

## Thallium toxicosis in a Pit Bull Terrier

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**Abstract.** Thallotoxicosis is described in an adult Pit Bull Terrier. The dog exhibited anorexia, emesis, weakness, conscious proprioceptive deficits, and a hemorrhagic diarrhea before death. A severe, acute necrotizing enterocolitis was evident upon histological examination, as was a multifocal to coalescing pulmonary edema. Liver and kidney thallium concentrations were 18 and 26 ppm, respectively. The source of the thallium was determined to be thallium sulfate obtained by a person with the intent to harm family members. Although thallium has not been produced in the United States for 20 years, this report demonstrates the need to consider thallium toxicosis as a differential diagnosis for animals presenting with vague and mixed gastrointestinal and neurological signs.

**Key words:** Necrotizing enterocolitis; thallium; thallium poisoning; thallotoxicosis.

Thallium salts were once widely used as rodenticides, but because of their notorious toxicity to non-target species, this use was banned in 1972. Today, animal poisonings from thallium in the United States are rare. The purpose of this report is to describe a recent case of fatal thallium toxicosis in a dog.

A 3-year-old intact male Pit Bull Terrier presented to a veterinary clinic with an acute onset and 1-day duration of anorexia, emesis, dehydration, and weakness. The dog was current on all vaccinations and heartworm preventive treatment. The owner reported that the dog was stumbling the previous day. The dog exhibited pain on ventroflexion, extension, and lateral movement of the neck. Signs of conscious proprioceptive deficits were noted on all four limbs. Body temperature, mucous membrane color, complete blood count, serum chemistries, and urinalysis were all normal upon initial examination. The patient was hospitalized. Tentative differential diagnoses included bacterial and/or viral meningitis, rabies, and poisoning. The dog's condition deteriorated and it developed hemorrhagic diarrhea. Despite symptomatic treatment, the dog died on the fourth day following presentation. A partial necropsy was performed by the attending veterinarian, tissues were collected and placed in formalin for histopathology, and the body was stored frozen for disposal.

The frozen remains of the dog were submitted to the University of Illinois, Veterinary Diagnostic Laboratory, for a more extensive necropsy examination after several human members of the dog's household were diagnosed with malicious thallium poisoning. The boyfriend of the owner's mother was suspected of

poisoning the mother, the owner, 2 of the owner's siblings, and several visitors. Thallium sulfate powder (99.8% pure) had been purchased from a chemical supply company through the Internet under false pretenses. Exposure of the human victims and the dog was a result of ingesting thallium-tainted food and beverage.

The formalin-fixed tissues (stomach, kidney, adrenal gland, spleen, large intestine) recovered at the initial necropsy examination were also submitted for evaluation. A determination of the dog's cause of death could not be made from gross examination of the remains. Tissues were also collected from the previously frozen carcass for histopathological, toxicological, and microbiological analysis.

Histologically, the large and small intestines contained numerous hypereosinophilic crypt epithelial cells with pyknotic nuclei along with small to moderate numbers of lymphocytes and plasma cells diffusely distributed throughout the entire lamina propria. The crypts were moderately dilated and contained small amounts of necrotic debris. Multifocally, within the lungs, alveolar spaces contained large amounts of hemorrhage and moderate to large amounts of edema fluid. Histopathological examination of the kidney, heart, liver, skeletal muscle, cerebral cortex, cerebellum, bone marrow, and spinal cord revealed no significant lesions. Rabies examination by fluorescent antibody was negative and anaerobic culture of the brain identified no pathogens.

Liver and kidney samples were analyzed for arsenic, lead, and thallium by inductively coupled argon plasma emission spectroscopy. Arsenic in the kidney was higher than normal background concentrations, but not suggestive of an arsenic toxicosis (As = 1.1 ppm, normal reference range less than 0.1–0.4 ppm, high 0.5–1.0 ppm).<sup>12</sup> Liver arsenic concentration and liver and kidney lead concentrations were consistent with nor-

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mal background levels. Liver thallium concentration was 18 ppm and kidney thallium concentration was 26 ppm. Thallium is normally not at all present in the body or, if present, it occurs at concentrations of less than 0.01 ppm tissue,<sup>4,14</sup> below the detection capabilities of many analytical instruments. Therefore, detection of any amount of thallium in tissues, along with appropriate clinical signs, is of diagnostic significance. Based on the tissue thallium concentrations, the clinical course, and the illnesses confirmed in the family members, a diagnosis of thallium toxicosis was made.

