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# CASE REPORTS

## Thallium Poisoning

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THALLIUM, a heavy metal, has been used mainly as a depilatory agent in favus and ringworm of the scalp,[1] but its therapeutic use has been discontinued because of its toxicity. It is still available commercially as a rodenticide, as an insecticide and in cosmetic depilatory preparations. Thallium poisoning in humans has been reported from many parts of the world, including the United States.[2, 3] In Canada, during the years 1958 to 1964, an average of 13 cases a year has been reported to the Poison Control Centres,[4] although to our knowledge no report has appeared in the medical literature. Diagnosis of this condition may be missed, especially in children without an obvious history of thallium ingestion, unless a high index of suspicion is maintained. It is our purpose to draw the attention of physicians to the possibility of thallium poisoning. The following case report of a child who presented with bizarre clinical manifestations and no history of ingestion of the offending agent illustrates the difficulty in diagnosis.

A 19-month-old white Canadian girl was brought to the outpatient department of the Montreal Children's Hospital. Her parents had noticed that in the previous four days she had become increasingly unsteady on her feet, that she was unable to open her left eye and that her hair had started to fall out. The child had no history of any serious illness. Her growth and motor development had been normal. She had always been irritable and had episodes of head banging and temper tantrums. Two days before the onset of her symptoms she had fallen on her head from a height of four feet. There had been no loss of consciousness.

On examination, the patient was conscious. She had moderate ataxia, mainly of her upper limbs and trunk, ptosis of her left eyelid and partial alopecia. Bruising was present over the left mastoid area. The patient was admitted to the neurosurgical service, where she was kept under observation for 24 hours.

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The next day her condition had deteriorated. She became extremely irritable and more ataxic. The possibility of an intracranial space-occupying lesion was entertained and a pneumoencephalogram was performed, which was normal. By evening her condition had further deteriorated. She was now delirious and had gross generalized ataxia and choreiform movements of the upper limbs. Muscular tone was decreased, but the deep tendon reflexes were all brisk; plantar responses were flexor. Examination of the cranial nerves was negative except for ptosis of her left eyelid. There was no nystagmus and the ocular fundi appeared normal. Her hair came out in great tufts; the eyelashes and eyebrows were not affected.

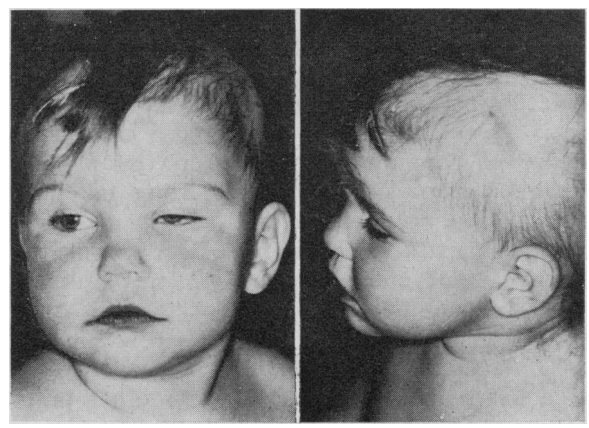

Fig. 1 Fig. 2

Fig. 1.—Front view of patient showing ptosis of left eye, alopecia and angular stomatitis. Fig. 2.—Profile of patient showing almost complete alopecia except for a tuft of hair in the mid-line of the scalp.

Confronted with these peculiar manifestations, we made further enquiries into the possible ingestion of a toxic agent. It transpired that the child had pica, but we were unable to obtain a history of recent ingestion of a specific toxin.

On the third day of hospitalization the patient was semicomatose with intermittent periods of delirium which were exacerbated by the slightest stimulation. She had lost all the hair on her scalp except for a narrow strip in the midline (Figs. 1 and 2). Angular stomatitis was present, but her skin and nails were unaffected. At this stage a presumptive diagnosis of thallium poisoning was made which was later confirmed by laboratory investigations.

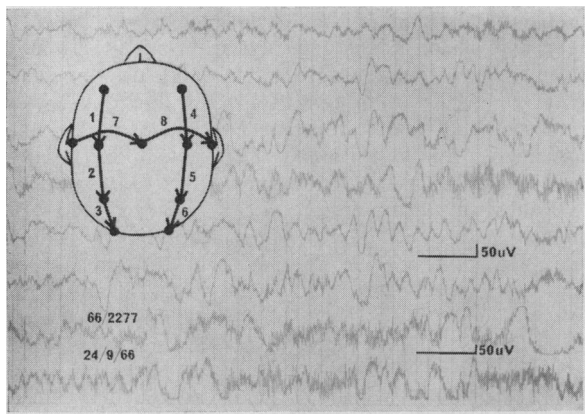


Fig. 3.—Electroencephalogram on admission showing severe diffuse disturbance of cerebral activity with abnormally high-voltage slow waves, 2 to 3 cycles per second.

