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Baclofen Pump Complications

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Case Report

A 5-year-old boy was referred to the Emergency Department from a skilled nursing facility for evaluation of a potential intrathecal baclofen pump infection. Erythema had been noted near the pump site on the child's abdomen one day previously. The patient's past medical history was significant for delivery at 24 weeks gestational age, glottic stenosis, and tracheostomy placement. The patient had subsequently suffered cardiopulmonary arrest due to tracheostomy plugging, resulting in anoxic brain injury and spastic quadriplegia. A baclofen pump had been placed three months prior to presentation to mitigate spasticity. Open Nissen fundoplication for gastroesophageal reflux had occurred one month previously. Initial vital signs were: blood pressure, 104/68 mm Hg; pulse, 111 / minute; respiratory rate, 32 / minute; rectal temperature, 99.0˚F; pulse oximetry, 99% receiving 28% FiO_2; weight, 24.1 kg. The physical exam revealed erythema overlying the pump site and mild edema of skin, without obvious fluctuance.

What is intrathecal baclofen (ITB) and why is it used?

Severe spasticity associated with upper motor neuron lesions is thought to result from decreased release of GABA in the dorsal horn of the spinal cord, which allows unregulated activation by glutamate and leads to muscle spasticity.[1] Baclofen, 4-amino-3-(4-chlorophenyl)butanoic acid, is an agonist at pre-and post-synaptic $GABA_B$ receptors. Pre-synaptically, baclofen prevents Ca^{2+} influx; post-synaptically, it increases K^+ efflux.[2] Clinically, this inhibition results in decreased muscle tone and suppression of muscle spasms.[1] Oral baclofen is used in combination with other therapies to treat spastic conditions of cerebral or spinal origin, but risks systemic adverse effects at higher doses needed to control symptoms. ITB is utilized due to its spinal cord selectivity: subarachnoid concentrations of baclofen injected intrathecally diminish in the cranial direction.[1] Dosing can thus be titrated to maximize spasm control while minimizing central effects, such as sedation, delirium, and seizure.

How is ITB administered?

ITB is delivered by a programmable pump. The pump is implanted in the anterolateral abdominal wall. It gives rise to a silicone rubber catheter that is subcutaneously tunneled catheter laterally around the patient's side to the midline lower back. The catheter then extends anteriorly to spinal canal, entering the intrathecal compartment at the mid-lumbar level. The spinal level in the thecal sac at which the catheter tip is placed depends upon

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clinical indication: the T1-T2 level for spastic quadriplegia, the T6-T10 level for spastic diplegia, and the mid-cervical region for dystonia.[1] Depending on the model, pump reservoirs may range from 10 to 60 mL, filled with commercially available baclofen concentrations of 50 µg/mL, 500 µg/mL, or 2000 µg/mL (although compounding pharmacies may provide concentrations up to 8000 µg/mL).[3-6] A wide range of delivery rates of 12 µg/day to over 2000 µg/day can thus be achieved via period bolus or continuous infusion, titrated to desired effect.[6]

Case Continuation

An emergency department physician attempted needle aspiration over the area of erythema to detect purulence from a potential abscess, but was unable to aspirate any fluid. A neurosurgical consultant determined that the area of erythema on the patient's abdomen was likely secondary to contact dermatitis from tape or a diaper and recommended neither laboratory analysis nor antibiotics. The patient returned to the skilled nursing facility.

The following day, the patient revisited the emergency department with clear fluid leaking from the aspiration site. He was febrile (101˚F), but otherwise hemodynamically stable. It was determined that the attempted needle aspiration had inadvertently punctured the catheter tubing; either cerebrospinal fluid (CSF) or baclofen was leaking from the wound. Chest and abdominal radiography revealed an appropriately place gastrostomy tube and a baclofen pump with catheter tip extending to T8-T9, as well as a new focal opacity in the right upper lobe.

What are some complications of ITB?

Complications may be related to surgical procedures, pump problems, and catheter malfunctions. Baclofen overdose may arise from inadvertent subcutaneous injection of baclofen during attempts to access and refill the baclofen pump reservoir or injection of an inappropriate concentration of baclofen solution. Peripheral accessory catheter-access port ("side port") access could result in direct injection into the CSF, either during refill or during contrast administration for fluoroscopic imaging. Overdose might also occur due to pump leak or malfunction. Failure to appreciate catheter space or the "dead space" that exists between the pump reservoir and catheter access port, as well as priming bolus miscalculations might lead to over- or under-dosing.[7] Pump malfunction, disconnection, migration, breakage or kinking of the catheter, or extravasation might result in insufficient ITB delivery and precipitate withdrawal.[8,9]

Why might ITB complications be difficult to diagnose, and what are key elements to distinguish overdose from withdrawal?

