

# Rapid Development of Life-Threatening Emamectin Benzoate Poisoning

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A 75-year-old man presented to the ED after he intentionally ingested a 200-mL bottle of an agricultural insecticide.

Emamectin benzoate (EB) is a semisynthetic derivative of avermectin that has acaricidal, nematocidal, and insecticidal action. Avermectin analogs are natural products from soil fungi (*Streptomyces avermitilis*).<sup>1</sup> Emamectin benzoate was initially developed to eradicate lepidopteran larvae, particularly armyworms, and is registered in the United States and Japan for use on vegetable crops.<sup>2-4</sup> In addition to its agricultural use, EB also has antiparasitic effects on sea lice (*Lepeophtheirus salmonis*) that affect Atlantic salmon, and has been registered for use in several countries since 1999.<sup>5-7</sup> Although a few studies have evaluated the toxic effects of avermectin on humans, there is a paucity of information regarding human toxicity associated with EB.<sup>7</sup> This case report describes rapid deterioration of a patient following ingestion of EB.

## Case

A 75-year-old man presented to the ED 20 minutes after intentionally ingesting an agricultural insecticide. Upon presentation, the patient stated that he drank a whole bottle (100 mL) of insecticide after consuming alcohol, but denied coingestion of other

toxic substances or any medications. The patient provided the empty bottle upon presentation, and the ingested product was identified as Affirm, an insecticide containing 2.15% EB as the active ingredient.

The patient's medical history was significant for major depressive disorder, for which he was on alprazolam, donepezil, paroxetine, and quetiapine. The patient stated that he also suffered from chronic back pain, noting that he only took analgesics intermittently as needed.

On examination, the patient was alert and oriented to time and place. Initially, he did not experience any physical discomfort. His vital signs were: blood pressure (BP), 126/74 mm Hg; pulse rate, 67 beats/minute; respiratory rate, mildly tachypneic at 23 breaths/minute; and temperature, 97.9°F. Oxygen saturation was 96% on room air.

Ocular examination revealed both pupils to be equally round, 3 mm in diameter, and reactive to light. Examination of the oropharynx was normal and without signs of mucosal injury. The lung sounds were clear bilaterally, and the heart was a regular rate and rhythm and without murmur. The patient's abdomen was soft and

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Table. Sequential Result of Arterial Blood Gas Analysis

	90 min	320 min	380 min	430 min	680 min	740 min
pH	7.33	7.27	7.15	7.21	6.87	7.04
PCO <sub>2</sub> (mm Hg)	22	23	23	19	59	55
PO <sub>2</sub> (mm Hg)	97	92	90	126	53	38
Bicarbonate (mEq/L)	11.6	10.6	8.0	7.6	10.8	14.9
Base excess (mEq/L)	-12.0	-14.2	-19.0	-17.9	-22.6	-16.0
O <sub>2</sub> saturation (%)	97	96	94	98	55	45

Abbreviations: O<sub>2</sub>, oxygen; PCO<sub>2</sub>, partial pressure of carbon dioxide; PO<sub>2</sub>, partial pressure of oxygen.

nontender. No deficits, such as ataxia, dysarthria, or tremor were found on the neurological examination.

Prompt gastric lavage via a nasogastric tube was performed, and activated charcoal was administered. Laboratory evaluation was significant for the following: white blood cell count, 22.77 x 10<sup>9</sup>/L with 78% neutrophils and 16% lymphocytes; sodium, 138 mEq/L; potassium, 3.1 mEq/L; chloride, 109 mEq/L; blood urea nitrogen, 19 mg/dL; and creatinine, 0.7 mg/dL. Arterial blood gas (ABG) results revealed a pH, 7.37; partial pressure of carbon dioxide, 25 mm Hg; partial pressure of oxygen, 93 mm Hg; bicarbonate, 14.5 mEq/L; base excess, -8.9 mEq/L; and an oxygen saturation, 97%. Serum creatine kinase (CK), CK-MB and troponin levels were both within normal range. Lactic acid, serum osmolality, and serum ethanol levels were not obtained. The patient's electrocardiogram (ECG) and chest radiograph findings were normal.

Approximately 1 hour after presentation, the patient complained of an epigastric burning sensation and continued to exhibit mild tachypnea. A subsequent ABG test revealed progressive metabolic acidosis (Table). Although the patient was given a total of 800 mL of normal saline intravenously (IV) upon arrival at the ED, his

total urinary output was less than 100 mL 7 hours afterward. Attempts to increase urinary output with IV furosemide were ineffective.

Along with the progressive metabolic acidosis, the patient became hypotensive, and did not respond to IV fluid resuscitation. A norepinephrine infusion was started to improve BP, but this was likewise ineffective. Serial ECGs did not show any specific abnormalities such as dysrhythmia or ischemia.