The parents eventually revealed that the child had been seen, two weeks before admission to hospital, playing with an open container of "Tat Ant Trap" which contains 1% thallium sulfate.

*Investigations*

Cerebrospinal fluid was normal. Viral cultures were negative. Total blood count and peripheral blood smear were normal. Repeated urinalyses throughout her hospital stay were normal. Urine for coproporphyrin was negative. Urine amino-acid chromatography, both before and during treatment, did not show any significant abnormality. The serum sodium, potassium, chloride, calcium, phosphorus and alkaline phosphatase were normal on repeated examinations. The blood glucose and urea nitrogen and liver function tests were normal. Radiographs of the skull, chest, long bones and abdomen were normal. An electrocardiogram was normal. Initially the electroencephalogram showed severe diffuse disturbance of cerebral activity with abnormally high-voltage slow waves, 2 to 3 cycles per second (Fig. 3). Two weeks later the EEG showed marked improvement. Minimal diffuse slow dysrhythmia was present with no lateralization or epileptiform activity. An electroencephalogram repeated three months later was within normal limits and follow-up EEG 10 months later was normal (Fig. 4).

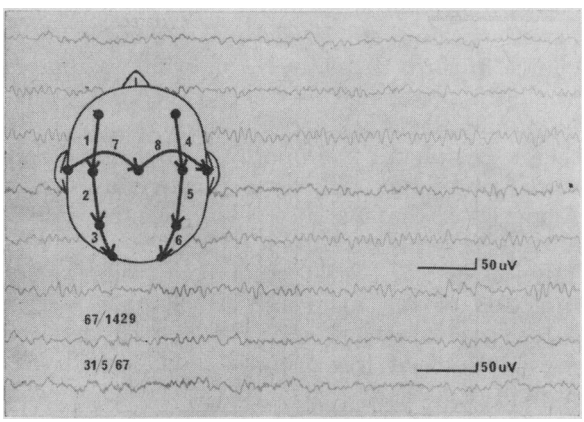


Fig. 4.—Electroencephalogram taken 10 months after initial illness showing complete return to normal.

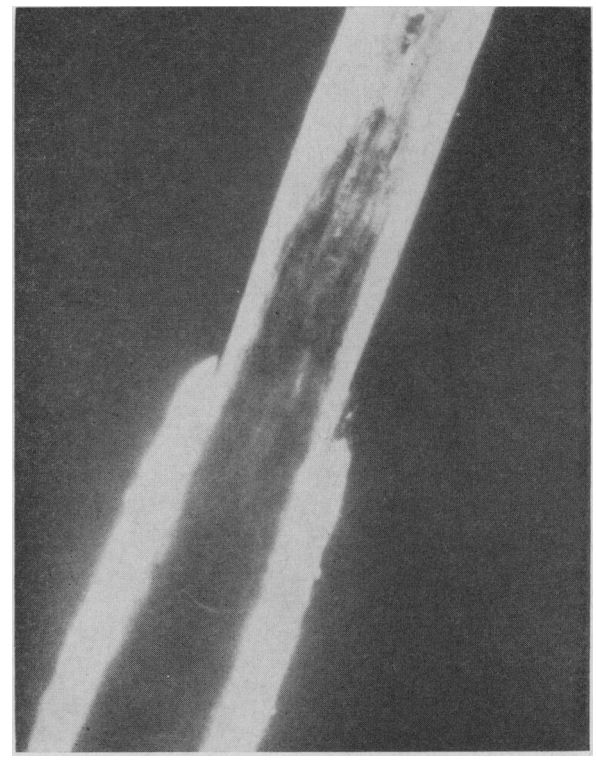

Fig. 5.—Hair root viewed by polarized light showing refractile root sheath and shaft with blackened hair root. (Original magnification × 80.)

Analysis of the patient's blood and urine* on the third day of hospitalization revealed a thallium content of the order of 10 to 50 ppm in the urine, but none was detected in the blood. (Normally thallium cannot be detected in urine or blood.) The patient's hair was examined microscopically. Close to the hair bulb for a distance of 0.5 mm. an abnormal brownish-black pigmentation was present (Figs. 5 and 6). Analysis† of the hair did not reveal any thallium. After laboratory confirmation of the diagnosis, 24-hour urine collections were made on four consecutive days for thallium estimation† (Table I).