Baclofen overdose and withdrawal may present with overlapping symptoms.[8] Both withdrawal and overdose may be heralded by hemodynamic instability and altered mental status or delirium. Seizures and rhabdomyolysis are described in both scenarios. Increased muscle rigidity and spasticity may be noted in withdrawal. However, evaluation of muscle tone is difficult, as patients with severe spasticity may remain relatively spastic even in overdose and baseline muscle tone may be unknown. Parent or caregiver input is often helpful in this case. Severe and untreated baclofen withdrawal may progress to multi-organ system failure and disseminated intravascular coagulation.[10] Bradycardia and respiratory depression are seen with overdose. A spectrum of CNS depression is described, depending on overdose severity. Hyporeflexia and flaccid muscle tone also may be evident. At its most severe, overdose can result in cardiac dysrhythmia and respiratory failure, requiring mechanical ventilation.[10]

Withdrawal symptoms have a more insidious onset than overdose and generally do not occur until 12-24 hours after the pump malfunction has occurred, while overdose tends to occur relatively quickly (minutes) after the pump malfunctions.[8] A patient with a recent pump refill with sudden onset of symptoms might suggest overdose.

How are ITB overdose and withdrawal managed?

Baclofen pumps are generally managed by Neurosurgery and/or Rehabilitation Medicine. Consultation for pump interrogation may be useful. Overdose is managed with aggressive supportive care including intubation and ventilation, as well as consideration of withdrawal of ITB solution from the pump. The ITB manufacturer also suggests consideration of 30-40 mL CSF withdrawal to reduce CSF baclofen concentrations.[6] Treatment with physostigmine has been described, but is not recommended since it may lower seizure threshold, increase pulmonary secretions, and exacerbate bradycardia.[11]

Management of withdrawal has been described using a variety of agents to counter-act spasticity, including: benzodiazepines, propofol, skeletal muscle relaxants (dantrolene), and tizanidine.[8] In severe cases, baclofen may be delivered via lumbar puncture.[11] Active thermoregulatory control (including external cooling) may be required. Neurosurgical intervention may be ultimately necessary following clinical stabilization.

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Rapid Toxicologic Collapse

Zhanna Livshits, MD, and Lewis S. Nelson, MD
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Case Presentation

Following a domestic dispute, a 41-year-old man injects his girlfriend, a 35-year-old woman, in her right buttock with a syringe containing a clear liquid. He then drinks some of the same liquid and collapses within 10 minutes. The woman's brother, who is nearby, responds to the woman's scream and is told the story, following which he calls 911. EMS finds the alleged assailant in asystole. They also find a bottle of household bleach and a bottle of ammonium on the table next to the partially filled syringe and an empty cup. Both patients are taken to the nearby hospital, where the man is immediately pronounced dead. The woman is in extremis.

In the ED, the woman is obtunded with the following vital signs: blood pressure, 80/40 mm Hg; heart rate, 40 beats/min; and respiratory rate, shallow. Her Spo_2 is 88% on 15 L oxygen. She is intubated and has persistent hypotension despite adequate volume resuscitation and rapid escalation of therapy to three vasopressors. Both EMS and the physician are under the impression that the patient was injected with a combination of ammonium and sodium hypochlorite (bleach), which were found on the kitchen table.

Which agents can lead to such rapid hemodynamic collapse?

The combination of aqueous ammonium and sodium hypochlorite, both common household cleaning agents, can lead to formation of chloramine, a gas under standard conditions. When inhaled, this gas may produce irritant pulmonary injury. If an aqueous solution is ingested or injected, tissue irritation and/or necrosis are likely sequelae, but rapid collapse would be unexpected (though chloramine injection appears to be unreported in the medical literature).

The differential diagnosis for rapid cardiovascular collapse after exposure to a toxin is rather narrow. Most common culprits are mitochondrial toxins that interfere with oxidative phosphorylation and cellular energy production. Following exposure to the toxin, cells cease aerobic respiration and shift to anaerobic glycolysis for energy production, which is much less efficient. Potent mitochondrial toxins that cause rapid demise in small doses include the following: carbon monoxide, hydrogen sulfide, sodium azide, phosphine, and cyanide. All of these toxins inhibit cytochrome complex IV in the electron transport chain.[1]

Other etiologies to consider include paralytic agents, potent opioids like fentanyl, or GABA-ergic sedatives. However, these agents typically produce cardiovascular collapse secondary to respiratory arrest, so despite the outward appearance of coma or collapse, the patient's hemodynamics are likely initially near normal. Convulsants, such as tetramine, or hypoglycemic agents, such as insulin, may similarly be associated with rapid collapse, but hemodynamic failure is a delayed consequence.

