis.

Diagnosis

Diagnosis is based on a characteristic clinical presentation and on laboratory confirmation of thallium in biological fluids.

· The triad of gastroenteritis, polyneuropathy and alopecia is regarded as the classic syndrome of thallium poisoning.
· Typical alopecia and Mee’s lines in the nails appear after 2 weeks [Figure 1].

Figure 1: Mee’s line and erosion of nails in a case of thallium poisoning
· Thallium levels are usually examined in urine, blood and hair samples.

**Episodes of thallium poisoning**

Chronic occupational thallium poisoning has been reported from Japan in a male worker who handled thallium containing raw materials for glass manufacturing over a period of four years and complained of alopecia, abdominal pain, diarrhea, and tingling in extremities. Mild glove stocking type polyneuropathy was found in this patient. Thallium content of hair as determined by ICP-MS method was found to be 20 ng/g.[8]

Acute thallium poisoning of eight people due to unknown cause has been reported from Poland where some cases have fatal outcome also.[9]

1. Thallium poisoning from maliciously contaminated food has been reported from New York, where thallium intake occurred through candy and the victims suffered from variable gastro intestinal symptoms and painful paraesthesia of hands and feet.[2]

2. A case of thallium poisoning is known from New York, where poisoning began during first trimester of pregnancy and resulted in fetal demise. This case documents that thallium passes through both placenta and breast milk.[10]

3. Thallium poisoning has been reported from Israel in the year 2000 after a gap of 30 years when an old man developed both acute and chronic symptoms concomitantly after ingestion of thallium compounds through alcoholic beverages.[11]

4. Not only is thallium poisoning occurring from occupational and nonoccupational sources, it is also taking place with suicidal and homicidal intentions. In some places, it is showing resurgence after a silence of even decades. Naturally, it is becoming a growing concern and a matter of toxicological interest. In such circumstances, the clinicians should keep the diagnostic features of thallium poisoning in mind in view of the fact that early suspicion of this poisoning and thereby early institution of specific therapy can save the life of the victims.

**Mortality in thallium poisoning**

There are numerous case reports of human lethality following acute oral exposure to thallium. Death occurred in one individual 9 days following intentional ingestion of a single estimated dose of 54–110 mg thallium/kg (as thallium nitrate). Cranial and peripheral nerves showed axonal degeneration with preservation of most of the overlying myelin, suggesting that thallium damaged axons.[12] Two of three subjects who ingested thallium (thallous acetate) also died, however death occurred 1 month after onset of symptoms. Dose could not be determined since exposure occurred in three divided doses for unspecified durations. Distal peripheral axon degeneration with preserved proximal fibers was reported in one case.[13]

Other studies[14–16] have reported that thallium (as thallium sulfate, dose not specified) is lethal following ingestion, and there was evidence for central–peripheral distal axonopathy.[16] Although the finding of neurological effects was consistent among case reports, death was attributable to cardiac or respiratory failure.

**Laboratory methods to determine thallium in body fluids and tissue samples**

Thallium concentration in environmental samples being very low, determination directly from the sample or from the digestion solution usually lacks sufficient accuracy. In such circumstances, preconcentration procedures are necessary. Sampling and sample preparation also needs special care because these can result in thallium loss or contamination. Thallium is almost always determined as total metal, rather than as specific thallium compounds. Among the analytical techniques that can be used are spectrophotometry, mass spectrophotometry (MS), atomic absorption spectrometry (AAS), voltametry, neutron activation analysis (NAA), X-ray fluorimetry, and inductively coupled plasma (ICP) techniques. Selection of analytical methods should be done carefully on the basis of character of sample in which thallium is to be estimated. To determine presence of thallium in water samples amperometric titration or ICP-MS can be useful. Inductively coupled plasma – atomic emission spectrometry (ICP–AES) is of use in analyzing biological materials as well as air particulates. Other useful methods for biological samples are ICP–MS and DPASV (differential pulse anodic stripping voltammetry). The ICP–MS can be used for analysis of rocks also and spectrometry may be used for environmental samples. Routine methods in use are GFAAS (graphite furnace atomic emission spectrometry), DPASV, ICP–MS, and photometry. As most of the techniques require a careful sample pretreatment/preconcentration step, it is strongly recommended that all analyses should be accompanied by a quality assurance program.

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**REFERENCES**

5. Mamoru H, Kazushi T, Mariko O, Mitsutoshi T, Naomi H. A probable