Case Files of the Medical Toxicology Fellowship at the New York City Poison Control: Bromism: Forgotten, but Not Gone

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CASE PRESENTATION

A 22-day-old girl was brought to the emergency department (ED) by her parents for excessive sleepiness and decreased oral intake over the prior 48 hours. Her birth history was unremarkable and her parents had no significant past medical history. Routine newborn exam and screens were also normal at birth. She had follow-up visits with a pediatrician and had been gaining weight appropriately. The parents stated that the child had some "colic" 2 weeks prior and her urine output was slightly decreased, but otherwise she had no recent illness, fever, chills, vomiting, diarrhea, rash, or excessive crying. All other systems reviews were negative.

Further questioning revealed that the parents had been adding Cordial de Monell, an "elixir" for colic, to each meal around the clock for about 12 days prior to the patient's current symptom onset. It was purchased locally, and is commonly used in the Dominican Republic and in the expatriate Dominican community in the US. The resident physician who was caring for this patient had a similar cultural background, was familiar with this product, and remembered it contained "bromuro de potasio." The parents later brought in the actual product, confirming potassium bromide as a listed ingredient (Figures 1 and 2). The New York City Poison Control Center was consulted regarding whether exposure to potassium bromide could explain this patient's presentation.

What is the History of Bromide's Medicinal Use?

Potassium bromide was first discovered in 1826; shortly afterward it was used medicinally for splenomegaly, because it was believed to have anti-inflammatory properties. It was not long after its introduction that many began to observe sedative-hypnotic effects. A textbook published in the late 1800s noted that bromide "caused much drowsiness, and in very large doses, want of power over extremities . . . acting as an anti-aphrodisiac, causing loss of virile power" [1].

In 1857, Sir Charles Locock, an obstetrician aware of the apparent suppressive effects bromide had on the libido, administered potassium bromide to several women with uncontrollable

Figure 1: Cordial de Monell, as sold on shelf with paper wrapping. (Photo credit: Ceila Dominguez, MD, Lincoln Medical and Mental Health Center)

Figure 2: Listed ingredients of Cordial de Monell. (Photo credit: Daniel M. Lugassy, MD, New York City Poison Control Center)

"onanism," one of whom suffered from epilepsy. It was believed at this time that masturbation was a cause of epilepsy. He observed great success in the suppression of seizures in this patient and has often been credited with discovering bromide's use in epilepsy. Locock never again played a role in the use of bromides to treat epilepsy; it was several other British and French physicians who accelerated this new treatment. In a span of 20 years, between 1855 and 1875, a hospital pharmacy in Paris saw its annual dispensing of potassium bromide increase 100-fold [1].

The worldwide use of bromides to treat epilepsy began to decline in 1912, when phenobarbital was introduced. The discovery in 1938 of phenytoin, which had a better safety profile than bromides, rendered them obsolete for the treatment of epilepsy. Despite this defeat, bromide remained a prominent component in many prescription and over-the-counter (OTC) preparations owing to its sedative effect [2]. Bromisovalum and carbromal were prescribed as sleep aids, and OTC items such as Bromo-Seltzer, Bromo-Quinine, and Dr. Miles' Nervine were extremely popular "nerve tonics" [3,4].

In 1938, sales of products containing bromide in the US were second only to aspirin [3]. In the 1930s and 40s, bromism (discussed in detail later) was recognized as a frequent cause of altered mental status, psychiatric complaints, and coma [3,5]. In 1965, up to 10% of patients admitted to a psychiatric hospital had a measurable serum bromide concentration, and 2% had clinically significant bromism [6]. Widespread abuse lead to the ban by the Food and Drug Administration (FDA) of bromide salts from OTC products in 1975, and later the removal of organic bromides from OTC sleep aids in 1989 [3].

How Can Patients Be Exposed to Bromide?

