



The New York State Poison Centers

TOXICOLOGY

LETTER

COMPRISING THE NEW YORK CITY AND UPSTATE NEW YORK POISON CENTERS

Physophobia

Contributed by: Nicholas Nacca, MD, Michael Hodgman, MD. Upstate NY Poison Center, Syracuse NY

Case Introduction:

A 57 year old male presented to an outlying facility confused and hallucinating. He was noted to be picking at the air. By history he had overdosed on an unknown amount of cyclobenzaprine which was prescribed to him for chronic back pain. His vital signs included the following: Temp 37.0 HR: 119, BP 158/102, RR 21, O2 sat 97% RA. In the Emergency Department he was given 4mg lorazepam intravenously for agitation, but no effect was noted. His EKG was noted to have narrow complexes. After 12 hours of observation he remained tachycardic, hallucinating and in 4 point restraints. His CK was trending up. At that time the primary team administered quetiapine for sedation in addition to another 2 mg of lorazepam. A trial of dexmedetomidine was instituted without any significant response, so the team continued with benzodiazepines for sedation. Early on in this patient's care the poison center was contacted and the toxicology consultant recommended physostigmine. In-house consultants from another service advised against the use of physostigmine for unclear reasons. More than 48 hours after admission to the hospital, and after multiple doses of benzodiazepines the patient aspirated and required intubation. He suffered aspiration pneumonia and remained intubated for 5 days. On the 8th hospital day he was extubated and after an additional 24 hours he became lucid.

The effects of drugs that have anticholinergic properties can be characterized by the memory device: "hot as a hare (febrile), red as a beat (cutaneous flushing), mad as a hatter (delirium), blind as a bat (mydriasis), dry as a bone (Anhidrosis), and the heart runs alone (tachycardia). Colloquially, we refer to these drugs as having anticholinergic effects but it is more precise to describe them as having antimuscarinic effects, given that antagonism at the nicotinic receptor is not manifested. There are some drugs we use specifically for their antimuscarinic effects which include atropine, scopolamine, and benztropine. There are many drugs that have unintended antimuscarinic effects such as antihistamines like diphenhydramine, antipsychotics such as olanzapine and quetiapine, and others such as cyclobenzaprine. The anticholinergic toxidrome is often difficult for physicians to identify. In addition to the above signs and symptoms these poisoned patients are frequently noted to exhibit Lilliputian hallucinations (visual hallucinations of small things, creatures, or people), picking at intravenous catheter insertion sites and telemetry leads, picking at things in the air, and urinary retention.

Physostigmine salicylate is a carbamate that reversibly binds to and inhibits the acetylcholinesterase enzyme. Thus the amount of acetylcholine in the synaptic cleft available to bind at the muscarinic receptors is increased in the presence of physostigmine. This drug can be used therapeutically in attempt to overcome a drug that is blocking the postsynaptic muscarinic receptors. The adverse effects of physostigmine are those symptoms one would expect with excess acetylcholine acting on the acetylcholine receptors. If given to a normal healthy person, a dose of 2mg administered over 5 minutes might be expected to produce some diaphoresis, hypersalivation and possibly relative bradycardia (secondary to stimula-

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tion of parasympathetic postganglionic nicotinic receptors). Conversely, in the context of a patient exhibiting an anticholinergic toxidrome, the same dose can be expected to have dramatic improvement of their level of consciousness and lucidity. Other benefits include resolution of anhidrosis which in severe cases can lead to hyperthermia in conjunction with the combative delirium. Additionally, the patients gain the ability to relax the urethral sphincter and contract the detrusor muscle, avoiding the need for foley catheter insertion to treat urinary retention.

Physostigmine is extracted from the legume *Physostigma Venenosum*, a plant native to Nigeria. At one time it was used in traditional judicial proceedings to “prove” innocence or guilt. It was believed that after eating the legume, the guilty would perish while the innocent would purge the poison and live. Physostigmine is a tertiary amine. As a tertiary amine, physostigmine is neutral at physiologic PH and can therefore cross the blood brain barrier, a property that allows it to reverse central antimuscarinic toxicity. The ability to reverse the central effects of antimuscarinic drugs is why the sensorium of poisoned patients clears dramatically after administration of physostigmine. Neostigmine is a quaternary amine and another carbamate acetylcholinesterase inhibitor. As a quaternary amine it is unable to cross the blood brain barrier and therefore has no effect on central antimuscarinic toxicity. Neostigmine is commonly used in the operating room by anesthesiologists to reverse the effects of neuromuscular blocking drugs.

