# Methemoglobinemia From Eating Meat With High Nitrite Content

## By J. D. ORGERON, M.P.H., J. D. MARTIN, M.D., C. T. CARAWAY, D.V.M., ROSE MARY MARTINE, B.S., and GEORGE H. HAUSER, M.D.

TEN CASES of methemoglobinemia occurred near New Orleans, La., in October 1955. From epidemiological and laboratory investigations, we determined that they were due to nitrite poisoning which resulted from eating wieners and bologna containing large amounts of the chemical.

Before detailing the circumstances of the outbreak, we shall review briefly the medical aspects of methemoglobinemia and consider the use of nitrites in meat.

#### Methemoglobin in the Blood

Methemoglobinemia is a condition in which a part of the hemoglobin has been oxidized to methemoglobin with a consequent reduction in the oxygen-combining and oxygen-carrying power of the blood. The oxidation may be caused by absorption, inhalation, or ingestion of large doses of certain chemicals, particularly the nitrites, nitrates, sulfonamides, and aniline derivatives.

Onset of symptoms is sudden, usually within 1 or 2 hours after contact with, or ingestion of,

Mr. Orgeron, Dr. Martin, Dr. Caraway, and Miss Martine are members of the epidemiology team, Louisiana State Department of Health. Mr. Orgeron is a sanitarian epidemiologist, Dr. Martin is chief of the epidemiology section, Dr. Caraway is a veterinary epidemiologist, and Miss Martine is a nurse epidemiologist. Dr. Hauser is director of the division of laboratories and acting director of the division of food and drugs and the chemicaltoxicological laboratory of the health department. the poison. The symptoms include nausea, vomiting, profuse sweating, and an intense cyanosis of the fingertips, nose, and ears.

Mild cases of methemoglobinemia result when less than 50 percent of the hemoglobin is oxidized to methemoglobin. After 70 to 80 percent is oxidized, there is a progression of ataxia, dyspnea, excessive salivation, prostration, and unconsciousness. Oxidation of 90 percent or more is fatal unless immediate treatment is given (1).

A presumptive diagnosis of methemoglobinemia should be made if there is a history of rapid onset of cyanosis without physical findings of cardiac, pulmonary, or intracranial disorder. A history of ingestion of a substance containing nitrites or nitrates within the past few hours aids in establishing the diagnosis. If cyanosis is unrelieved by oxygen therapy and if blood withdrawn from a vein shows the characteristic chocolate-brown coloration, the diagnosis is almost certain (2).

A definitive diagnosis of methemoglobinemia can be made with the laboratory procedure reported by Evelyn and Malloy (3). This procedure, which uses a single sample of blood from the finger, is an accurate photoelectric method of determining the oxyhemoglobin, methemoglobin, and sulfhemoglobin levels of the blood.

Methylene blue is an effective antidote for toxic methemoglobinemia. The recommended dosages are 1 mg. of methylene blue per kilogram of body weight for adults and 2 mg. of methylene blue per kilogram of body weight for children. These amounts should be injected intravenously over a 5-minute period. Dosages should not exceed 7 mg. per kilogram since toxic effects such as dyspnea, precardial pain, restlessness, a sense of oppression, apprehension, and fibrillar tremors may occur (1).

Numerous cases of methemoglobinemia have been traced to the consumption of well water containing large amounts of nitrates (4-7), contact with aniline dyes used in crayons (8-11) and laundry marking ink (12, 13), accidental ingestion of leather dyes and furniture polish (2), and ingestion or absorption of varied medications containing hemoglobin oxidizing components (14-16). Only a few outbreaks have been reported in which the causative agent was contained in food. One of these was an outbreak in New York City in which 11 aged men who had eaten breakfast at the same cafeteria were affected. Investigation showed that sodium nitrite was used in place of table salt in the seasoning of the oatmeal they had eaten (17). Another was an outbreak of acute toxic methemoglobinemia among a group of people who had eaten wheatcakes and "maple sirup" at a diner in Syracuse, N.Y. In this outbreak. investigation revealed that a commercially prepared corning extract containing 8 percent nitrites, 4 percent nitrates, and sucrose was inadvertently served as maple sirup to the affected individuals (18).