Delayed-onset toxins administered parenterally with harmful intent include methotrexate, ricin, and chemotherapeutic agents.

How can the differential diagnosis be narrowed?

The implicated toxin in this case is in a liquid form. Liquids are generally either chemicals that exist in this form under standard conditions or aqueous (water-based) or nonaqueous solutions. Almost any toxin that has the capacity to dissolve in a liquid (whether water or another liquid) could be considered as an etiology in this case. Of the agents mentioned above, only cyanide and sodium azide are typically found in liquid form.

Although carbon monoxide poisoning could readily explain the clinical findings in this patient, carbon monoxide is an odorless and colorless gas. Sources of exposure include coal burners, engines, hibachi grills, and, most importantly, fires.[2] The context of the story excludes carbon monoxide as a cause.

Hydrogen sulfide is a colorless gas with a characteristic odor similar to that of rotten eggs. It is produced by bacterial decomposition of proteins or decay of sulfur-containing products such as sewage, fish, and manure. With exposure to higher hydrogen sulfide concentrations, olfactory nerve paralysis ensues, decreasing the ability to detect the rotten-egg odor, thereby increasing the risk of poisoning. The dramatic collapse and demise following exposure is described as the "slaughterhouse sledgehammer effect." Of note, there has been a recent trend, primarily in Japan, to commit suicide using hydrogen sulfide generated in situ by combining chemicals within the confines of a motor vehicle or other enclosed space.[3,4]

Sodium azide is an inorganic salt, formerly widely used in automotive airbag systems and commonly found as a preservative in laboratory solutions. It is soluble in water, in which it forms hydrazoic acid, which itself is volatile and may be inhaled.

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Rapid Toxicologic Collapse

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Phosphine is a gas that forms upon contact of a phosphide salt (such as zinc or aluminum phosphide) with water. The gas can also be stored in compressed cylinders for industrial use. The phosphides are used in grain storage processes and during methamphetamine synthesis, and phosphine poisoning is associated with both situations.

Cyanide may also exist in the gaseous or aqueous forms. It can be found in the precursor form (eg, cyanogenic glycosides) in plants such as cassava (linamarin) and *Prunus* species (amygdalin) and in commercial liquids (eg, nitriles). Poisoning by a precursor form of cyanide has delayed onset (hours), while rapid demise occurs when cyanide is either inhaled (hydrogen cyanide), ingested, or injected as an aqueous salt solution (eg, sodium cyanide).

Ancillary information can be a valuable tool in clinical practice. In addition to medical history, current medication regimens, use of illicit drugs, and family history, the patient's occupational information can be revealing and may help the clinical team to home in on a diagnosis. It was discovered much later in the management of this case that the male patient was a jeweler. A simple investigation into compounds commonly used by jewelers could rapidly implicate cyanide salts, which are used for electroplating and metal cleaning.

What are the clinical implications of various routes of cyanide administration?

The most important clinical implication is the difference in onset of toxicity and time to death. Faster onset decreases the chance for timely antidote administration and therefore increases the likelihood of death.[5]

Cyanide gas, commonly in the form of hydrogen cyanide, is quickly absorbed and swiftly (within a minute or two) affects all the organs. Death occurs within minutes of exposure. This form of cyanide poisoning is the most rapid.

Ingestion of cyanide-containing liquid leads to rapid absorption and distribution to target organs. Additionally, aqueous solutions of cyanide salts are caustic and may lead to direct mucosal injury of the gastrointestinal tract. Clinical effects begin with a few minutes of ingestion, and death ensues several minutes thereafter without therapy.

Intramuscular injection of cyanide is poorly described in the literature, though its kinetics are likely similar to those resulting from ingestion. Absorption is the rate-limiting step. Therefore, onset of toxicity may take longer than onset following inhalation or ingestion. The female patient, who received an intragluteal injection, was able to relate her story to her brother after the boyfriend succumbed to the effects of cyanide.

What are the potentially lifesaving prehospital measures in cases of sudden collapse from a presumed toxin?

There are limited therapies available to prehospital providers for the management of victims of exposure who have had rapid clinical decompensation/demise. EMS should consider contacting the local poison control centers from the scene or while en route to the hospital. The administration of a cyanide antidote is critical in the early course of toxicity.[6-8] Once cyanide distributes to target organs, which happens rapidly, the antidotes may not be as effective.