TABLE I.—DAILY URINARY EXCRETION OF THALLIUM DURING TREATMENT WITH DIPHENYLTHIOCARBAZONE (DITHIZONE), 20 mg. PER kg. PER DAY ORALLY

| *Days of collection* | *Volume of urine (ml. per 24 hours)* | *Thallium (μg. per 100 ml. of urine)* | *24-hour excretion of thallium (μg.)* |
|---|---|---|---|
| 1 | 875 | 7.6 | 66.5 |
| 2 | 495 | 155 | 765.05 |
| 3 | 745 | 56.8 | 433.16 |
| 4 | 385 | 203 | 781.55 |

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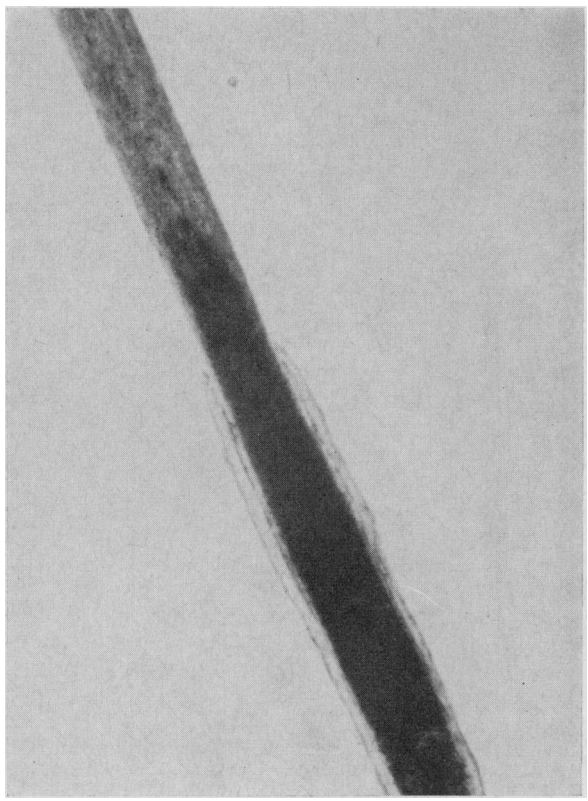

Fig. 6.—Hair root viewed by ordinary light showing blackening. (Original magnification × 32.)

*Treatment and Progress*

While we awaited the results of thallium estimation in the urine, a dose of calcium disodium edetate (EDTA) was given intravenously, 200 mg. in 200 ml. of 10% dextrose in one hour. The same evening, after confirmation of the diagnosis, treatment was started with diphenylthiocarbazone (Dithizone), 20 mg. per kg. per day in two divided doses administered in suspension in 100 ml. of 10% dextrose by nasogastric tube.

Two days later the patient's condition had noticeably improved. She regained consciousness, was able to sit up with support, and appeared to recognize her parents. A week later she was tolerating a normal diet. She was now interested in her surroundings and smiled occasionally. She was able to sit up unaided, and with assistance was able to take a few steps. Her gait was still very ataxic and she had marked intention tremor of her upper limbs. Her recovery was interrupted when she developed pneumonia after her fourth week in hospital. This, however, rapidly improved with penicillin therapy and the patient was discharged shortly afterwards.

Follow-up examination at 2 months and 10 months after discharge from hospital showed a normal well-developed child with no residual neurological or psychological sequelae (Figs. 7 and 8).

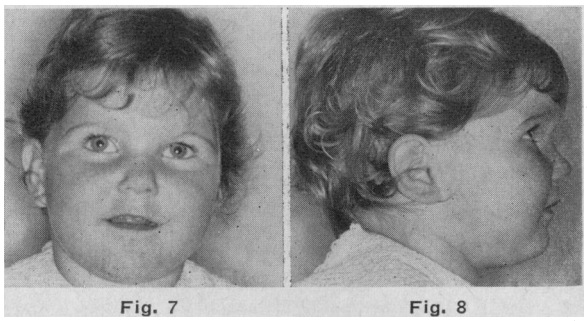

Fig. 7 Fig. 8

Figs. 7 and 8.—Front view and profile of patient 10 months after her acute thallium poisoning (29 months of age) showing complete recovery.