#### Nitrites in Meat

Nitrites and nitrates are used in curing meats mainly because of their color-fixing qualities, although these substances also have some preservative properties. When added to meat, sodium nitrate (Chile saltpeter) or potassium nitrate (saltpeter) is reduced to the corresponding nitrite by the action of certain bacteria that occur naturally in the meat and on processing equipment. The nitrites are further broken down by hydrolysis to form nitric oxide. This simple compound combines with the muscle hemoglobin (myoglobin) of the meat to form a more permanent pink substance, nitric oxide myoglobin. This pigment is more stable than the natural pigment found in blood and muscle fibers and is also more resistant to the action of air, heat, and bacteria (19).

Federal meat regulations and most of the

State food and drug regulations prohibit the use of more than 200 p.p.m. of nitrite in meat products for human consumption. These regulations also require that products containing nitrates and nitrites be labeled to that effect.

The amount of nitrite that can be utilized by meat is limited by the amount of myoglobin originally in the muscle tissues. The addition of excessive amounts of nitrites will not increase or intensify the color, but it may have an adverse effect on the meat.

## **Circumstances of the Outbreak**

The Louisiana State Department of Health first learned of the outbreak of methemoglobinemia in the New Orleans area from a report of two cases from a practicing pediatrician.

The first patient was a 2-year-old girl who became ill about 2 hours after eating 2 wieners. Symptoms, as observed by the child's mother, included profuse sweating, vomiting, and a bluish-gray cyanosis around the lips and nails. The family physician was called immediately, and the child was hospitalized with a presumptive diagnosis of methemoglobinemia. The child responded well to an intravenous injection of methylene blue and was discharged from the hospital the following day.

Specimens of the vomitus, which contained particles of wieners, and samples of wieners obtained from the same package from which the meal was prepared were submitted to the chemical-toxicological laboratory of the State health department for determination of the nitrite content. Chemical analysis showed that the vomitus contained 11.8 p.p.m. of nitrite and that the wieners contained 5,420 p.p.m. of nitrite.

The following day the second case of methemoglobinemia was reported in a 3-year-old boy. Speech disturbance and cyanosis of the lips and nails were observed about 2 hours after the child had eaten 2 wieners manufactured by the same meat plant that prepared the ones eaten by the first patient. The child recovered rapidly after hospitalization and treatment with methylene blue injected intravenously. Samples of the wieners obtained from the same package as those eaten by this child contained 5,420 p.p.m. of nitrite. The remaining 8 patients exhibited symptoms similar to the first 2, and all responded well to treatment with methylene blue. Seven had eaten wieners and one had eaten bologna, all manufactured at the same plant.

Of the 10 persons ill in this outbreak, 8 were between the ages of  $1\frac{1}{2}$  and 5 years. For this group the interval between eating the meat and onset of symptoms was 2 hours. The other 2 patients were 10-year-olds, and the time lapse between eating the meat and onset of symptoms was about 6 hours.

#### Inspection of the Plant

After the report of the third case and the finding of excessive quantities of nitrite in the wieners, State and local health department sanitarians were notified to place under seizure all retail stocks of wieners manufactured by the meat plant in question. Later, when the case in which bologna appeared to be the cause was reported, some retail stocks of bologna manufactured by this plant were also seized. One or more samples from each lot of meat placed under seizure were sent to the State chemicaltoxicological laboratory for nitrite determinations.

In 131 samples of the assorted meat products, nitrite concentrations varied from 3.3 p.p.m. to 6,570 p.p.m. Seventeen of the samples (14 of wieners and 3 of bologna) contained nitrites in excess of the maximum allowable of 200 p.p.m. The lots from which these samples were taken were destroyed by burning.

In an effort to determine the conditions responsible for the excessive amounts of nitrites in these meat products, we subsequently made an inspectional tour of the manufacturing plant. (This plant does not use Federal, State, or local meat inspection services.) The general manager and the sausage production manager of the plant explained each operation in the wiener and bologna manufacturing process, with particular emphasis on the mixing and blending operations.

In preparing wieners or bologna, approximately 400 pounds of coarsely ground meat and meat products are added to a silent cutter, along with ice for cooling, a prepackaged spice preparation, and 1.5 pounds of a commercially prepared powder containing nitrite and nitrate. This powder is composed of approximately 6 percent sodium nitrite, 4 percent sodium nitrate, 87 percent sodium chloride, and 3 percent moisture. After 12 to 20 minutes in the silent cutter, the material is conveyed to the stuffing room, where the artificial casings are filled. Samples of the artificial casing contained only a trace of nitrite.