Case Conclusion

The female patient's venous blood gas analysis showed a profound metabolic acidosis (pH, 6.96) with a serum lactate concentration greater than 20 mmol/L. Based on her history of injection followed by rapid clinical decompensation, treatment for cyanide toxicity was recommended by the poison control center. The ED, however, did not have either hydroxocobalamin or the original three-part cyanide antidote kit, and antidote administration was delayed by 2.5 hours while a courier was dispatched to another hospital. The patient eventually received two doses of 5 g of hydroxocobalamin but died within 24 hours of hospital arrival. Initial blood cyanide concentration was 0.76 mg/L. Investigation confirmed that cyanide was present in both the drinking cup and the syringe.

The man's postmortem blood cyanide concentration was 335 mg/L, and the stomach contained 597 mg of cyanide. Autopsy demonstrated pharyngeal mucosal injury and gastric hemorrhage, which were likely a result of caustic injury induced by the ingested cyanide salt. He had red skin discoloration of the back.

The woman's postmortem blood cyanide concentration was 0.4 mg/L. Her autopsy demonstrated red-purple skin discoloration and organ decomposition. The site of injection in the buttock contained subcutaneous hemorrhage. Although red skin discoloration has been described postmortem in victims of cyanide poisoning, hydroxocobalamin is a red dye and may lead to red discoloration of the skin, as well.[9,10]

Conclusion

There are few toxins that result in rapid clinical deterioration and demise shortly after exposure. Cyanide is easily obtained, and effective antidotes are available.

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Bronchiolitis Obliterans and Microwave Popcorn Worker's Lung

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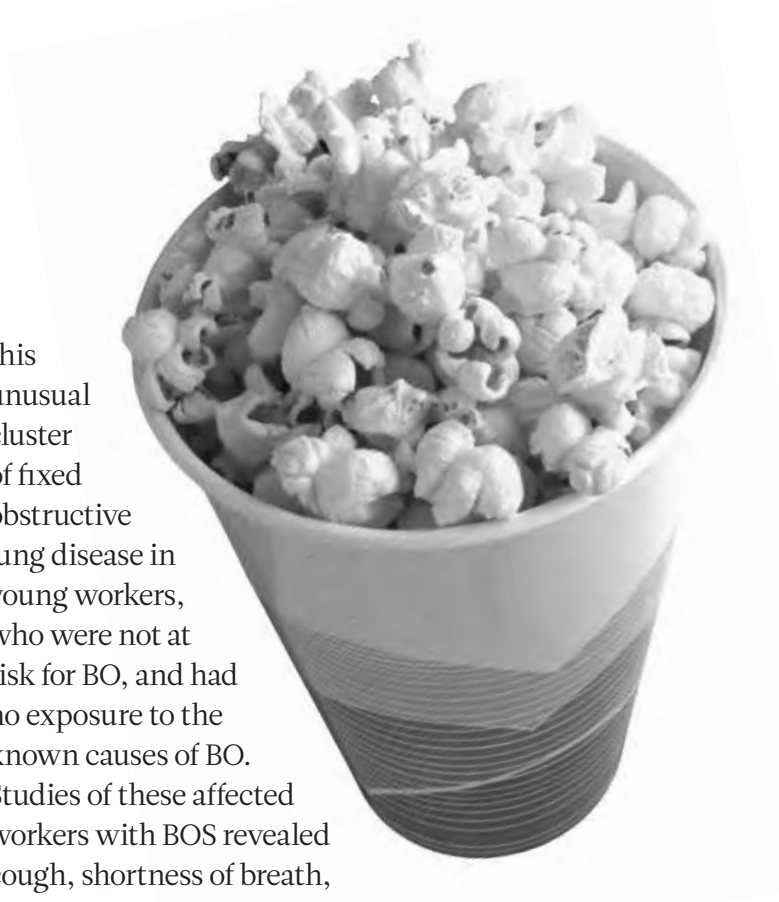

Bronchiolitis obliterans (BO) is a relatively rare, fixed-obstructive lung disease. It can however, be caused by occupational or environmental exposures. These exposures were heretofore almost exclusively as a result of high level, accidental/unanticipated exposures to irritant gases, notably oxides of nitrogen but also chlorine, anhydrous ammonia, phosgene, ozone, hydrogen sulfide, and sulfur dioxide as well as organic and inorganic dusts.[1] The initial inflammatory disease of the small airways from these exposures results in fibrotic healing in the small airways, and thus a fixed obstructive defect on spirometry that is not reversible by bronchodilator administration. When large exposures to these known noxious gases occur at work, the causal relationship is usually recognized when workers subsequently develop fixed airways obstruction a few weeks after the initial inhalational injury. It should be noted that bronchiolitis obliterans is also a common finding of rejection in lung transplant recipients, and develops via a different mechanism than in the inhalational injuries.