The patient was admitted to the intensive care unit approximately 10.5 hours after presentation where he received continuous renal replacement therapy (CRRT) to correct the severe metabolic acidosis and poor circulation. Metabolic acidosis persisted despite CRRT, and the patient remained hypotensive even after receiving high-dose IV norepinephrine (Figure).

About 12.5 hours after his presentation to the ED, the patient began to vomit profusely and went into cardiac arrest. The cardiac monitor demonstrated pulseless ventricular tachycardia. Aggressive resuscitative efforts were initiated, but failed to restore spontaneous circulation.

### Discussion

As an avermectin analog, EB interacts with  $\gamma$ -aminobutyric acid (GABA) receptors and

enhances membrane chloride permeability.<sup>8</sup> In mammals, GABA-containing neurons and receptors are found in the central nervous system (CNS), but not in the peripheral nervous system. In cases of high-dose avermectin ingestion in humans, CNS toxicity, including agitation and depressed mental status, have been reported, as well as death resulting from respiratory failure.<sup>9</sup>

With respect to human EB toxicity, there is only one other documented case in the literature by Yen and Lin.<sup>7</sup> In their case, the authors report on a patient who ingested 100 mL of Proclaim, which contained 2.15% EB diluted with 400 mL of tap water.<sup>7</sup> They note that the patient in their case presented with mild confusion and gastrointestinal (GI) symptoms of nausea, vomiting, and cramping discomfort. Following laboratory and radiological investigation, the patient was found to have aspiration pneumonitis and admitted to the inpatient hospital. On hospital day 2, the patient's GI symptoms abated and he became alert and oriented. He was discharged 1 week from initial presentation and experienced no sequelae.

In our case, the patient ingested 100 mL of 2.15% EB without dilution. He also experienced GI symptoms, but did not have any CNS depression. The metabolic acidosis rapidly worsened, and could not be corrected, even with intensive therapy. This rapid life-threatening course has not previously been reported with avermectin or EB poisoning. In the avermectin poisoning cases in the literature, seven out of 19 patients (37%) exhibited severe effects, such as hypotension, coma, and aspiration with respiratory failure.<sup>9</sup> Six of the seven patients experienced a full recovery; the remaining patient died 18 days after ingestion from multiple organ failure.

The reason for our patient's rapid progression to metabolic acidosis and progressive deterioration (hypotension and hypoxemia) is not clear. One possible theory is that the solvents or other additives aside from EB in the ingested insecticide

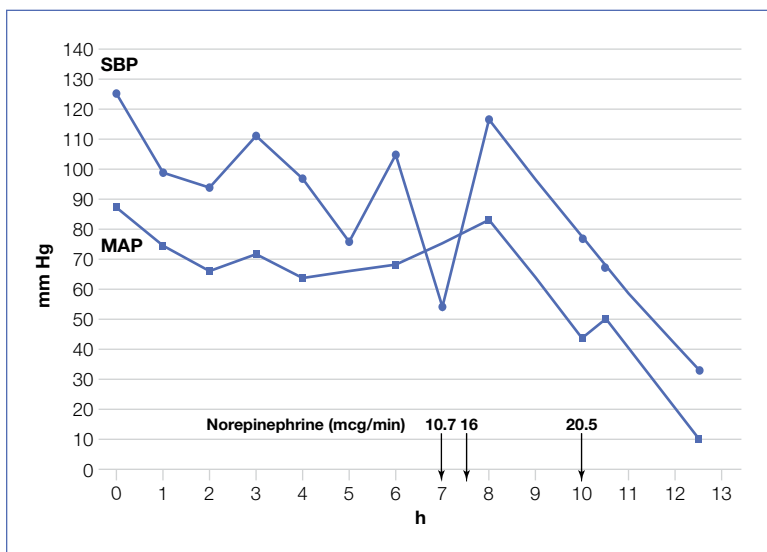


Figure. Chart detailing the persistent downward trend in the patient's systolic blood pressure (SBP) and mean arterial pressure (MAP) despite continuous renal replacement therapy and high-dose norepinephrine.

might make EB more toxic. In our case, the patient's rapid deterioration alone or asphyxia by vomitus might have been the cause of the cardiac arrest. Future reports and studies about EB toxicity in humans are warranted to investigate the pathogenesis of toxicity and appropriate treatment.

### Conclusion

This is the first report of a human death caused by EB poisoning; the patient experienced severe metabolic acidosis without CNS depression, ultimately leading to death. Emergency physicians should be aware of the possibility of rapid deterioration in patients who present after ingestion of EB and related substances.

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