Despite all of these benefits of rational use of this antidote, there remains a great deal of hesitancy and discomfort with the use of physostigmine in the patient poisoned with an antimuscarinic drug. Physostigmine was originally marketed as “Antilirium,” a name which provides some insight into the perception of its utility. Administration of this antileptic drug will cause some degree of arousal from most sedative intoxications. In the 1970’s it was often used as part of the “coma cocktail,” which included some variation of the drugs physostigmine, naloxone, and dextrose. This “coma cocktail,” was at times used indiscriminately and without careful identification of the patient history and physical exam findings. At one time it was also thought to be the ideal antidote for the treatment of tricyclic antidepressant (TCA) toxicity.

A sentinel publication in 1980 reported two asystolic events temporally associated with the administration of physostigmine to patients with TCA poisoning (*Pentel and Peterson 1980*). Looking back on these cases, both patients were relatively bradycardic with wide QRS complex on their electrocardiograms. There are only two other similar cases reported in the medical literature, both of which involve TCA overdose (*Tong et al 1976, Shannon et al 1998*). We now understand the wide QRS complex on the electrocardiogram to be a manifestation of sodium channel blockade from the TCA. The heart rates in the two cases reported by Pentel and Peterson were unexpectedly slow, given that anticholinergic toxidromes tend to manifest tachycardia. One of these patients had co-ingested a beta blocker, which likely contributed to the bradycardic presentation. Alternatively, these patients represent severely poisoned patients in a peri-mortem state. In truth, TCAs are “dirty” drugs. They are known to block sodium channels, alpha adrenergic receptors, GABA receptors, and muscarinic receptors, all in addition to their effects on the serotonergic pathway. There are several theories as to why physostigmine treatment in the setting of TCA poisoning with cardiac conduction disturbance was reported to precipitate bradydysrhythmia and ultimately asystole. Interpretation of this observation has been complicated by the fact that some data from animal studies suggests that physostigmine can actually narrow the QRS prolongation associated with TCA overdose (*Suchard 2003*). Alternatively, it has been argued that the adverse outcomes noted in these scattered case reports were part of the natural progression of severe TCA poisoning and had nothing to do with physostigmine administration (*Kulig and Rumack 1981*).

Regardless of why and how, after the Pentel and Peterson publication in 1980 physostigmine entered a dark age where its use was discouraged and even incited accusations of heresy if it was suggested in the management of a poisoned patient. Thus, the liberal use of physostigmine in the 1970s was followed by over a decade of infrequent use. Lately however, there has been a resurgence of the use of physostigmine. Though it may seem logical in retrospect, indiscriminant administration of any drug is a bad idea. A careful history and physical examination can usually identify an anticholinergic toxidrome. Examination of a poisoned patient’s electrocardiogram can reliably rule out significant sodium channel blockade as is manifested by a wide QRS complex. The benefits of physostigmine are evident in the literature. A study performed in 1999 evaluated 52 patients presenting with anticholinergic toxidrome. The patients treated with physostigmine had better reversal of delirium, lower incidence of complications, and shorter time to recovery over those treated with benzodiazepines (*Burns et al. 1999*). A retrospective review of 39 patients treated with physostigmine concluded only 1 potential complication, and it is unclear if the physostigmine played a causal role (*Schneir 2003*). Interestingly, 4 of those 39 cases were actually TCA overdoses, none of whom had cardiac conduction disturbance prior to treatment, and none had adverse effects from physostigmine administration. A literature review by Suchard in 2002 concluded that the available published evidence is insufficient to draw any solid conclusions about the use of physostigmine in treatment of TCA overdose. It is the opinion of this author that physostigmine be avoided in patients suspected of

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The Physophobia Pendulum

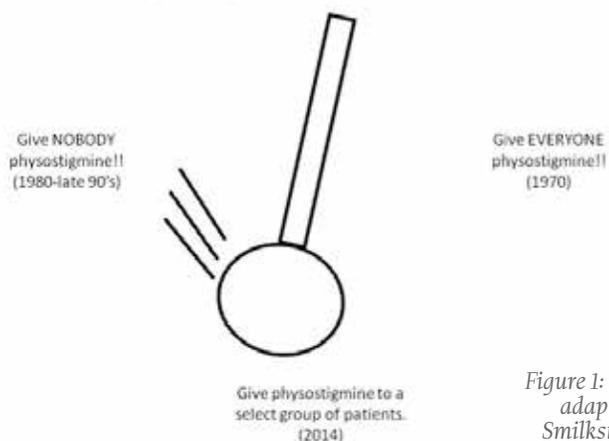


Figure 1: Concept adapted from Smilkstein 1991



There's No Place Like Home... for Carbon Monoxide Poisoning

Jason West, MD; Michael McGregor, MD; Michael Touger, MD

Case:

An 84-year-old woman with a history of hypertension and dyslipidemia and her husband, an 88-year-old man with a history of dementia and coronary artery disease, presented to the ED via EMS after neighbors discovered the woman lying on her living room floor, responding only to painful stimuli. Earlier in the evening, the same neighbors had helped the husband to bed after noticing that he had become lethargic. The EMS report indicated that a car had been left running in a closed garage of the patients' home. The fire department identified an ambient carbon monoxide (CO) concentration of 88 ppm.

Upon arrival to the ED, the woman's vital signs were: blood pressure (BP), 130/74 mm Hg; heart rate (HR), 63 beats/minute; respiratory rate (RR), 16 breaths/minute; temperature, 99°F. Oxygen saturation was 99% on room air. Her husband's vital signs were: BP, 150/66 mm Hg; HR, 59 beats/minute; RR, 19 breaths/minute; temperature, 98°F; oxygen saturation was 98% on room air.

What is carbon monoxide poisoning?

Carbon monoxide is a colorless and odorless toxic gas produced by incomplete combustion of carbon-based fuel. Common sources in the United States include portable generators, gas-powered furnaces, cooking appliances, poorly ventilated home-heating systems, and motor vehicles (**Box 1**).¹

Carbon monoxide is the leading cause of unintentional poisoning deaths in the United States,¹ resulting in more than 20,000 ED visits and 2,000 hospital admissions. Nearly three-fourths of these deaths are due to exposures in the home, with more than half occurring during the months of November through February.^{2,3} The average cost of a hospital admission for confirmed CO poisoning is over \$11,000, with a cumulative nationwide total cost of over \$26 million per year. While the hospitalization rate for persons aged 18 to 44 years is only 6.7%, the admittance rates for persons aged 65 to 84 years and older than 85 years are 33% and 43%, respectively.³ Although there has been a slight decline in the incidence of CO poisoning over the past 10 years, it is still a public health concern (**Figure 1**).²

Who is most susceptible to motor vehicle-related carbon monoxide poisoning?

The US Centers for Disease Control and Prevention (CDC) reports that motor vehicles are the second most common source of CO exposure.⁴ A study of US news media reports covering a 2.5-year period revealed that 8% of such poisonings were the result of a motor vehicle left running in a garage—the overall mortality rate of which is suggested to be significantly higher than that of other sources of CO exposure.⁵

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Carbon Monoxide

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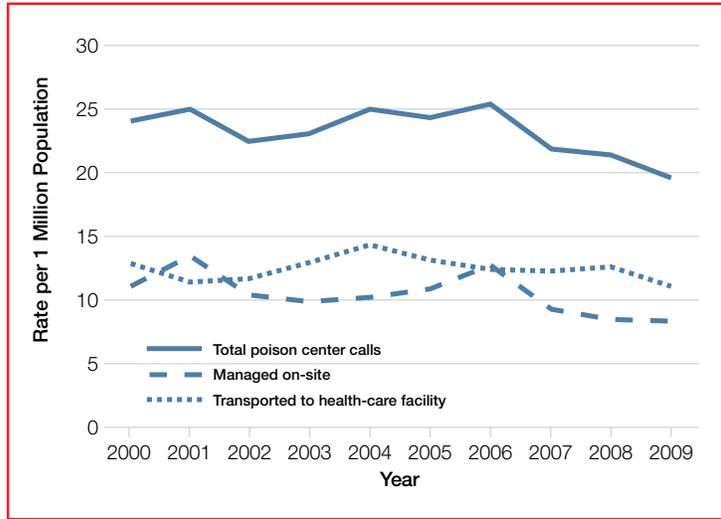


Figure 1. Annual Rate* of Reported Carbon Monoxide Exposures—National Poison Data System, United States 2000–2009^a

Source: US Census Bureau. Annual estimates of the resident population for the United States, regions, states, and Puerto Rico: April 1, 2000 to July 1, 2009. Washington, DC: US Census Bureau, Population Division; 2010.

* Per 1 million population.