In 2002, the first reports of a new syndrome of butter flavoring-associated bronchiolitis obliterans (BO) affecting microwave popcorn workers (MWPCW) appeared in the literature. This rare syndrome has also subsequently been reported in clusters of workers in various plants who were also exposed to artificial butter flavorings.[2, 3]

This newly described MWPCW lung disease appeared to be due to an environmental exposure to a workplace toxin that caused a unique and previously unrecognized form of rapidly progressive obstructive lung disease.[4] In direct contrast to other occupational lung diseases, neither the workers, their supervisors, their physicians, or plant officials were aware of any temporal relationship between working at the plant and the severity of symptoms over the course of the workday or workweek (i.e., no exacerbations such as those seen with occupational asthma); thus no one suspected an exposure at work as being the cause of this lung disease.[5, 6] An astute occupational physician working near the index plant noticed this unusual cluster of fixed obstructive lung disease in young workers, who were not at risk for BO, and had no exposure to the known causes of BO. Studies of these affected workers with BOS revealed cough, shortness of breath, and spirometry with fixed airways obstruction and poor response to bronchodilators; normal diffusion capacity (DLco); stabilization (but not much improvement) of the obstructive defect after leaving the plant, and poor-to-no response to corticosteroids.[7, 8, 9]

Current focus of this association is on the naturally-occurring chemical diacetyl (2,3 butane dione) a highly water-soluble diketone which gives natural butter its buttery flavor, and is added to foods and beverages to impart this butter-like flavor. It is found naturally in beer, wine, cheeses, and other dairy products. Workers most severely affected worked near heated soybean oil where they added concentrated diacetyl to the heated oil (packaging workers also may be affected, but at a lower incidence). Diacetyl had not been listed as a hazardous chemical by any governmental agency, or been previously described as an inhalational hazard.[10] In fact, the chemical characteristics of diacetyl, i.e., its high water solubility, do not indicate it would be a cause of deep lung injury.[11] It has been suggested that the diacetyl may actually simply be a marker of exposure to flavoring mixtures, and the culprit chemical which causes deep lung injury remains unknown. Other plausible candidates are the poorly water-soluble components of the heated oils, which theoretically would not be trapped by

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upper air way moisture, and would therefore have easier penetration to deeper lung spaces. While many authors have more recently concluded that diacetyl is not simply the marker but rather is the culprit chemical, there is still some debate regarding this point in the current scientific literature. There is a new theory that there may be an immune basis for MWPCW Lung disease: a new laboratory study showed that diacetyl can form protein adducts with argenine; theses adducts are known to stimulate autoimmune reactions. This theory could possibly explain why the disease is similar to the BO seen in chronic lung transplant rejection,[12] but would not explain how this highly water-soluble compound would not be trapped in the water-bathed mucous membranes of the upper airways, and how it would penetrate to the terminal bronchioles to exert this effect. Interestingly, non-smoking workers seem to be much more severely affected than smokers, suggesting a possible "protective effect" of cigarette smoking.[13, 14] This lower incidence in smokers has also been seen in other lung diseases, namely hypersensitivity pneumonitis, sarcoidosis, and radiation pneumonitis. [15, 16]

The working diagnostic criteria for MWPCW Lung includes appropriate exposure cohort, fixed obstructive lung disease that is unresponsive to bronchodilators or corticosteroids, and appropriate findings on inspiratory and expiratory HRCT (in a person without COPD or refractory asthma) or lung biopsy. Lung biopsy was required for the diagnosis of BO in lung transplant recipients, but is not currently routinely performed in MWPCW lung case investigations. [17] However, if HRCT scans are not conclusive for BO in a worker with the characteristic exposure, symptoms, and PFT findings, then a lung biopsy may be necessary for a diagnosis of BO.

