Heavy Metal Neuropathies

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CASES OF HEAVY METAL POISONING, although uncommon, do occur in ordinary clinical practice. The manifestations can be subtle or devastating, depending on the exposure, and the diagnosis can be difficult. The following three cases illustrate some of the possible presentations:

CASE 1

A 19-year-old man presented to the emergency room after having ingested 5–10 g of thallium nitrate in a suicidal attempt. He was treated with gastric lavage, activated charcoal, and hemodialysis to try to remove the thallium. On the second day, he complained of severe paresthesias, and experienced progressive muscular weakness. Respiratory insufficiency necessitated intubation. Sensory and motor deficits grew steadily worse over the next four days. The patient became anuric, and cardiac enzymes rose. He suffered a cardiac arrest and died. Peripheral nerves examined at biopsy two days before death and at autopsy showed a severe peripheral neuropathy with axonal degeneration, compatible with thallium intoxication.

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CASE 2

A 64-year-old man suffered three episodes of acute arsenic intoxication. His symptoms included nausea and vomiting, diarrhea, a skin rash, white lines across the nails, and a severe peripheral neuropathy with marked loss of sensory and motor function in the distal extremities. Twenty-four hour urine arsenic levels after the second and third episodes were 480 μg/l and 15,200 μg/l. A nerve biopsy at the time of the second episode showed a peripheral neuropathy with axonal degeneration. In spite of numerous efforts to determine the source of the poisoning, none was ever identified.

CASE 3

A 68-year-old man died of a hypertensive brainstem hemorrhage. At the time of autopsy, his daughter expressed concern that he might have had mercury poisoning. His hobby was to mine for gold and try to extract the gold from ores using elemental mercury to form an amalgam. Postmortem blood levels of mercury were 8.4 μg/100 ml, in the toxic range. Examination of peripheral nerves at autopsy showed a peripheral neuropathy with axonal degeneration. Since the patient also abused alcohol, a definitive diagnosis of mercury intox-
cation could not be made, but could be suspected from the blood levels.

Heavy metals can damage many organ systems, most often the nervous system, the gastrointestinal tract, and the kidney. This review will focus on the effects of certain heavy metals on the peripheral nervous system. Because the effects of lead and mercury have been most clearly described, they will be considered first. Arsenic and thallium, two well-known neurotoxins whose ingestion is often accidental or deliberate, will be discussed next. Finally, the effects of platinum and gold, two therapeutic agents with neurotoxic potential, will be described. Clinical and morphologic findings will be summarized, with an attempt to describe the mechanism(s) of toxicity, where possible. Several excellent general reviews of heavy metal toxicity, from both the toxicologic and neuropathologic viewpoints, are available.

Because biopsy of a peripheral nerve is a relatively noninvasive technique that can yield substantial information in appropriate cases, it is often performed in cases of suspected heavy metal poisoning. Thus, general guidelines for handling nerve biopsies are given. A brief review of the histology of the peripheral nerve and its reaction to injury follow.

**HANDLING THE NERVE BIOPSY SPECIMEN**

The procedure of nerve biopsy is a fairly simple one, and can be done on an outpatient basis, usually under local anesthetic. The sural nerve is almost universally used, because it is a purely sensory nerve, and its removal results only in loss of sensation to the lateral lower leg and foot. After a small skin incision is made, the nerve is identified lateral to the Achilles tendon on the posterior lateral leg. The normal nerve is fairly large, often 3 mm or more in diameter; a diseased nerve may be smaller due to atrophy. A segment, at least 3 cm long, is removed and immediately sent fresh to the laboratory for processing. Each end is tied with a piece of suture and the nerve is gently stretched, in one of two fashions (Fig. 1). The nerve can be stretched over a portion of a wooden tongue depressor, attaching the two sutures to the ends of the blade. Alternatively, the nerve can be suspended in a vial of fixative and stretched by attaching a small fishing weight to the lower suture. The specimen is fixed in an appropriate fixative, usually 2.5% glutaraldehyde, for 24 hours at 4°C. This technique also can be used for peripheral nerve taken at autopsy. Stretching a segment of nerve results in longitudinally oriented fibers that can be more easily examined.

Tissue from a nerve biopsy should be processed for evaluation by both light and electron microscopy. Thus, after removal of the ends, where crushing may have occurred, the specimen is divided into two approximately equal pieces (A and B, Fig. 2), depending on the actual length of the specimen. One-half of the tissue (A) is processed routinely in paraffin. A small segment is cut...