Pure thallium is a bluish-white metal that is found in trace amounts in the earth's crust. It is a rare but ubiquitous element with no known beneficial biological functions.<sup>10</sup> The mean concentration of thallium in the earth's crust is about 1 ppm. In the past, thallium was obtained as a by-product from smelting other metals (zinc, lead, copper); however, it is no longer produced in the United States. All thallium used in the United States since 1984 has been obtained from imports and from thallium reserves.<sup>1</sup> Thallium is used mostly in manufacturing electronic devices, switches, and closures, primarily for the semiconductor industry. It also has limited use in the manufacture of special highly refractive optical glass and for cardiac imaging.<sup>1</sup> Pure thallium and thallium sulfate are odorless and tasteless.<sup>1,9</sup> Thallium compounds are soluble in warm water, and vapors of boiling solutions are poisonous.<sup>9</sup> Thallium sulfate was widely used as a rodenticide, but because of its toxicity to children and pets, household use was barred in 1965,<sup>3,9</sup> and complete use as a rodenticide was banned in 1972.<sup>1</sup>

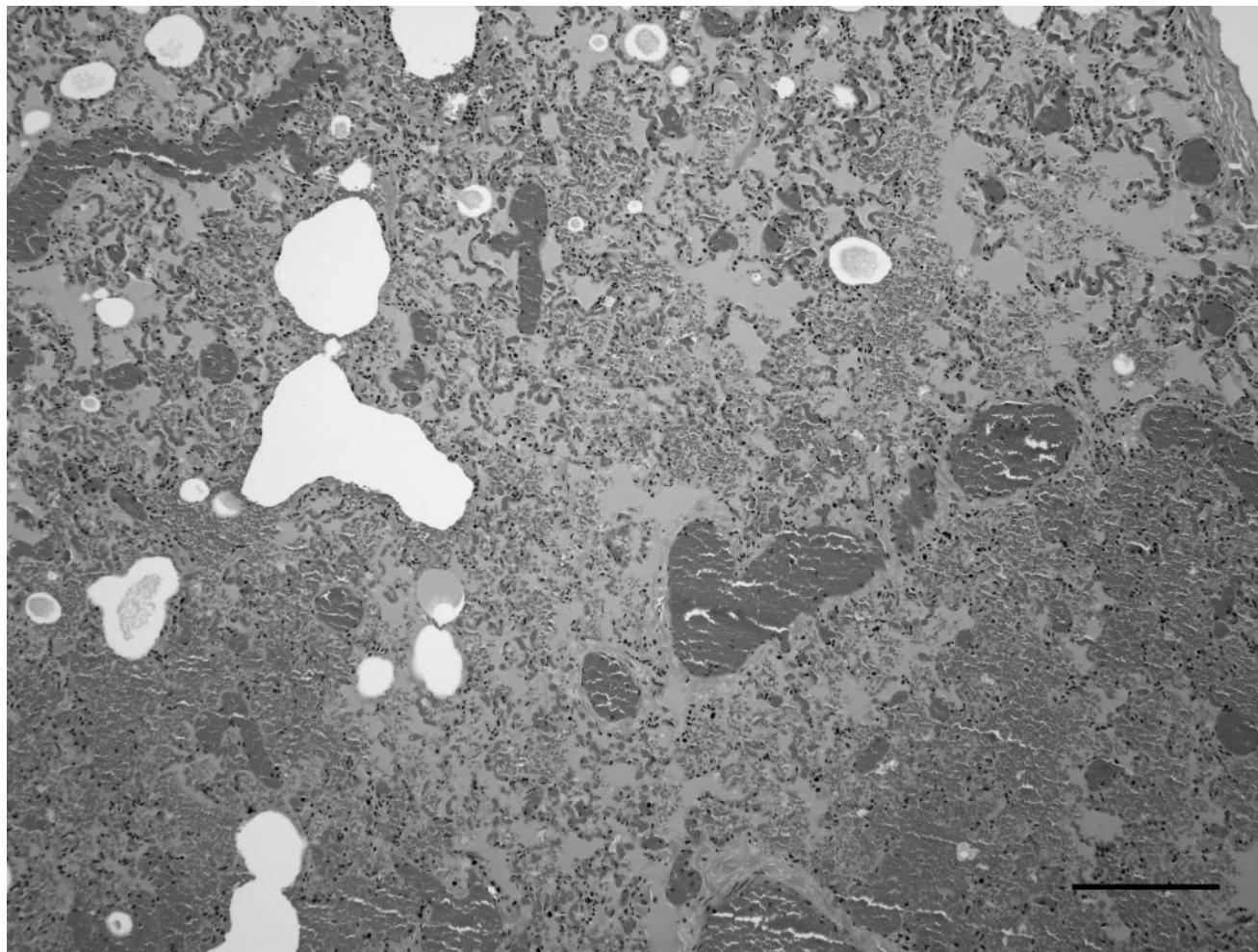
Thallium is considered a cumulative poison. Thallium salts are readily absorbed by the gastrointestinal tract, respiratory tract, and skin. Thallium rapidly enters tissue cells, widely distributing to brain, heart, kidney, skeletal muscle, testes, intestine, thyroid, and salivary glands.<sup>10,11</sup> Like other heavy metals, thallium binds to sulfhydryl groups of proteins and mitochondrial membranes, thereby inhibiting a range of enzyme reactions and leading to a generalized poisoning.<sup>13</sup> Possible toxic mechanisms of thallium include ligand formation with protein sulfhydryl groups, inhibition of cellular respiration, interaction with riboflavin and riboflavin-based cofactors, and disruption of calcium homeostasis.<sup>11</sup>