^a Adapted from the Centers for Disease Control and Prevention.²

Approximately 430 deaths per year are caused by unintentional, nonfire-related CO poisoning,⁶ and the CDC reports the death rate is highest in persons older than age 65 years.¹ The death rate from these exposures is more than three times higher in men than women (Figure 2).⁶ In addition, older patients are disproportionately affected: In US news media-reported cases of CO poisoning that included patient age, 29% occurred in persons older than age 80 years.⁵ Moreover, in approximately one-third of motor vehicle-related deaths due to CO poisoning, nearly all of patients older than age 80 years were found dead at the scene of exposure. These reports suggest that the elderly are at greater risk for CO exposure due to age-related cognitive changes, physical inability to escape a toxic environment once becoming symptomatic, and a greater susceptibility to poisoning due to comorbid conditions.⁵

Case Continued

The husband and wife’s initial carboxyhemoglobin concentrations in this case were 35% and 13%, respectively. Both were treated with hyperbaric oxygen (HBO) without complication. During their inpatient stay, the woman noted that their home did not have a CO detector.

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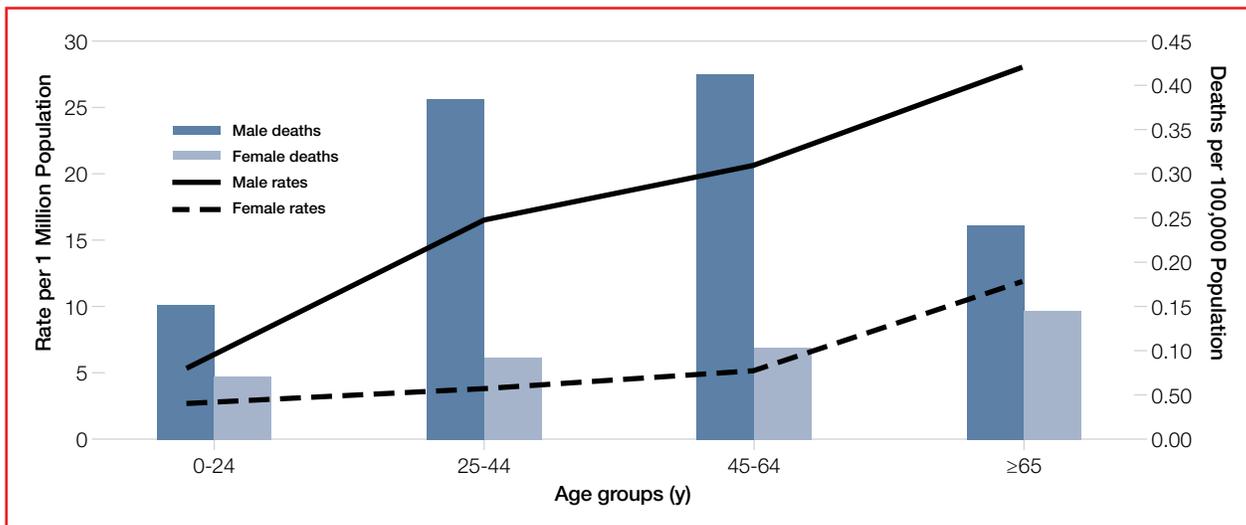


Figure 2. Average Annual Number of Deaths and Death Rates From Unintentional, Nonfire-Related Carbon Monoxide Poisoning,* † by Sex and Age Group—United States, 1999–2010^a

Source: National Vital Statistics System. Mortality public use data files, 1999–2010.

* Unintentional, nonfire-related carbon monoxide poisoning is defined both as (1) accidental poisoning by and exposure to gases or vapors (code X47) listed as the underlying cause, and (2) toxic effect of carbon monoxide (code T58) listed as the contributing cause, according to the International Classification of Diseases, 10th Revision. All deaths caused by intentional exposure (X67), exposure of undetermined intent (Y17), or fire-related exposure to carbon monoxide (codes X00–X09, X76, X97, and Y26) were excluded.

† Deaths are 12-year annual averages, and death rates are per 100,000 12-year annual average population.

^a Adapted from the Centers for Disease Control and Prevention.⁶

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Carbon Monoxide

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What is the role of hyperbaric oxygen therapy as a treatment option for CO poisoning?

Hyperbaric oxygen therapy greatly accelerates the dissociation of hemoglobin from CO, reduces free radical-related cellular damage, and may have a role in preventing adverse neurological sequelae in the setting of CO poisoning. Although controversy exists, HBO therapy is generally indicated in select patients with elevated CO levels and abnormal neurological findings, cardiovascular findings, or persistent metabolic acidosis. While few ED patients with CO exposure receive HBO therapy, over 20% of patients requiring inpatient hospitalization receive treatment.³

What preventive measures can be taken to reduce motor vehicle-related CO poisoning?