The initial diagnosis of an obstructive lung disease is made with the aid of spirometry. Many of the initial index cases were initially diagnosed as much more common ailments such as asthma or COPD, due to the presence of obstructive defect on spirometric testing. When there is no response to bronchodilator, a fixed obstructive defect must be considered. However, since fixed obstructive diseases are rare, and quality of office-based spirometry can be quite variable, many times a minimal response to bronchodilator is erroneously interpreted as a reversible airways disease process and treated as such. The quality of the spirometry is critical, a factor that is often overlooked in surveillance studies of occupational lung diseases is that and must be taken into account when interpreting results. Spirometry is very effort-dependent, and therefore good compliance by the subject being tested is crucial. For this reason the ATS has developed expert consensus guidelines for acceptable tests, which include the duration of the FVC effort, plateau, test-to-test variability and reproducibility. It is well-known that submaximal effort by the subject can lead to erroneous diagnoses of lung function decrements, when the abnormal test results may in fact be due to intentional poor effort. This should especially be suspected when there are wide swings in the values from one surveillance test to the next. The most difficult part of spirometry interpretation is the response to bronchodilator, or lack thereof. This is because there is no clear consensus about what constitutes reversibility in subjects with airflow obstruction. Since there is also no consensus on how a bronchodilator response should be expressed, the variables to be used, and, finally, the kind, dose and inhalation mode of bronchodilator medication, it is no wonder there is no consensus. Generally, most experts would agree that improvement of <8% of the baseline value of of the forced expiratory value in one second (FEV_1) is not considered significantly different than normal test-to-test variability.[18] It is generally accepted that 12% or more increase in the FEV1 and/or FVC constitutes a positive response to bronchodilator, but many experts use 10% as a significant response.

Inspiratory and expiratory HRCT scans can be helpful for making the diagnosis of MWPCW Lung in workers with occupational exposure to heated diacetyl who have fixed obstructive defects on spirometry if they also have the characteristic findings on HRCT. The primary CT feature of bronchiolitis obliterans on inspiratory HRCT is a mosaic pattern of lung attenuation, which shows segmental areas of decreased lung density, as well air trapping. Expiratory imaging can confirm the presence of diffuse or focal air trapping and may be abnormal even if inspiratory CT results are normal. Mild cylindrical bronchiectasis is also common seen, and presence of a tree-in-bud pattern should suggest the presence of a more active inflammatory bronchiolitis.[19] Indeed, multiple epidemiological studies of these workers and review

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Taking the Lead with Lead Poisoning

David H. Jang, MD, and Lewis S. Nelson, MD
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A child whose blood lead level is elevated for the third time in a year is brought to the ED. This case study reviews common sources of lead exposure, signs of lead poisoning, and guidelines for management in the pediatric population.

Case

A 2-year-old boy presents to the ED after his mother is informed that her son's venous blood lead level (BLL), which was obtained 3 days prior, is 59 µg/dL (normal, <10). Further history provided in the ED includes two previous episodes of elevated BLLs in the past year that required outpatient treatment with succimer. During these past two episodes, it was suspected that the child may have been exposed to lead from paint chips, although evaluation of the home was unable to identify a source. The patient's last treatment was approximately 4 to 5 months earlier and he has since undergone periodic testing for lead. His mother denies that the child has any symptoms consistent with chronic lead poisoning, such as constipation or abdominal pain, and feels the child has both normal behavior and development.

Physical examination reveals a well-developed child with the following vital signs: blood pressure, 90/50 mm Hg; pulse, 100 beats/min; respiratory rate, 15 breaths/min; and temperature, 98.9˚F. Findings on cardiac, pulmonary, and abdominal examinations are normal. Neurologic examination demonstrates normal attentiveness, motor function, and developmental milestones. The patient's initial blood analysis reveals a hemoglobin level of 8.1 g/dL and a mean corpuscular volume of 50 fL (normal, 80 to 100 fL); a peripheral blood smear is negative for red blood cell basophilic stippling. (Note that the patient's blood was obtained by venipuncture, not from a capillary blood source. Dermal contamination may lead to unreliable results with capillary testing, but low results are considered acceptable.) Urinalysis results are normal. Radiographic studies are negative for radiopaque foreign bodies within the abdomen but positive for dense metaphyseal bands at the distal radius.

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What are important sources of lead exposure to consider in children?

In addition to identifying and managing patients who present with lead poisoning (whether acute or chronic), the clinician must also attempt to locate the source of lead exposure. Unless the child is removed from exposure to the source, he or she is at continued risk. It is possible that other family members, such as siblings, may also be exposed. Sources of lead exposure can generally be classified as environmental, occupational, and miscellaneous (such as ethnic-related foods or supplements). Lead-based paints (typically containing the white pigment lead carbonate) still remain an important source of lead poisoning in children, especially in homes built before 1978.[1,2] Table 1 lists important sources of lead.[3]

What are the signs and symptoms of lead poisoning in children?

The signs and symptoms of lead poisoning are diverse and depend on both the dose and duration of exposure.