During our inspection of the spice storage room, we noticed an unopened container of "pure" sodium nitrate powder. On close questioning concerning the use of this powder, the sausage production manager stated that this material was just recently obtained. The commercially prepared nitrite-nitrate powder produced too fast a "cure" on some products, he explained, and he had ordered the "pure" sodium nitrate to correct this difficulty. He knew of no "pure" sodium nitrate compounds ever having been used in the plant.

Since the commercially prepared powder contained only 10 percent sodium nitrite and sodium nitrate, about 36 to 40 pounds of this material would have to be added to a 400-pound batch of meat to provide the concentration of 6,570 p.p.m. found in one sample of wieners. The amount of sodium chloride contained in 36 to 40 pounds of the commercial preparation would have made the wieners very distasteful. Hence, it would seem that a product containing a larger concentration of nitrate or nitrite (or both) than the powder would have had to be used to result in the quantities of nitrite reported by the laboratory.

After our tour of the plant, we obtained information regarding personnel changes during recent months, disposition of broken and imperfect wieners, records of nitrite and nitrate inventories, and routine laboratory controls on the meat products. Investigations of these items, however, did not help us determine how the excessive quantity of nitrite got into the wieners and bologna.

Many safeguards were taken to insure the accuracy of the chemical analyses. Two laboratories in addition to the State chemical-toxicological laboratory analyzed samples of the meat products, and all found similar nitrite concentrations. Laboratory examination of the commercially prepared powder used at the plant indicated that it did not contain more than the 10 percent sodium nitrite and sodium nitrate indicated on the label. The salt content of the wieners manufactured by the plant was found to be within normal limits.

Laboratory analysis of samples of wieners manufactured by other plants using the same commercial nitrite-nitrate preparation did not show the excessive amounts of nitrites found in the products of the plant under suspicion.

Bacteriological examination of samples of the suspected meat products did not reveal any organisms of the food-poisoning type.

Although we were unable to determine exactly how the additives were applied to the meat products to result in the excessive concentrations of nitrite, it seems most likely that a product containing a large quantity of nitrate or nitrite (or both) was mistakenly added to one or more batches of the wiener and bologna mixtures. Since the inventory controls of the additives were haphazard and the code dating of the meat products was unreliable, we were unable to learn the date that the incident occurred. Had this information been available, we could have directed our investigations to the events of the day in question.

#### **Summary and Conclusion**

In October 1955, an outbreak of 10 cases of methemoglobinemia occurred in the New Orleans, La., area. Early evidence pointed to the ingestion of large amounts of nitrite in wieners and bologna as the cause.

Investigation revealed that 9 victims had eaten wieners and 1 had eaten bologna manufactured by the same plant. Laboratory analysis of 131 samples from retail stocks of meat products manufactured by this plant indicated that 17 samples contained nitrite concentrations in excess of 200 p.p.m., the maximum amount permissible under Federal and State regulations. The concentrations ranged up to 6,570 p.p.m. A commercially prepared powder containing 10 percent sodium nitrite and sodium nitrate was used routinely in preparing the wieners and bologna.

Exactly how the excessive quantity of nitrite got into the meat products could not be determined. It seems likely, however, that a product containing a larger quantity of nitrate or nitrite (or both) than the commercially prepared powder had been added by mistake to one or more batches of the wiener and bologna mixtures.

This outbreak demonstrates the need for effective meat inspection services in all meat packing plants. An official meat inspection program should be the aim and eventual goal of every State and municipality. In the meantime, all owners and employees of meat plants should be made aware of the dangers of careless handling of nitrates, nitrites, and other chemical additives.

• • •

Since the occurrence of this outbreak, a similar incident was reported in Florida. Two children, a 4-year-old boy and a 15-month-old girl, from the same household became ill after eating uncooked wieners. The subsequent death of the 4-year-old child has been attributed to eating the uncooked wieners.

