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CLINICAL CASE

Physicians' Duty to Be Aware of and Report Environmental Toxins

Commentary by Gina M. Solomon, MD, MPH, and Steven R. Kirkhorn, MD, MPH

Miguel's mother brought her 3-month-old son to a rural clinic for an urgent care visit. Miguel was vomiting and had diarrhea. Among his other worrisome symptoms were cyanosis, drowsiness, and rapid breathing. His physician told his mother he needed to go to the nearest ER by ambulance and she agreed. At the ER, they were rushed into an exam room, with the baby on oxygen.

Miguel was found to have central cyanosis which had not improved despite the oxygen. After talking to his mother about the baby and their living situation, the ER physician ordered some specialized blood tests, co-oximetry, and a methemoglobin level. The infant was diagnosed with methemoglobinemia, and therapy was started, alleviating the cyanosis almost immediately. Miguel went home on the second hospital day with no evidence of brain damage from hypoxia.

Miguel was the fifth child seen in the hospital over an 8-week period with methemoglobinemia. The doctors believed all the cases were caused by nitrate toxicity. The widespread use of nitrate fertilizers increases the risk of water contamination in rural areas. Infants under 4 months of age are at particular risk of nitrate toxicity from contaminated water. Physicians suspected that the water Miguel's mother was mixing with his powdered formula was contaminated with nitrates.

Her primary doctor at the rural clinic told her, "your well water is probably contaminated. So you see, Miguel's blood has been changed by this water; it can't transport oxygen from the air he breathes around his body. So, that's why he was turning blue. It was dangerous. He needs safe water in his formula. Try finding some bottled water for now."

Commentary 1

by Gina M. Solomon, MD, MPH

Diagnosis of methemoglobinemia means that an infant has been exposed to a toxicant in the environment that has seriously endangered his or her health. In a rural environment, by far the most common cause of this disease is nitrate-contaminated water. Depending on the source of the contamination, large numbers of infants may be in danger of illness or death. From an ethical perspective, it is as unconscionable to fail to address the root cause of this problem.

In fact, this case already demonstrates a serious lapse of medical ethics, given that four infants have been seen at this hospital over 2 months with the disease, yet apparently no action has been taken. The proper course would be to act after an index case is diagnosed. If the physicians had already acted on their ethical obligation, Miguel might not have become ill.

Nitrate contamination has been an increasing problem in water systems in the United States, probably due to the growing use of synthetic fertilizers since the 1950s [1]. Nitrogen contamination also results from intensive livestock operations, leaking septic systems, and municipal wastewater discharges. The most commonly contaminated water supplies come from shallow groundwater aquifers. According to the U.S. Environmental Protection Agency (EPA), about 4.5 million people—almost all in rural areas—have nitrate levels in their water supply in excess of the legal limit (maximum contaminant level) of 10 mg/L of nitrate [2].

Infants are the most susceptible to methemoglobinemia for a variety of physiological reasons [3]. High exposures cause Blue Baby Syndrome (the characteristic blue-gray cyanosis as seen in this case); but lower levels of exposure are also harmful, decreasing oxygenation of the central nervous system, impairing neurodevelopment, and potentially resulting in the formation of carcinogenic nitrosamines in the stomach [2]. Public health action is therefore required not only to prevent the acute presentation, but also to protect a larger portion of the population against more subtle or delayed health effects.

First and foremost, the physician has a direct obligation to Miguel and his family. Obviously it is of paramount importance to educate the family about the problem [4]. Once the physician is assured that the family will not continue to consume the tap water, there are several possible courses of action, depending on the exact circumstances in the community.

If the family is served by a public water system, the system is in violation of the EPA drinking water standard and must be reported to both the local water utility and the EPA for investigation. In this case, the physician must educate the family and report the problem to these two authorities in order to discharge his or her ethical obligation. The EPA would follow up and work with the utility to address the violation and warn others who are served by the contaminated water system.

Many people in rural areas drink from private wells, which poses another problem. Well water is not regulated by any government agency. The expense of testing the water and purchasing a reverse osmosis filtration system falls completely on the family. The fact that 5 cases of nitrate poisoning have been seen in this hospital clearly indicates that, if well water is the source of contamination, the affected aquifer is tapped by numerous wells in the community. In a poor community, the cost of addressing this contamination can be prohibitive for the families involved. Here is where the physician must decide whether to act as an advocate for the health and well-being of the community. The Principles of Medical Ethics state that "A physician shall recognize a responsibility to participate in activities contributing to the improvement of the community and the betterment of public health" [5]. The physician's obligation therefore clearly extends beyond his or her own patient to the broader community.