The most dramatic presentation of acute pediatric plumbism (clinical lead poisoning) is lead encephalopathy. It is characterized by pernicious vomiting, altered mental status, seizures due to cerebral edema, and increased intracranial pressure. Physical exam findings may reveal oculomotor palsy, papilledema, and other signs of increased intracranial pressure. Acute lead encephalopathy occurs most often in children ages 15 to 30 months and often is associated with a BLL of greater than 100 µg/dL.[4]

Subencephalopathic symptomatic plumbism is associated with BLLs greater than 70 µg/dL, but it can occur at BLLs as low as 50 µg/dL. Signs and symptoms can range from chronic hyperactive behavior to developmental delay. Less common features can include seizures and peripheral neuropathy.[5]

The largest group of children with chronic lead poisoning comprises those with elevated BLL without any overt symptoms. The primary concerns with children in this group are the subclinical effects of chronic, lowlevel lead exposure. Subtle effects can include disturbances in growth, hearing, fine motor movement, and neurocognitive development.[6]

Table. Environmental Lead Sources*

Source	
Leaded paint	Indoors, particularly in homes built before 1978 (still used outdoors)
Dust	From deteriorated lead paint
Soil	From areas tainted with deteriorated lead paint/industrial lead or leaded gasoline emissions from previous era (banned in US since 1976; still in use worldwide)
Water	Leached from lead-containing plumbing (pipes, solder), cooking utensils, water coolers
Air	Industrial emissions
Food	Lead solder in cans (pre-1991 US; still found in some imported canned foods), "natural" calcium supplements, "moonshine" whisky, lead-foil-covered wine bottles, contaminated flour, paprika

**Adapted from Henretig.*[3]

What are the critical actions to consider in the management of lead poisoning in children?

The treatment of lead poisoning in children may require an aggressive approach. For most patients, the critical action is the removal of the child from the source of the lead exposure, which in many cases may be the child's home. If the child is asymptomatic, placement in the home of a family or friend will avert admission to the hospital. Children with large gastrointestinal burdens of lead paint chips may benefit from prompt initiation of whole-bowel irrigation to reduce absorption.

Therapy with chelators, considered a mainstay of therapy for symptomatic patients, involves a complicated risk-benefit decision for asymptomatic children with an elevated BLL. Chelation therapy increases lead excretion, reduces BLLs, and allows reversal of hematologic markers of toxicity during therapy. The use of combination chelation in the treatment of acute lead encephalopathy in the 1960s contributed to a large decline in mortality. The role of chelation in subclinically symptomatic patients with mild to moderate lead burdens is less clear, with lingering questions regarding both efficacy and safety.[7]

A large multicenter trial evaluated the effect of chelation therapy with succimer on neuropsychological test scores in children with no overt symptoms but moderately elevated BLLs (20 to 44 µg/dL).[8] All children in the study were removed from the source of lead exposure and were randomized to receive either succimer or placebo.

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Children who received succimer initially had a rapid and significant decrease in BLLs, but a rebound was observed within 1 week, likely due to mobilization of lead from bone. The placebo group also had a decrease in BLLs, probably due to removal from the exposure. At the end of the study period, the two groups had similar BLLs, and no differential improvement in cognition, behavior, or neuropsychological function was demonstrated. Given the lack of clear benefit and the cost of treatment, the findings from this study suggest that the use of chelation in asymptomatic patients should be undertaken only after careful consideration. However, it should be noted that determining that a young child is truly asymptomatic is fraught with difficulty, as the baseline level of function is limited, complicating assessment of subtle changes.[8]

What is the recommended chelation protocol for children?

The decision to use chelation therapy for childhood lead poisoning, as well as the selection of a chelator, depends on many factors, such as age, BLL, and clinical findings. Decision making should involve consultation with a medical toxicologist, a department of health, or a pediatrician with experience in management of lead poisoning. Three chelating agents are currently recommended for the treatment of lead poisoning. BAL (British anti-Lewisite), also called dimercaprol, is an intramuscular drug that is formulated in peanut oil due to its insolubility in water; it is associated with painful injection. Edetate calcium disodium (CaNa2EDTA) is administered intravenously, either alone or in combination with BAL, for symptomatic patients and asymptomatic patients with extreme elevations in BLL. Succimer, or dimercaptosuccinic acid (DMSA), is available for oral therapy and is used in patients with mild to moderate poisoning.[9] Treatment guidelines from the New York City Department of Health and Mental Hygiene *(www.nyc.gov/html/doh/downloads/pdf/lead/ lead-chelation.pdf)*[10] and the American Academy of Pediatrics[6] are also valuable resources.

