CASE REPORT
cyanide poisoning, laetrile;
laetrile, cyanide poisoning

Acute Cyanide Poisoning from Laetrile Ingestion

Wilson C. Beamer, MD*†
Winston-Salem, North Carolina
Ralph M. Shealy, MD‡
Charleston, South Carolina
Donald S. Prough, MD*
Winston-Salem, North Carolina

From the Department of Anesthesia,* and the Section of Emergency Medical Services,† Department of Surgery, Bowman Gray School of Medicine, Winston-Salem, North Carolina; and the Emergency Department, Roper Hospital,‡ Charleston, South Carolina.

Submitted for publication August 23, 1982.
Revision received January 24, 1983.
Accepted for publication March 4, 1983.

Address for reprints: Wilson C. Beamer, MD, Department of Anesthesia, Bowman Gray School of Medicine, 300 South Hawthorne Road, Winston-Salem, North Carolina 27103.

A case of cyanide poisoning from laetrile ingestion is presented as an illustration of the recognition and treatment of cyanide intoxication. The pharmacology of laetrile, of cyanide, and of antidotes to cyanide intoxication are discussed as they relate to the acute management and successful treatment of this patient after this highly lethal ingestion. [Beamer WC, Shealy RM, Prough DS: Acute cyanide poisoning from laetrile ingestion. Ann Emerg Med 12:449-451, July 1983.]

INTRODUCTION

Intoxication with cyanide is fatal unless treated rapidly. Cyanide poisoning is one of the few potentially lethal poisonings in which early intervention with the correct antidotes may prevent death.

Cyanide is a metabolite of laetrile,[1] large doses of which may produce fatal poisoning.[2]

We recently encountered a nearly fatal case of cyanide poisoning secondary to laetrile ingestion in which rapid diagnosis and therapy led to a successful outcome.

CASE REPORT

A 22-year-old man was brought to the emergency department because of the acute onset of grand mal seizures. No history was obtainable. Blood pressure was 140/100 mm Hg, heart rate was 88 beats/min, and respirations were very deep at a rate of 32/min. The patient was comatose, unresponsive to pain, and demonstrated muscle rigidity with intermittent tonic clonic seizure activity. The pupils were fixed and dilated. The skin was pink. The lungs were clear to auscultation. There were no cardiac gallops or murmurs and the peripheral pulses were full. Blood glucose was 90 mg% by Dextrostix® (Ames, Division of Miles Laboratories, Elkhart, IN). A peripheral IV catheter was in place and naloxone hydrochloride 1.6 mg was given intravenously without response.

At that time an odor similar to that of almonds was noted on the patient's breath. Arterial blood gases drawn shortly after admission on room air were as follows: pH, 7.09; PaO_2, 135 mm Hg; $PaCO_2$, 9 mm Hg; HCO_3, 3 mEq; and O_2 saturation, 98.4%. Because of the combination of severe metabolic acidosis, normoglycemia, and the almond odor, a presumptive diagnosis of cyanide intoxication was made. Amyl nitrite was administered, 15 to 30 sec/min, by inhalation for approximately three minutes. Shortly thereafter, the patient was nasotracheally intubated and ventilated with 100% oxygen.

He received sodium nitrite 300 mg intravenously, followed by 12.5 g sodium thiosulfate IV. Five minutes after infusion of the thiosulfate, arterial blood gases were as follows: pH, 6.82; PaO_2, 143 mm Hg; $PaCO_2$, 23 mm Hg; HCO_3, 4 mEq; and O_2 saturation, 98%. The methemoglobin level was 3.3%. Sodium bicarbonate 88 mEq was given IV. Five minutes later arterial blood gases were as follows: pH, 6.99; PaO_2, 582 mm Hg; $PaCO_2$, 20 mm Hg; and HCO_3, 10 mEq. The methemoglobin level had increased to 6.6%. An additional 88 mEq sodium bicarbonate and 300 mg sodium nitrite were administered intravenously. Five minutes later arterial blood gases were as follows:

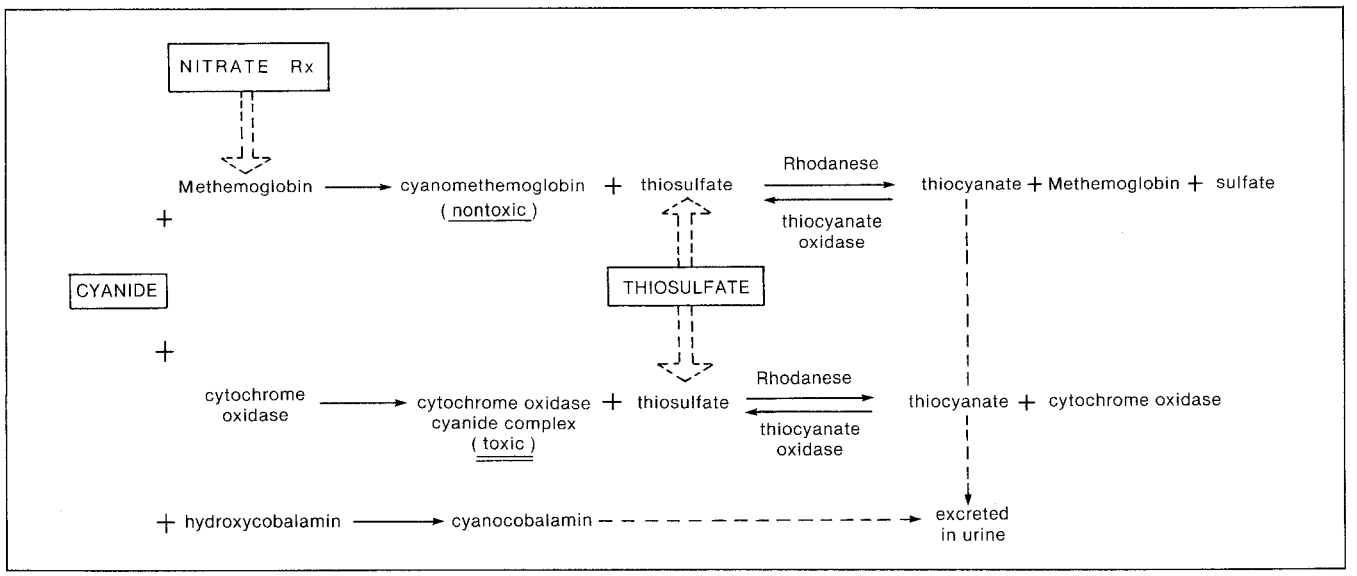

Fig. *Cyanide detoxification.*

pH, 7.21; PaO_2, 562; $PaCO_2$, 26 mm Hg; and HCO_3, 10 mEq. The methemoglobin level was 10.5%. Additional supportive measures instituted included gastric lavage, urinary catheterization, and neuromuscular blockade with 8 mg pancuronium bromide. The latter was necessary due to persistent violent seizure activity refractory to therapy with diazepam.

No further specific treatment was administered. Supportive care with mechanical ventilation was continued. Metabolic acidosis progressively cleared. The patient rapidly recovered full neurological function and was extubated 20 hours after admission. Routine urine toxicology and heavy metal screening were normal.

It was later learned that the patient had undergone a thoracotomy for carcinoma approximately one year prior to admission and, after refusing the recommended radiation therapy, had gone to Mexico to obtain laetrile. The patient admitted to missing several days of his medication after which he took 12 to 18 tablets in order to "catch up."

DISCUSSION

This case illustrates the favorable outcome that may occur if cyanide intoxication is expeditiously diagnosed and treated. Unfortunately, recognition of cyanide poisoning may be delayed because the majority of clinical and laboratory findings are nonspecific.

Headache, vomiting, hyperventilation, tachycardia, coma, seizures, hypotension, and death are common clinical presentations.[2-5] Graham[3] reported a case in which pulmonary edema, apparently secondary to left ventricular failure, also occurred. Evidence of anaerobic metabolism is prominent, including metabolic acidosis, elevated blood lactate levels, and a widened anion gap reflecting inhibition of cellular respiration.[1,3]

Metabolic acidosis stimulates hyperventilation, as was evident in our patient. Two physical findings said to be of some value include bright-red retinal veins and the odor of almonds on the patient's breath.[6] However, the sensitivity of these two findings has been questioned.[3,7] The retinal arteries and veins might be equally red only in massive poisoning,[3] and there is apparently marked individual variation in the ability to recognize the odor of cyanide or, for that matter, the odor of essence of almond.[7] In our case, the diagnosis was based on the combination of neurological findings, metabolic acidosis, and recognition of the odor of almonds.