Poisoning has resulted from several classes of bromide-containing compounds, all of which ultimately release bromide ions. Soluble bromide salts, such as potassium bromide and sodium bromide, are still used for the treatment of epilepsy in dogs and in photographic developing chemicals [7]. Our case also illustrates that despite FDA regulations, bromide salts may also still find their way into public use. In 2007, an outbreak of an unknown neurological disease occurred in Angola, where ~500 people exhibited symptoms of tiredness, blurred vision, dizziness, weakness, and trouble with speech and walking. An investigation revealed that several patients had significantly elevated serum bromide concentrations, and the local dietary salt supply was found to have a large amount of sodium bromide. If confirmed, this will have been the largest outbreak of bromide poisoning ever reported [8].

Bromoureides, organic structures containing bromide ions, were previously popular as sedative-hypnotics, and although prohibited in the US, they are still used widely in Europe and other parts of the world [3,9,10]. Bromisovalum, bromvalerylurea, and carbromal are three bromoureides that have been reported to cause bromism with chronic use [2,11,12].

Numerous xenobiotics today exist as bromide salts, and their intended clinical effects are unrelated to the bromide ion. Bromide is present in trivial amounts, and therapeutic dosing of such medications does not cause any of the features associated with bromide toxicity. However, when chronically consumed or abused, bromism can occur. For example, bromism has occurred from the abuse of dextromethorphan hydrobromide, as well as with the chronic use of pyridostigmine bromide [2,9,13,14].

At least two cases of bromide toxicity have been linked to soft drink intake. Brominated vegetable oil acting as an emulsifier to enhance the citrus flavor of soft drinks has resulted in significant serum bromide accumulation [15]. Bromism was seen from excess cola consumption and bromoderma in a patient who consumed nearly 8 L of Ruby Red Squirt soda daily for several months [3,15]. Table 1 lists some of the products clinicians may encounter that patients have ingested that contain bromide.

Table 1: Xenobiotics containing bromide

Bromide Salts	Medications (existing as bromide salts)
Ammonium bromide	
Potassium bromide	Dextromethorphan hydrobromide
Sodium bromide	Homatropine hydrobromide
	Neostigmine bromide
Bromoureides	Pancuronium bromide
	Propantheline bromide
Bromisovalum	Pyridostigmine bromide
Bromocriptine	Quinine hydrobromide
Brompheniramine	Scopolamine hydrobromide
Bromvaleryurea	Vecuronium bromide
Calcium bromogalactogluconate	
Carbromal	**Miscellaneous**
Pamabrom	
	Halothane
	Brominated vegetable oil

CASE CONTINUATION

The infant's vital signs were: blood pressure 84/35 mmHg, heart rate 159 beats/minute, respiratory rate 38 breaths/minute, and temperature 36.6°C (97.9°F). Pertinent physical exam findings included lethargy, hypotonia, and slightly diminished reflexes. The infant hardly responded to peripheral intravenous catheter placement and did not cry during examination. The patient had normal skin turgor, mucous membranes were slightly dry, had a supple neck, and the fontanels were not depressed; there were no signs of trauma.

What Are the Features of Bromide Toxicity, and Do They Fit with the Presentation of This Case?

Bromides at therapeutic doses commonly produce sedation without significant alteration in vital signs, mental status, or other physiological functions. Acute overdose of bromide salts typically results in nausea and vomiting due to the irritating effect of bromide ions on the gastrointestinal tract. Therefore, even massive single ingestions rarely allow enough to be absorbed to result in significant systemic toxicity [16]. Poisoning is often due to chronic repeated exposure and can develop gradually over weeks to months [2].

Bromide toxicity primarily manifests in its adverse effects on neurological and psychiatric functioning. Bromism describes patients who display the debilitating neuropsychiatric effects from chronic exposure to bromides, who are found to have concurrent elevated serum bromide concentration. Neurological depression presents as lethargy, slurred speech, confusion, ataxia, and coma [3,4]. Other features such as tremor, headache, ptosis, hypotonia, mydriasis, visual changes, myoclonus, and alteration of deep tendon reflexes (either increased or decreased) can also be present [3,17,18]. Weak cry, poor suck, diminished Moro reflex, lethargy, and hypotonia have been described in infants with bromism [7]. There are no consistent vital sign abnormalities noted in bromism, and if found they are usually related to severe sedation or other underlying conditions.