The well-known mechanism behind thallium toxicity is related to its similarity to potassium and the interference with vital potassium-dependent processes. Both are univalent ions with similar ionic radii, and thallium mimics potassium in its intracellular movements. Thallium's similarity to potassium is responsible for the disruption of a number of potassium-dependent enzymes, including  $\text{Na}^+\text{-K}^+$  ATPase and pyruvate kinase. Once intracellular, thallium is less rap-

idly released than potassium. Because of this and its large volume of distribution, thallium is released slowly from the body. Residues of thallium can be detected for months following exposure. The slow rate of excretion enables accumulation of thallium even at low levels of exposure.<sup>10,11</sup>

Experimental oral dosing of thallium sulfate to dogs provides an estimated minimum lethal dose of thallium in this species of approximately 12–15 mg/kg.<sup>4</sup> Dogs in this dose range died by 5 days after exposure. In another study, a dog dosed orally with 9.2 mg thallium sulfate/kg body weight developed vomiting and bloody diarrhea by day 5 and hair loss and reddening of the skin over the rump by 7 days.<sup>5</sup> The signs gradually lessened and the dog improved by 14 days. Another dog in the same study<sup>5</sup> dosed at 20 mg/kg developed more severe signs, including vomiting, bloody diarrhea, dyspnea, weak pulse, redness of the lips, drying of the epidermis, profound hair loss, weakness, stumbling, collapse, and death at 12 days. In both studies, the time to death decreased with increasing doses, so that a dog dosed at 135 mg/kg died within 24 hours.<sup>4</sup>

The clinical signs of thallium toxicosis in dogs depend on the duration of exposure, the amount ingested, and the duration of time after ingestion. Because thallium affects many body systems, it can result in a complex clinical picture. In general, acute toxicoses are characterized by the development of a severe gastroenteritis. Emesis and anorexia are often accompanied by hemorrhagic diarrhea and abdominal pain, usually developing within 4 days of ingestion.<sup>16</sup> Severe colic, brick-red mucous membranes, ulcerative stomatitis, and death may ensue. Microscopic gastrointestinal lesions can include a mucosal epithelial necrosis with focal ulceration, submucosal edema, erythema, hemorrhage, and infiltration of submucosa by inflammatory cells.<sup>6</sup> At lower levels of exposure, the onset of signs may be delayed for several weeks; the clinical signs include gastrointestinal and neurological manifestations, as well as dermal lesions. Paresthesia and hyperesthesia of the extremities, ataxia, weakness, tremors, and progressive motor neuropathy resulting in respiratory paralysis may develop.<sup>6</sup> Myelinated nerves may exhibit degenerative changes characterized by focal distension of the myelin sheaths, with swelling and occasional fragmentation of axons.<sup>19</sup> Focal areas of necrosis within the mesencephalon may be noted, as well as cerebral and cerebellar edema. Cutaneous lesions can be characterized as erythema, hyperkeratosis, alopecia, scaling, exudation, often beginning at the commissures of the lips, the nasal cleft, and the ear margins in dogs.<sup>6</sup> Histologically, intense congestion of dermal vessels, focal necrosis of apocrine and sebaceous glands, focal necrotizing folliculitis, and peri-



**Figure 1.** Lung. Alveoli are filled with hemorrhage and/or edema. The vasculature is congested. HE. Bar = 200  $\mu$ m.

follicular inflammation can be seen.<sup>19</sup> Skin lesions may progress to severe epidermal and follicular parakeratosis, acanthosis, and edema of the spinous layer, and mild hyperkeratosis.<sup>19</sup>

The presentation and clinical course for this dog is typical of acute thallotoxicoses previously reported in the literature, where severe gastrointestinal effects predominate.<sup>2,7,8,15–19</sup> In a review of 34 cases of confirmed thallium toxicosis in dogs by Zook et al.,<sup>19</sup> emesis was the most commonly reported sign (82%) followed by cutaneous alterations (71%), depression (62%), anorexia (53%), and nervous disorders (47%). The dog in this case presented with a mixture of gastrointestinal and neurological signs. Severe hemorrhagic gastroenteritis and a neuropathy were apparent clinically. No dermal lesions developed, and no neural lesions were identified. The gastrointestinal changes were consistent with a necrotizing enterocolitis. In the report by Zook et al.,<sup>19</sup> edema of the lungs was found in all histologic sections of the lungs. Macrophages were increased in number within alveoli in a high percentage of dogs.

Several of the dogs had exudative bronchopneumonia characterized by neutrophils, macrophages, edema, and hemorrhage. The dog in this case had pulmonary hemorrhage and edema (Fig. 1).

The case described herein demonstrates the need to consider thallium toxicosis as a differential diagnosis for animals presenting with vague and mixed gastrointestinal and neurological signs, even though the metal has not been produced in the United States for 20 years and has not been marketed as a rodenticide for 30 years.

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