The following steps should be taken prior to initiation of chelation therapy in children with a BLL of 45 µg/d[10]: (1) a venous blood specimen should be taken and processed emergently (unless encephalopathy is apparent) to confirm that the child's BLL is 45 µg/dL or greater; (2) abdominal radiography should be performed to rule out ingestion of solid lead; if radioopaque particles are detected or if the child was seen ingesting lead, a cathartic should be given; (3) admission and chelation therapy should be arranged in a hospital with experience in the treatment of children with lead poisoning; (4) ensure that the child will be discharged to an environment that is lead-safe; the local department of health should be informed of hospitalization of lead poisoning and should inspect the child's home prior to discharge.

Case Conclusion

The child received oral succimer and was admitted to the hospital for further evaluation. On the third day of succimer therapy, results of a repeat specimen taken on admission revealed a BLL of 71 µg/dL. At this time, the intravenous chelating agent $CaNa_2EDTA$ was added. The repeat BLL, drawn on the third hospital day, with results known the following day (4 days after initiation of this therapy), was 21 µg/dL, prompting discontinuation of the $CaNa_2EDTA$. Succimer was continued for the full 21-day course. Further investigation by the department of health confirmed that the home was not the source of lead, and questioning for other sources, such as home remedies, was inconclusive. Results of testing in one sibling were unremarkable.

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articles indicate that high resolution computed tomography showing typical findings such as air trapping on expiratory films is required to make a diagnosis of BOS.[20, 21, 22] However, (but not sufficient) COPD and severe asthma can also have these same HRCT findings mentioned above, and these HRCT findings alone are not considered specific for or exclusively found in BOS. For instance, air trapping can be seen in asthma, hypersensitivity pneumonitis, as well as in some normal individuals. [23]

The differential diagnosis of BO in butter flavoring-exposed workers includes COPD and chronic persistent asthma, which can have similar spirometric and HRCT findings. Since smoking and occupational asthma are far more common diseases, these should always be considered, especially when a case is seen in isolation (i.e., no cluster within an exposure group) and/or not in an appropriate exposure group. Advanced asthma can also present as a chronic, incapacitating process, eventually leading to irreversible obstructive pulmonary disease. Bronchial wall thickening and expiratory air trapping are also common to asthma and BO. [24]

MWPCW Lung is a new, fascinating disorder that was discovered and reported by an astute primary care physician who recognized the unusual clustering of a rare disorder in a group of workers with similar exposures at the same jobsite. Poison centers and toxicologists understand the value of this type of disease surveillance, and should strive to develop relationships with local occupational medicine colleagues to more rapidly report such cases. While it is not definite that diacetyl is the culprit chemical, it seems likely that it is responsible. If so, it could break the paradigm of water solubility and area of lungs at risk for injury. More strict controls over worker exposures have reduced the incidence; fortunately there is no evidence of any risk to consumers due to exposures to the finished products. Many manufacturers of microwave popcorn have reformulated their butter flavoring, eliminating diacetyl altogether. However, many other chemical flavorings are also untested for safety.

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Baclofen Pump Complications

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Case Conclusion

The patient was admitted to intensive care to monitor for potential withdrawal. With assistance from Rehabilitation Medicine, the patient was weaned from the ITB, with an initial 25% dose reduction from the pump and advanced with oral baclofen to the maximum recommended dose for the patient's age, 40 mg/day in three dosage intervals. Vancomycin and cefepime were administered for meningitis prophylaxis, given the presence of fever and catheter violation. Operative pump removal was accomplished the following day, with the catheter left in place for emergency ITB administration should withdrawal symptoms develop. The patient was successfully weaned from baclofen over five days without requiring intrathecal injections, and the catheter was subsequently removed. CSF cultures were positive for MRSA, and the patient completed a 2 week course of vancomycin and was discharged at his baseline state to a skilled nursing facility.

Postscript: what other medications might be encountered in intrathecal drug delivery systems for pain or spasticity?

Medications from diverse pharmaceutical classes have been used. These include alpha$_2$ adrenergic receptor agonists (clonidine), benzodiazepines (midazolam), conotoxins (ziconotide), "local" anesthetics (bupivicaine, ropivicaine), NSAIDs (keterolac), and opioids (fentanyl, hydromorphone, meperidine, morphine, sufentanyl).[4] Complications may be seen in both overdose and withdrawal. Aggressive supportive care as well as specific antidotes may be required for management.

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Thus, cyanide poisoning should be considered when clinical history is suggestive of such. The availability of cyanide antidotes to emergency medicine may facilitate early lifesaving treatment, and EMS or medical control should attempt contact with the poison control center as early as possible when cyanide poisoning is suspected.

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