The psychiatric features of bromism vary by patient, but the following have been seen: irritability, agitation, memory impairment, decreased ability to concentrate, auditory and visual hallucinations, depression, mania, crying spells, persecutory delusions, and schizophreniform psychosis [2,4,9,19]. None of the features listed are particularly specific to bromide toxicity, therefore the diagnosis can be difficult to confirm by exam. The protean neuropsychiatric features of bromism frequently lead to either delayed or missed diagnosis, often misinterpreted as senility or dementia in elderly patients [4,19].

Bromoderma is a rash that occurs in patients chronically exposed to bromides. Classically described as an acneiform rash, it can also include pustular lesions, granulomatous plaques, ulcers, or bullae [20]. It is commonly found on the face and trunk, but also occurs on arms, legs, and hands [15]. Bromoderma is only found in 25–30% of patients with significant bromide exposure [21,22]. Patients may exhibit bromoderma without any of the neuropsy-

chiatric features of bromism [3,15,20]. Skin eruptions from halides such as bromide and iodide are believed to be a hypersensitivity-type reaction, but the accumulation of these halides in abnormally high amounts also seems to be a key factor [20].

What Is the Pharmacology of Bromides?

Soluble bromide salts have nearly 100% bioavailability when ingested [16]. Other forms of bromides have various bioavailabilities depending on their physicochemical properties, such as solubility and acid stability [10]. Bromide ions rapidly distribute into extracellular fluids, erythrocytes, muscles, liver, and neural tissues in a similar pattern to chloride ions [16,23]. Bromide has a volume of distribution of 0.35 to 0.48 L/kg [16]. Bromide ions are predominantly eliminated by the kidneys and in healthy individuals the half-life is approximately 12 days [2,3]. With chronic use, intake often exceeds elimination and serum bromide concentrations will rise. This causes a significant increase in the urinary excretion of chloride, as the renal tubules preferentially reabsorb bromide [23]. Chloride stores can be severely depleted and up to 45% of total body chloride may be replaced by bromide [16]. This effect on chloride distribution is believed to alter intrinsic cellular conductance, most significantly neuronal, leading to the neuropsychiatric abnormalities of bromism [1,10,16].

A more likely neuronal mechanism of action of bromide ions is their indirect effect on the gamma-aminobutyric acid (GABA)–linked ligand-gated chloride channel, the GABA$_A$ receptor. Normally, binding of GABA to the GABA$_A$ receptor increases chloride conductance, causing hyperpolarization of the intracellular electrical potential. Since bromide has a smaller hydrated diameter than chloride, it diffuses through this channel with less resistance and in greater quantity. Bromides therefore enhance the inhibitory clinical effects mediated by this channel, which explain many of the GABA-ergic manifestations of bromism [1,16].

CASE CONTINUATION

While in the ED, a newborn septic workup was initiated, including obtaining blood, cerebrospinal fluid (CSF), and urine cultures. Antibiotics were started empirically and the patient was admitted to the pediatric ICU. Initial pertinent laboratory results were: peripheral white blood cell count, 10,500 cells/mm^3; sodium, 140 mEq/L; potassium, 5.8 mEq/L; chloride, 105 mEq/L; bicarbonate, 26 mEq/L; blood urea nitrogen, 2.5 mmol/L (7 mg/dL); creatinine, 0.027 μmol/L (0.3 mg/dL); glucose, 3.5 mmol/L (64 mg/dL); anion gap, 9 mEq/L. After a traumatic lumbar puncture, CSF analysis revealed: white blood cell count, 6 cells/mm^3; red blood cells, 23,000 cells/mm^3; glucose, 55 mg/dL; protein, 40 mg/dL; no organisms on Gram stain. Urinalysis was normal.

If the Clinical Exam Findings in Bromism Are Nonspecific, What Other Features Can Help Make This Diagnosis?

In the presence of an elevated serum bromide concentration, the reported serum chloride concentration can be falsely elevated, in

some reports >200 mEq/L [24]. This can cause anion gaps to be low or even negative, and have been reported to reach values as low as –60 mEq/L and –97 mEq/L [25–27]. Bromism may not even appear in the differential diagnosis in many cases until these findings are seen on laboratory analysis [13].