## DISCUSSION

The present report demonstrates that thallium can be encountered in practice. Similar accidents in the United States have resulted in legislation by the Department of Agriculture prohibiting the sale of thallium sulfate for household use.[5] The authors believe that there should be legislation in Canada restricting the use of thallium sulfate in household products. The following is a list of some of the household products available commercially in Canada that contain thallium sulfate: Antcheck Ant Trap, Antrol Ant Trap, Ant-X Ant Trap, Black Flag Ant Traps, Beacon Ant Killer, Tant Ant Poison, Tat Ant Trap Insecticide, Havok Ant-Trap, Noxall Ant Trap, Tat Roach Trap.

Thallium sulfate is a white, tasteless and odourless powder. It is one of the most toxic heavy metals. Absorption is through the gastrointestinal tract. It also gains access to the circulation when applied to the skin as a depilatory ointment. The lethal dose in man is between 0.2 and 1.0 g.[6] The clinical manifestations have been well described by various authors.[7-11] Neurological and gastrointestinal symptoms dominate the picture.

Gastrointestinal symptoms may develop within 2 to 12 hours of an acute intoxication. Nausea, vomiting and diarrhea are commonly present, and occasionally hematemesis and melena may occur. The neurological manifestations are apparent within 7 to 10 days and dominate the clinical picture thereafter. Almost any symptom or sign is possible. Headaches, weakness, irritability and ataxia are early manifestations. Paresthesia, peripheral neuropathy, chorea, athetosis, coma, respiratory arrest and death may ensue. Alopecia is the most constant feature and is always present in chronic thallium poisoning. The loss of hair begins from 10 to 15 days after ingestion of the toxin and is complete within 3 to 4 weeks. Pubic and axillary hair and the medial third of the eyebrows are spared. Regrowth of hair usually begins at 4 weeks and is complete at 3 months. Thyresson,[12] using radioactive thallium in rats, was able to demonstrate

by radioautographs of the skin that the metal accumulates in the hair follicles and postulates interference with the formation of keratin. Other dermatological manifestations are angular stomatitis, dystrophic nail changes and hypohidrosis. Renal involvement has been reported by Fischl,[13] and three out of four cases of thallium intoxication were found to have renal aminoaciduria. Winter, Laron and Michaelson[14] report the case of a 9-year-old boy who developed hypertension, renal dysfunction and retinal changes following thallium poisoning. Hemolytic anemia was reported by Löhr and his colleagues[15, 16] and by Sunderman.[17]

Reed *et al.*[18] performed electroencephalograms on 13 patients who had thallium intoxication. In 9 of these there was severe diffuse disturbance of cerebral activity, and the same patients showed signs of encephalopathy, the clinical severity of which correlated well with the EEG changes. Seven of these nine patients died or had neurological sequelae, while all four with a normal EEG were normal at follow-up examination.

Grunfeld, Aldana and Hinostroza[19] found an increased radiodensity of the liver in a number of their patients with thallium poisoning. This has also been observed in experiments with animals.

Our patient showed most of the features of thallium poisoning. We were unable to demonstrate any hepatorenal involvement and did not observe any increased density of the liver on radiography. Although we obtained pictures of the hair follicles similar to those of Thyresson, we were unable to demonstrate that the pigmentation in the hair bulb contained thallium.

There is no unanimous agreement on the treatment of thallium poisoning. In cases diagnosed soon after ingestion of the toxin, gastric lavage with sodium iodide has been used to precipitate the thallium as thallium iodide. Intravenous fluids and oral potassium chloride and cystine may increase urinary excretion of thallium,[20] although they do not seem to give protection against thallium toxicity.

Dimercaprol (BAL) and calcium disodium edetate (EDTA) have been used with doubtful benefit. There is no evidence to suggest that they increase excretion of thallium. Diphenylthiocarbazone (Dithizone) has been used by Chamberlain *et al.*[7] and by Smith and Doherty,[21] and although there was no increase in thallium excretion, therapy was accompanied by clinical improvement. Our patient showed dramatic improvement in her clinical condition within 48 hours of treatment with diphenylthiocarbazone (Dithizone).

We are grateful to Drs. Alan Ross and Elizabeth Hillman for their valuable assistance in the care of this patient and in bringing this case to the attention of the Poison Control Centre; to Dr. E. R. Harpur for arranging the various biochemical investigations; to Dr. D. E. Douglas and Mr. R. M. Yanchinski for the analyses of thallium; to Dr. K. Metrakos for interpreting the EEG's; and to Dr. J. S. Fawcett for examination of the hair.

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