No simple, rapid confirmatory test for cyanide intoxication is readily available. Lee-Jones et al[8] described a test that will rapidly distinguish cyanide from other common intoxicants. Confusion with salicylate poisoning, in which the clinical presentation might be quite similar, could still occur.[3] Cyanide blood levels are not readily available. If obtained, normal levels are less than 0.20 μg/mL[9] and levels of greater than 3 μg/mL are associated with mortality.[10]

A history of laetrile ingestion, when it can be elicited, can be of considerable assistance. The principal constituent of laetrile is amygdalin, one of a group of cyanogenic compounds found in fruit pits, plants and berries.[11] Apricot pits and bitter almonds contain especially high concentrations of amygdalin that, when broken down to cyanide, can be lethal if sufficient quantities are ingested.[1] Breakdown depends on the enzyme emulsin, contained in the fruit pit, or beta glucosidase, an enzyme found in the gastrointestinal tract. Consequently laetrile is toxic only if administered orally or rectally, because conversion must occur in the gastrointestinal tract. Intravenous laetrile does not produce cyanide intoxication. After a toxic dose of laetrile is ingested, there may be a delay in the development of symptoms because emulsin does not maximally hydrolyze amygdalin until it is transported into the alkaline environment of the small intestine.[11]

Other sources of cyanide include industrial and chemical compounds, photographic processing materials, fumigants, insecticides, the combustion of hydroxyurethanes and nylons, and administration of excess quantities of nitroprusside.[12-16]

Treatment of cyanide intoxication is a combination of effective supportive therapy and administration of chemical antidotes. Appropriate supportive therapy consists of oxygen, ventilation if necessary, sodium bicarbonate for severe metabolic acidosis and, when indicated, cardiovascular support. In addition gastric lavage should be ini-

tiated with a large bore tube once the airway has been protected. Charcoal may be given in case other toxic products have been ingested. In our case, muscle paralysis may have been useful in limiting oxygen consumption and anaerobic metabolism produced by violent seizure activity.

The antidotal treatment of cyanide intoxication is still based on a description by Chen in 1933.[17] Sodium thiosulfate is administered to prevent depletion of endogenous thiosulfate, a compound that combines with the toxic complex of cytochrome oxidase and cyanide to produce thiocyanate and to regenerate cytochrome oxidase. This reaction is mediated by the enzyme rhodanese (Figure). Depletion of endogenous thiosulfate may cause the reaction to proceed in the reverse direction, through the enzyme thiocyanate oxidase, accounting for several reports of reintoxication.[18] Administration of thiosulfate is apparently nontoxic.[3] The other two classical antidotes are the nitrite compounds, amyl nitrite and sodium nitrite. These compounds cause an increase in methemoglobin concentration above the normal 1% level.[19]

Methemoglobin differs from normal hemoglobin in that the iron is in the ferric rather than the ferrous state. Ferric iron binds cyanide to produce cyanomethemoglobin, which in turn combines with thiosulfate and, in a reaction again mediated by rhodanese, is broken down into thiocyanate and methemoglobin (Figure). Thiocyanate is excreted in the urine. Adequate thiosulfate is necessary for the metabolism of cyanomethemoglobin. The sequence of therapy recommended in the Lilly Cyanide Poisoning Kit, number N-76 (Eli Lilly and Company, Indianapolis, IN), suggests the administration of amyl nitrite by inhalation, 15 to 30 sec/min, followed by intravenous administration of sodium nitrite (300 mg for an adult) and the intravenous administration of sodium thiosulfate (12.5 g for an adult). Pediatric dosage has been defined by Berlin.[20]

Therapy with nitrites is not benign. Methemoglobin does not carry oxygen; consequently levels greater than 30% to 40% of circulating hemoglobin are themselves toxic, with evidence of tissue hypoxia appearing at levels of greater than 60% of circulating hemoglobin.[21] In addition, both amyl nitrite and sodium nitrite may cause severe hypotension.[3]

Other therapy of cyanide intoxication has been reported. Hydroxycobalamin (vitamin B_{12a}), an apparently nontoxic drug, is effective in treating cyanide intoxication by formation of the compound cyanocobalamin (vitamin B_{12})[3,22] (Figure). Dicobalt EDTA has been popularized in Europe under the name Kelocyanor®. Cobalt is a good chelating agent of cyanide but has significant toxicity of its own and has not been approved for use in this country.[23]

Our case is an example of successful treatment of cyanide intoxication secondary to laetrile ingestion, in which the diagnosis was made and therapy instituted quickly based on a high index of suspicion.