The physician should contact the state or county health department and press them to provide free testing of drinking water for families on private wells living in the area and to issue warnings in the local press. Warning and informational signs should be posted in the hospital and local clinics in all languages spoken in the area. Practitioners in the hospital and community should be educated to provide anticipatory guidance to families and to recognize the early signs of methemoglobinemia. Although these activities are partially the responsibility of the health department, physicians have an obligation to educate their patients and push the health department to act if it does not do so quickly.

One ethical responsibility not commonly discussed is physicians' duty to know the communities in which they practice. This obligation encompasses the need to understand social and cultural practices, socioeconomic challenges, and environmental hazards prevalent in the local community. In a rural agricultural community, hazards associated with farming, as well as specific hazards such as nitrate contamination, pesticide drift, and common allergens, should be well-understood by local practitioners. This knowledge promotes correct and rapid diagnosis when problems occur and enhances the physician's ability to practice prevention through anticipatory guidance and patient education.

In summary, the physician's ethical obligation goes beyond educating the individual family affected in this case and extends to reporting to appropriate authorities. If there are no regulatory authorities, the physician may have the duty to advocate for the families that might be affected to ensure investigation, remediation, and education. If a polluter is identified, that entity may be held responsible for the cost of investigating and remediating the problem, medical expenses, and permanent injuries to the affected infants. Finally, physicians have a responsibility to inform themselves about the communities in which they practice, so they are prepared for environmental health threats that may arise.

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Commentary 2
by Steven R. Kirkhorn, MD, MPH

The case of Miguel illustrates how exposure to a toxin that can be lethal for infants may be overlooked because the resulting condition is not a reportable disease. Miguel responded to treatment for a diagnosis secondary to nitrate exposure with no recognized sequelae. The hospital staff was attuned to the condition because Miguel was the fifth child seen with a diagnosis of methemoglobinemia during an 8-week period. By contrast, Wisconsin, a state which has had an active surveillance program for methemoglobinemia, identified eight cases from 1990 to 1999, three of which involved infants with formula prepared with water from nitrate-contaminated wells [1].

This extremely high incidence could be considered a public health threat, so it is appropriate for the hospital staff or pediatrics department that recognized the trend to notify the county or state public health department. More than 2,000 cases have been reported worldwide and sporadically in the United States since the first case of a fatal ingestion by an Iowa infant of nitrate-contaminated well water was reported in 1945 [2, 3]. Other sources of acquired methemoglobinemia include nitrate-contaminated food and medications such as benzocaine (used for teething), lidocaine, sulfonamides, and topical silver nitrates used for burns [2, 4, 5].

Physicians who see infants 6 months and younger with cyanosis in agricultural or rural areas should consider the possibility of nitrate-contaminated rural drinking water. The disease is more common in infants who are bottle-fed with formula that has been diluted with water from private wells than in breast-fed infants. Boiling water used to dilute formula increases the concentration of nitrates, but breast milk does not appear to be affected by maternal consumption of contaminated water [6].

Nitrates are one of the most common water contaminants found in agricultural states. An estimated 43 million U.S. citizens—15 percent of the population—are served by private well water, and 4 percent of the wells in one national sample had nitrates above the federal drinking-water standard of 10 mg/L nitrates [7]. In Wisconsin, 6.5 percent of private wells sampled had nitrate levels above the federal standard [8].

This study identified the following associations with elevated well water nitrate levels: (1) living on a farm, (2) lower annual incomes, and (3) older and shallower wells than families whose wells were low in nitrates [8]. A study in upstate New York identified 15.7 percent of sampled wells as having above-standard levels and found a positive association between larger farms and higher percentages of samples with elevated nitrate levels [9].

An environmental health history should be obtained from the parents of children diagnosed with methemoglobinemia, asking where their water supply comes from, whether other household members have had similar problems, and what the parents' occupations are [10]. Further questioning of medications used, folk remedies, and breast-feeding status of the infant is a critical component of the environmental history. Infants may have other illnesses and may have dehydration, acidosis, and diarrhea from wells contaminated from coliforms, often associated with elevated nitrate levels. Where these conditions are present, physicians may fail to consider a diagnosis of methemoglobinemia.

Infants less than 4 months old are susceptible to methemoglobinemia due to a number of physiological factors: (1) alkaline gastric conditions increase gastrointestinal microflora which convert nitrates to nitrites; (2) lower circulating hemoglobin levels and higher fetal hemoglobin, which is more susceptible to oxidation; and (3) decreased amount of methemoglobin reductase [4, 5, 11]. Methemoglobin is oxidized hemoglobin and is incapable of carrying oxygen to tissues. After 4 months of age the gastrointestinal environment becomes more acidic and alters the microbial flora, methemoglobin reductase levels increase, and the proportion of fetal hemoglobin decreases to the point that there is less susceptibility to methemoglobinemia. The normal level of circulating methemoglobin in healthy individuals is less than 1 percent [5].