#### REFERENCES

- Doctor, L.: The classification and treatment of methemoglobinemia. Quart. Bull. Northwestern Univ. M. School 27:134-137 (1953).
- (2) Macdonald, W. B.: Methaemoglobinaemia resulting from poisoning in children. M. J. Australia 1:145-147 (1951).
- (3) Evelyn, K., and Malloy, H.: Microdetermination of oxyhemoglobin, methemoglobin and sulfhemoglobin in a single sample of blood. J. Biol. Chem. 126:655 (1938).
- (4) Methaemoglobinaemia due to nitrites in water— Report of one case history. Brit. M. J. No. 4887; 575-576, Sept. 4, 1954.
- (5) Fawcett, R. C., and Miller, H. C.: Methemoglobinemia in infants fed milk diluted with well water high in nitrate content. J. Pediat. 29: 593-596, November 1946.
- (6) Comly, H. H.: Cyanosis in infants caused by nitrates in well water. J. A. M. A. 129:112-116 (1945).
- (7) Ferrant, M.: Methemoglobinemia—Two cases in newborn infants caused by nitrates in well waters. J. Pediat. 29: 585-592 (1946).
- (8) Rieders, F., and Brieger, H.: Mechanism of poisoning from wax crayons. J. A. M. A. 151:1490, April 1953.
- (9) Brieger, H.: Poisoning due to ingestion of wax crayons. Am. J. Pub. Health 39:1023 (1949).

- (10) Jones, J. A., and Brieger, H.: Poisoning due to ingestion of wax crayons. J. Pediat. 30:422 (1947).
- (11) Clark, E. B.: Poisoning due to ingestion of wax crayons. J. A. M. A. 135:917 (1947).
- (12) Pickup, J. D., and Eeles, J.: Cyanosis in infants caused by aniline dye poisoning. Lancet 265:118, July 18, 1953.
- (13) Etteldorf, J.: Methylene blue in the treatment of methemoglobinemia in premature infants caused by marking ink. J. Pediat. 38: 24-27, January 1951.
- (14) Wallace, W. W.: Methemoglobinemia in an infant as a result of the administration of bismuth subnitrate. J. A. M. A. 133: 1280 (1947).
- (15) Rozenfeld, I. H.: Methemoglobinemia resulting

from the absorption of sodium nitrite. J. A. M. A. 152: 706, June 20, 1953.

- (16) Oppe, T. E.: Methaemoglobinaemia due to sodium nitrite. Lancet 261:1051, May 12, 1951.
- (17) Greenberg, M., Brinkrant, W. B., and Schiftner, J. J.: Outbreak of sodium nitrite poisoning. Am. J. Pub. Health 35: 1217-1220, November 1945.
- (18) Tepperman, J., Marquardt, R., Reifenstein, G., and Lozner, E.: Methemoglobinemic cyanosis— Report of an epidemic due to corning extract substituted for maple syrup. J. A. M. A. 146:923-925, July 7, 1951.
- (19) Institute of American Meat Packers: Sausage and ready to serve meats. Chicago, Institute of Meat Packing, Haskell Hall, University of Chicago, 1938.

# techniques

## Soda Fountain School

Employees of Cleveland's 600 drug stores will be trained at the School of Soda Fountain Sanitation operated in the city hall by the Cleveland Division of Health. Graduates will receive a food-handler's button to wear on their uniforms.

Designed to reduce the need for enforcement of sanitary regulations, the school's short course combines audience participation, group discussion, and role playing in four 2hour sessions. Students are told and shown why a clean, colorful fountain will attract new customers, establish a regular clientele, increase sales for the drug store, and add pennies to their own pockets.

Classes began January 2, 1957. They are open to fountain employees of independent and chain stores throughout the Cleveland area in first-come, first-served order. Owner-manager representatives of the drug stores are encouraged to attend at times not used by their employees. Eventually, the course



will be offered to applicants attending high school.

The classroom seats 35. To one side is a fully equipped luncheonette, complete with mechanical dishwashing, refrigeration, and cooking facilities. All of the equipment has been donated by manufacturers and associations. Teaching aides include motion pictures, slides, flip charts, bulletin boards, pamphlets, checklists, and self-inventory sheets. Three regular and two guest instructors conduct the classes and give everyone individual attention when needed.

On completing the course, each graduate receives a permanent number, a card, and a button. Some of the stores have agreed not to employ new help until they have earned the food-handler's button.

Every store sending all of its employees through the course receives a certificate for public display if it also has had no sanitary violations. The certificate is revokable when violations are found.