The literature supports the enforcement of motor vehicle emissions standards and the proper use of home CO detectors as primary preventive strategies. Computerized data from the CDC, US Census Bureau, and US Environmental Protection Agency from 1968 to 1998 were used to evaluate the influence of national vehicle emissions policies on CO-related mortality. The Clean Air Act of 1970 set environmental limits on CO emissions from automobiles at 15.0 g/mile in 1975; the EPA further reduced this standard to 3.4 g/mile for automobiles manufac-

ured after 1981. After the enforcement of standards set forth by the Clean Air Act and the introduction of the catalytic converter in 1975, CO emissions from automobiles decreased by an estimated 76.3%, and unintentional motor vehicle-related CO deaths declined by 81.3% (Figure 3).⁷ (Catalytic converters contain elements [eg, platinum] that catalyze the oxidation of CO to carbon dioxide.)

Since CO exposure occurs primarily in the home, the installation of battery-powered or battery-backed CO alarms—both in the home and garage—can prevent poisoning. These detectors are inexpensive and available at common retail stores. Unfortunately, despite the easy availability and access to CO detectors, only 39 states currently have legislation mandating their use, and approximately two-thirds of the states with existing legislation only require CO detectors in newly built structures.⁸

In 2010, the state of New York enacted legislation known as “Amanda’s Law,” (named after a teenaged girl whose death was caused by CO poisoning from a defective boiler) mandating CO detectors in all one- and two-family homes with heating sources that may emit CO or have attached garages. However, an industry survey in 2011 found that nearly half of New York families were not aware of this law.⁹ The two largest

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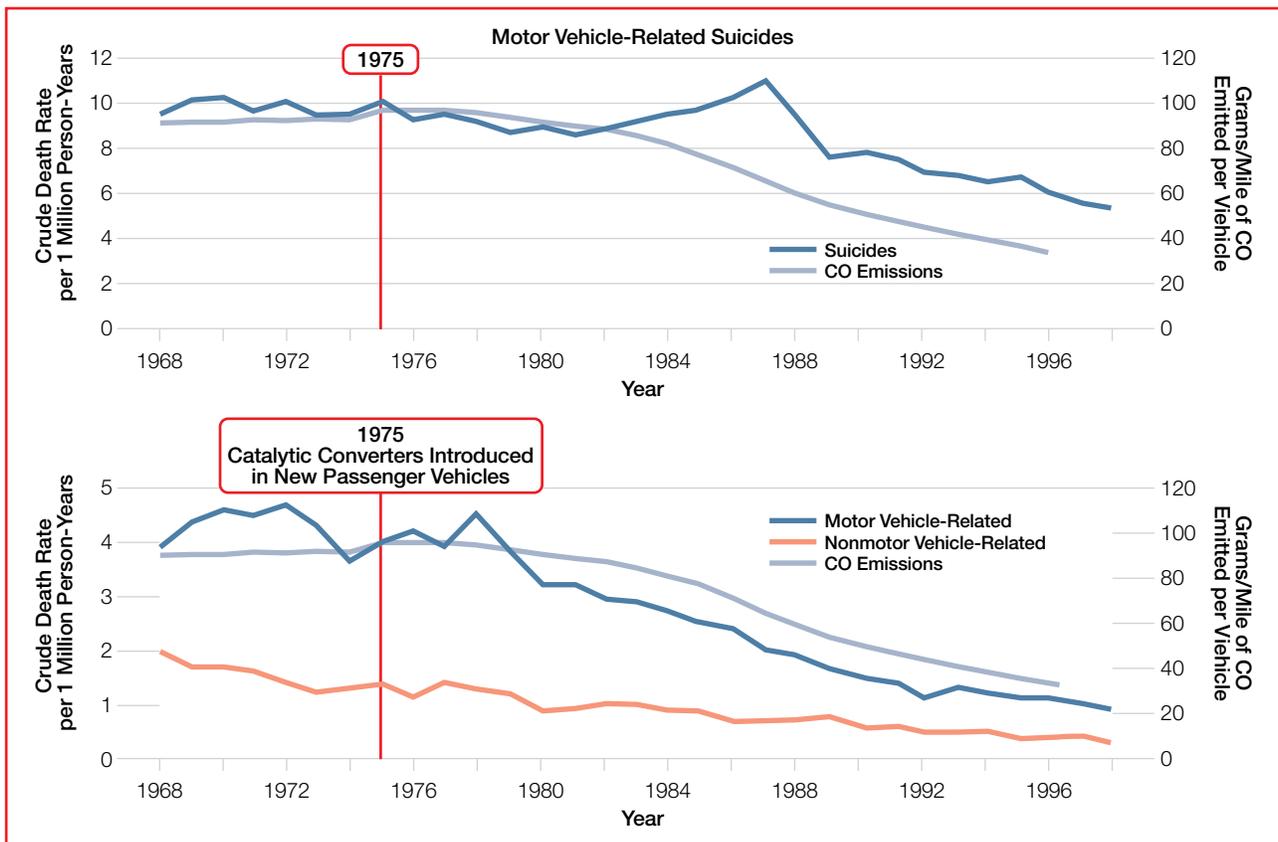