The maximum contaminant level (MCL) standard for nitrates set by the Environmental Protection Agency applies only to municipal water supplies since private wells are not subject to federal regulation [12]. Private water supplies do, however, fall under state health advisories in many if not all states. The advisories recommend that private well owners monitor nitrate levels every 2 to 3 years—or yearly if elevated nitrate levels have been previously detected—test for coliforms, and maintain nitrate levels below 10 mg/L nitrate. Monitoring annually is also recommended if there are infants under 6 months of age in the household or pregnancy is anticipated. Routine testing should be scheduled during the late spring or early fall of the year when the nitrate levels would be at the highest due to fertilizer application or rainfall [13].

Discharge planning should include education of the parents about environmental contamination of drinking water and safe drinking water for the family members at risk. Questions have been raised about chronic consumption of nitrate-contaminated drinking water and illnesses such as cancer and reproductive health concerns, but evidence is equivocal for such associations [2, 14]. Reproductive concerns include complications and adverse outcomes such as anemia, preeclampsia, threatened spontaneous abortions, premature labor, neural-tube defects, low birth weight, congenital cardiac defects, and other congenital malformations. Not all studies identify sufficient evidence of a causal relationship between these outcomes and exposure to nitrates in drinking water [15]. Nevertheless, the goal should be avoidance of exposure above the federal standard, which is set to prevent methemoglobinemia in infants. Resuming the same patterns of diluting the infant's formula with water contaminated with high levels of nitrates will increase the likelihood of a recurrence of methemoglobinemia.

The drinking water source should not be used until the water has been tested for nitrates. Testing can be arranged by contacting the public health department and requesting that the county public health nurse arrange for evaluation of the water supply at the family's residence and take steps to coordinate the evaluation of the drinking water source of the other children with observed methemoglobinemia. If the family has not given permission to share its information with public agencies, be sure to review HIPAA regulations on release of personal health information.

Methemoglobinemia is generally not a reportable disease; few states have surveillance programs for methemoglobinemia, and there may not be another method for informing public health professionals that a community environmental health risk may exist. Because Miguel, in our case scenario, is the fifth child to have this diagnosis in a short period of time and in the same region, a common source of nitrate contamination that could lead to additional cases of toxicity should be sought. Mapping of the recent cases of methemoglobinemia and the associated water supplies to identify a common point source of pollution falls under the responsibility of the state epidemiologist of the public health department or state environmental control agency. An excellent account of the classic work of John Snow and others in unraveling the source of cholera in London and the role of epidemiological mapping was published in 2006 [16].

If the families of affected infants are migrant workers living in camps or other housing provided by their employers, the Occupational Safety and Health Administration (OSHA) should be contacted by the health professional or the employees of the agricultural operation. OSHA regulates migrant housing, and the housing inspection checklist addresses proper location and maintenance of wells and requires that the housing have an adequate water supply that has been approved by the appropriate health authority [17]. Some states, such as Ohio, also mandate testing of potable water for coliforms and nitrates on a regular basis as part of migrant labor-camp oversight [18].

Families that are not documented and do not have valid visas or worker permits may not cooperate with a public health referral. *Promotores*—lay health educators serving the Hispanic community—are excellent community resources who aid in health efforts and outreach and may help persuade the families to allow public health or environmental regulatory agencies to test the water and provide abatement. Migrant labor camps, federally funded neighborhood clinics, and community health centers in many states have *promotores* [19, 20]. Testing well water for coliforms and nitrates (usually done together) costs from $7 to $25 and $20 to $40, respectively, per test and is usually carried out at the well owner's expense [21].

The only effective methods of lowering nitrate levels at the point of entry into the house are reverse osmosis, ion exchange, or distillation devices [22]. These devices are expensive and must be monitored because they can fail. Activated charcoal filters at the faucet or point-of-use are not effective. The end result may be that the family must move or buy bottled water to prepare formula for bottle feeding.

Practitioners who are not experienced in treating methemoglobinemia should consult the regional poison-control center or a medical toxicologist for aid in managing cases of methemoglobinemia. The hospital staff treating the children with methemoglobinemia in our case scenario should offer continuing medical education and public outreach to address a significant environmental health concern in their service area and increase awareness of potentially lethal exposures not otherwise commonly seen by the majority of practitioners. For online resources, see the CDC Agency for Toxic Substance and Disease Registry Case Studies in Environmental Medicine, nitrate/nitrite toxicity [2], the CDC National Agricultural Safety Database [23], and the EPA safewater homepage [12].

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