REFERENCES

1. Morse DL, Harrington JM, Heath CW: Laetrile, apricot pits, and cyanide poisoning. *N Engl J Med* **295**:1264, 1976.

2. Braico KT, Humbert JR, Terplan KL, et al: Laetrile intoxication. Report of a fatal case. *N Engl J Med* **300**:238-240, 1979.

3. Graham DL, Laman D, Theodore T, et al: Acute cyanide poisoning complicated by lactic acidosis and pulmonary edema. *Arch Intern Med* **137**:1051-1055, 1977.

4. Morse DL, Boros L, Findley PA: More on cyanide poisoning from laetrile, (letter). *N Engl J Med* **301**:892, 1979.

5. Ortega JA, Creek JE: Acute cyanide poisoning following administration of laetrile enemas. *J Pediatr* **93**:1059, 1978.

6. De-Busk RF, Seidl LG: Attempted suicide by cyanide. A report of two cases. *California Medicine* **110**:394-396, 1969.

7. Buchanan IS, Dhamee MS, Griffiths FE, et al: Abnormal fundal appearances in a case of poisoning by a cyanide capsule. *Med Sci Law* **16**:29-32, 1976.

8. Lee-Jones M, Bennett MA, Sherwell JM: Cyanide self-poisoning. *Br Med J* **4**:780-781, 1970.

9. Halstrom F, Moller KO: Content of cyanide in human organs. *Acta Pharmacol* **1**:18, 1945.

10. Bonnischen R, Maehly AC: Poisoning by volatile compounds. III. Hydrocyanic acid with reports of 40 lethal cases of intoxication. *J Forensic Sci* **11**:516-528, 1966.

11. Dorr RT, Paxinos J: The current status of laetrile. *Ann Intern Med* **89**:389-397, 1978.

12. Toxicity of laetrile. *FDA Drug Bull* 7:26-32, 1977.

13. Winek CL, Fusia E, Collom WD, et al: Cyanide poisoning as a mode of suicide. *Forensic Sci* **11**:51-55, 1978.

14. Goldfrank LR, Kirstein R: *Toxicologic Emergencies: A Handbook in Problem Solving*. New York, Appleton-Century-Crofts, 1978.

15. Symington IS, Anderson RA, Oliver JS, et al: Cyanide exposure in fires. *Lancet* **2**:91-92, 1978.

16. Cohn JN, Burke LP: Nitroprusside. *Ann Intern Med* **91**:752-757, 1979.

17. Chen KK, Rose CL, Clowes GHA: Amyl nitrate and cyanide poisoning. *JAMA* **11**:1920-1922, 1933.

18. Naughton M: Acute cyanide poisoning. *Anaesth Intensive Care* **2**:351-356, 1974.

19. Curry S: Methemoglobinemia. *Ann Emerg Med* **11**:214-221, 1982.

20. Berlin CM Jr: The treatment of cyanide poisoning in children. *Pediatrics* **46**:793-796, 1970.

21. Done AK: The toxic emergency. Blue skin and chocolate lips. *Emergency Medicine* **8**:283-286, 1976.

22. Posner MA, Tobey RE, McElroy H: Hydroxycobalamin therapy of cyanide intoxication in guinea pigs. *Anesthesiology* **44**:157-160, 1976.

23. Evans CL: Cobalt compounds as antidotes for hydrocyanic acid. *Br J Pharmacol* **23**:455-475, 1964.

In the article entitled "Rupture of the Right Hemidiaphragm Due to Blunt Trauma," by Phyllis L. Leaman, MD, (**12**:351-357, June 1983) Figure 1 was incorrectly labeled Figure 2 and Figure 2 was incorrectly labeled Figure 1. The editors regret any inconvenience caused by this error.