Figure 3. Crude Annual Unintentional Death Rates From Carbon Monoxide-Related Poisoning and Annual Estimated Carbon Monoxide Emission Rates per Light-Duty Motor Vehicle^a

Abbreviation: CO, carbon monoxide.

^aAdapted with permission from the Journal of the American Medical Association.⁷

Carbon Monoxide

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surveys on home CO detector use—those conducted by the US Census Bureau and CDC—estimate the national rate of having a working CO detector in a home is 32% to 40%, with a lower prevalence among those living in manufactured housing, renting a home, or living below the poverty level.¹⁰

What is the utilization of CO detectors by ED patients?

The United States Consumer Product Safety Commission, the National Fire Protection Agency, and most CO detector manufacturers recommend that CO detectors be installed in close proximity to sleeping areas. A convenience cross-sectional survey in Connecticut found that less than half of residents polled had CO detectors installed, and only 17.2% had a detector installed in the proper location.¹¹ Interestingly, nearly 98% of the 1,000 people surveyed had smoke detectors installed.¹¹ The authors of the survey noted a direct, near linear relationship between household income and CO detector installment with rates of low-income and high-income CO detector use of 27% and 82%, respectively (Figure 4).¹¹ The reasons survey participants gave for lack of CO detector use were varied, yet all were consistent with a lack of understanding CO poisoning and an awareness of the importance of CO detection.¹¹

Case conclusion

After hospital admission and treatment, both patients were discharged on hospital day 2 with a return to a baseline mental status. Neither patient reported neurological sequelae or new cognitive changes when a follow up call was placed more than 6 months after HBO treatment. The couple furthermore reported that they installed a CO detector upon their return home.

Box 1. Common Sources of Carbon Monoxide Poisoning

- Charcoal grills
- Furnaces, hot water heaters
- Gasoline-powered engines (boats and generators)*
- Propane-powered equipment (heaters, ice-resurfacing machines)
- *automobiles less important due to advances in emission control (ie, catalytic converters)*



Box 2. General Indications for Hyperbaric Oxygen Therapy*

- Syncope
- Altered mental status
- Carboxyhemoglobin > 25% (without symptoms)
- Prolonged carbon monoxide exposure (soaking)
- Older age
- Pregnancy with fetal distress
- *Risk factors for poor neurological outcomes, though regional approaches differ.*

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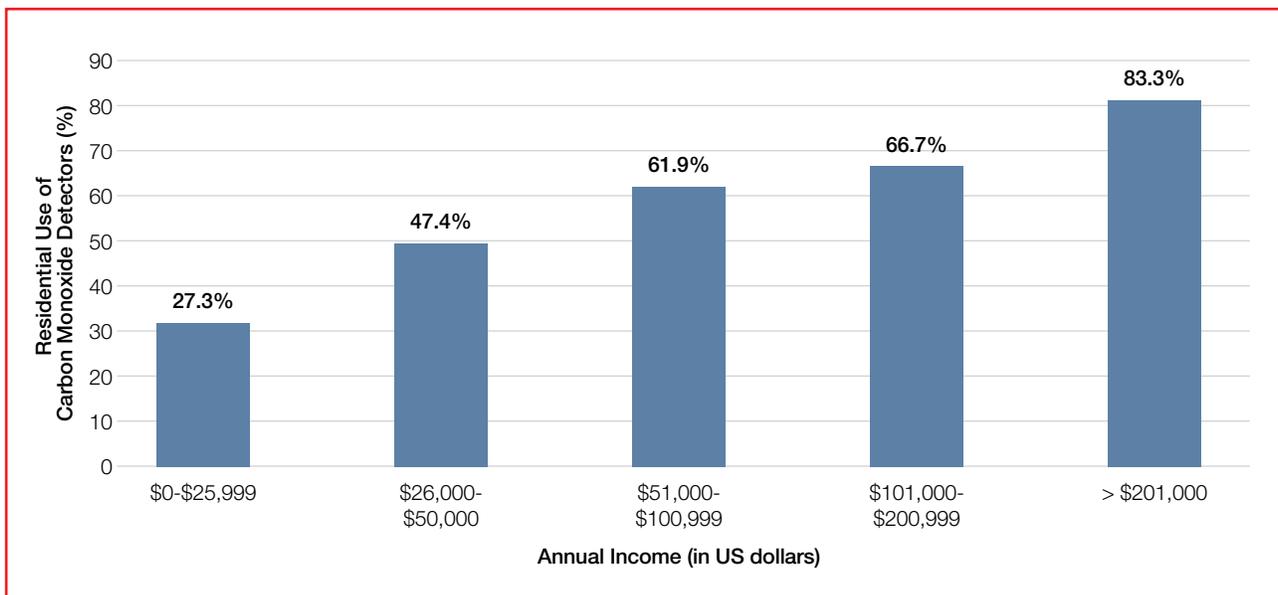


Figure 4. Residential Use of Carbon Monoxide Detectors by Annual Income^a
^a Adapted with permission from *Clinical Toxicology*.¹¹

Methemoglobinemia in the Pediatric Population

Contributed by: Katherine M Nacca, MD, Pediatric Emergency Medicine Fellow, Upstate Medical University



Methemoglobinemia is a rare but important cause of cyanosis in both the pediatric and adult populations. This disease entity may be caused by a toxic ingestion or by a congenital enzyme deficiency, though toxic causes are more common. Methemoglobinemia may be noted more often in the pediatric population. This is secondary to a relative, not congenital, enzyme deficiency compared to adults that resolves with age, but children under 36 months of age are considered at higher risk.¹

Under normal physiological circumstances, small amounts of hemoglobin contain iron in its ferric state (Fe^{3+}). Approximately 1% of hemoglobin is in this state at any given time. This methemoglobin is created as ferrous state hemoglobin (Fe^{2+}) combines with water and is oxidized. Intracellularly, methemoglobin is reduced back by Cytochrome B5. Intracellular reduction occurs much more efficiently than the oxidative process and therefore build-up of methemoglobin and side effects do not occur physiologically. Certain stressors such as anemia and acidosis may make a patient more prone to excessive methemoglobin, and added toxins exacerbate this as well. In addition, as previously mentioned, infants are relatively deficient in Cytochrome B5 and therefore more susceptible to insult. To further this, fetal hemoglobin, or hemoglobin f, which is still present around 6 months of age, is more susceptible to oxidation and therefore more readily forms into methemoglobin. Lastly, the infant gut has a less acidic environment than in adults which allows for more growth of nitrite-producing bacteria.²

Nitrites, converted from Nitrates in the gut, are known as strong oxidizing agents which are found in a variety of sources. Well water is a common source because of contaminants from fertilizers, human waste products, and animal waste products. Well water is sometimes used for home mixed infant formulas and is a not an uncommon cause of methemoglobinemia.¹ Gastroenteritis may lead to methemoglobinemia secondary to the increased production of nitrates by gut flora as well as dehydration. Medications that are nitrous based include Nitroglycerin, Nitroprusside, and Nitrous or Nitric oxide. Silver nitrites and Sodium nitrite also have nitrous bases.^{1,2} Nitrous oxide is an important and interesting intervention to consider. Case reports describe methemoglobinemia after the use of NO for pulmonary hypertension postoperatively in children with congenital cardiac anomalies.^{3,4} In addition, NO is used frequently for dental procedures and with increasing popularity in the emergency department for sedation.

Topical anesthetics have also been known to be responsible for methemoglobinemia. Benzocaine, Prilocaine, EMLA and Lidocaine are all common causes. Local anesthetics are broken down into Aniline which in and of itself is used occasion-

ally as a dye but is also a strong oxidizing agent. Methemoglobinemia from these drugs has been seen with both higher than normal dosing and with typical dosing. These medications use for dental procedures and is seen in use for teething babies as well. Phenyzypridine, used as an anesthetic for urinary tract infections, as well as Dapsone are well known causes of oxidation of hemoglobin as are Sulfonamides and Metochlopramide.

Medications and well water are not the only source of oxidizing agents that lead to methemoglobinemia. Automobile exhaust as well as certain foods may be other sources. Nitrous oxide is present in many types of exhaust. Cauliflower, carrots, spinach and broccoli as well as preservatives in hot dogs and sausage all contain higher levels of Nitrates. Nitroethane is present in certain rubber adhesives, resins and nail polish remover that may create problems with inappropriate exposures. As mentioned, it is thought that certain conditions may lead to increased susceptibility to these agents in otherwise healthy children. This includes conditions such as acidosis and dehydration.^{1,2}

Methemoglobinemia presents initially as cyanosis and with increasing exposure, more serious symptoms. Vitals in these patient remain around 85% despite supplemental oxygenation. Elevated PaO_2 on blood gas and “chocolate” colored blood on blood draws may help to further clue one in to the diagnosis but serum measurements of methemoglobin give the definitive diagnosis.

15% methemoglobin results in toxic doses leading to cyanosis. As this percentage increases, dyspnea, headaches, tachycardia and tachypnea result. Further levels lead to acidosis, lethargy, coma, seizures and subsequent death.⁵

At levels less than 20% removal of the offending agent is adequate without necessitating further treatment. If treatment is required, Methylene Blue is the treatment of choice. Dosages are 1 to 2 mg/kg as the initial dose which may be repeated with inadequate response. Methylene Blue is reduced to Leukomethylene blue which then may reduce Ferric to Ferrous hemoglobin. The reduction of Methylene blue requires NADH and therefore may be ineffective in G6PD deficiency due to poor production of NADH. Use of Methylene Blue in G6PD or in high doses may actually be harmful. In this situation, the treatment of choice is exchange transfusion and/or hyperbarics.^{1,2}

Chronic Ascorbic Acid treatment is used for treatment of Congenital Methemoglobinemia with Cytochrome B5 deficiency. This treatment has been proposed for treatment of toxic Methemoglobinemia as well. Ascorbic Acid acts as a reducing agent as well but is thought to be less effective than

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Methylene Blue. Despite this, in situations of renal failure, Methylene Blue failure, G6PD deficiency, and in situations of poor resources where Methylene Blue is not available, Ascorbic Acid may be useful.^{6,7} Case reports do describe failure with treatment with Methylene Blue.⁸ A retrospective study of 5 patients, 4 with exposure to oral contamination and one with exposure to Dapsone, showed full recover with the use of Ascorbic Acid in a resource poor area.⁶ Case reports describe similar outcomes.⁷

Methemoglobinemia is a serious condition that may be life threatening if not identified and treated early. Many common medications including Nitrates and Nitrites as well as Topical Anesthetics may be responsible but contaminants must also be considered. History of well water and exposure to certain food preservatives as well as health conditions leading to acidosis and dehydration may contribute. Early recognition and subsequent treatment with Methylene Blue are the mainstays of therapy but exchange transfusion and hyperbarics must be utilized with treatment failure. Ascorbic Acid may play a role but further research is required.

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having overdosed on TCAs, and any patients with conduction disturbance evident on EKG. In general, it is recommended to involve a toxicologist or other experienced clinician in the care of an anticholinergic patient requiring physostigmine reversal.

It is important to note that the antimuscarinic toxidrome is a spectrum disease. A pleasantly delirious, cooperative, afebrile patient without difficulty urinating does not require reversal with physostigmine. Conversely, the patient who exhibits a clear antimuscarinic toxidrome with combative delirium requiring physical and chemical restraint, active cooling, and foley catheter insertion is the optimal candidate for treatment. A common mistake is attempting to treat these patients with antipsychotics, which themselves confer some antimuscarinic activity. This intervention would more than likely worsen the patient's condition. In these patients, an electrocardiogram should be carefully reviewed for evidence of conduction disturbance independent of a baseline bundle branch block. Prolongation of the PR or QRS interval is a relative contraindication to treatment with physostigmine. Barring an abnormal electrocardiogram, physostigmine should be administered at a dose of 1mg intravenously over 5 minutes. If the patient has only mild improvement then a second dose of 1mg over 5 minutes should be repeated. Though it is very unlikely to be used, atropine should be readily available for the rare event of bradycardia. Seizures have been reported with the administration of physostigmine, but are likely related to a fast rate of administration (*Schneir 2003*). The patient should be monitored continuously during administration for signs of excessive salivation, bronchorexia, or bradycardia. These findings should prompt the physician to stop treating with physostigmine and reconsider the toxidrome. The half life of physostigmine is very short, but the reversal often lasts for an hour or more. Many patients do not require repeat dosing, but if necessary the above procedure can be repeated. Medical and clinical toxicologists are available through the poison center hotline, and consultation is recommended prior to reversal of an antimuscarinic toxidrome.

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