The similar physicochemical properties of bromide cause interference of serum chemistry analysis of chloride. It is important that hospital laboratories report any abnormal chloride values, as some may choose to discard the sample results as erroneous or contaminated [16]. There are only a few causes of falsely elevated serum chloride, including simple laboratory error, nitrate excess, hypertriglyceridemia, and elevated serum concentrations of halides such as bromide and iodide [26,28].

The 3 most common methods used to determine serum chloride concentration are coulometry, colorimetry, and use of an ion-selective electrode [13,26]. Coulometry measures chloride by creating a direct current of silver ions between 2 electrodes in the solution being tested. Chloride binds these available silver cations, creating silver chloride. Bromide and other halides can also bind silver in the same manner. Therefore this method provides the total halide concentration [27,29].

By the colorimetric method, chloride ions displace thiocyanate from mercuric thiocyanate. This free thiocyanate binds iron, creating ferric thiocyanate, and the amount of this complex in solution is determined photometrically. The concentration of iron-thiocyanate complexes correlates with the chloride concentration. Bromides bind with higher affinity to mercury than does chloride, enabling more thiocyanate liberation [29].

The ion-selective method is composed of solid-state electrodes of silver chloride and a semi-permeable membrane that is "selective" for chloride. As chloride ions flow across this membrane, a concentration gradient is created. A charge potential is also produced and a chloride concentration is determined. Interference occurs in this method because the membrane is not truly "selective" for chloride, and bromide ion, with its similar chemical properties, crosses quite easily [24,30]. This is the method most commonly used in clinical chemistry laboratories today.

All 3 methods have some interference in reporting chloride concentrations in the presence of bromides, and there can be great discrepancy between methods of chloride determination in the same sample [2,24,26]. For example, in a reported case of bromism, the chloride concentrations determined in the same sample were 109 mEq/L by coulimetry and 190 mEq/L by the ion-selective method, respectively [25]. The extent of interference in each method has been extensively studied in patients poisoned with bromides and by in vitro analysis [24,25]. The least interference is seen with coulometry, while the greatest is by the ion-selective method, in which the ratio of bromide misinterpreted as chloride is about 1:3 (i.e., for every bromide ion, it appears that 3 chloride ions are present) [24]. The colorimetric method interference ratio is reported to be 1.6 [24]. The coulometric measurement provides the most accurate serum chloride concentration in the presence of bromides, with an interference ratio close to 1 [24,31].

However, assuming that bromide will always produce abnormally elevated chloride values may lead to missed diagnoses of bromism. Severe bromide poisoning can deplete total body chloride, so even if bromide ions will falsely elevate the chloride, the net reported value may be normal [31]. A normal chloride concentration can be reported regardless of the method, even in the presence of significant bromide concentrations [10,17,25].

What Other Diagnoses Must Be Considered When There Is a Low or Even Negative Anion Gap?

A low or negative anion gap can occur via several mechanisms. More than 90% of the time, a low anion gap results from laboratory error [27]. A decrease in sodium and increases in chloride or bicarbonate will decrease the calculated anion gap. Reasons for falsely elevated chloride were discussed earlier. Sodium concentrations are prone to factitious decrease by hypernatremia itself, hypertriglyceridemia or dysproteinemia, and severe macroglobulinemia. Bicarbonate is determined by measuring carbon dioxide release, and if serum is not separated from the cellular elements shortly after phlebotomy, leukocytes may continue to produce carbon dioxide in vitro, falsely elevating the reported bicarbonate concentration [27].

Above we have described conditions that may cause factitious lowering of the anion gap, but there are conditions that exist in which it is truly low or negative. Unmeasured anions are largely complexed to proteins, and hypoalbuminemia is a well-established cause of a low anion gap. A decrease in the anion gap of 1.5–2.5 mEq/L may be seen with each 1 g/dL drop in plasma albumin. Overproduction of IgG immunoglobulins can also cause alterations in the anion gap as they tend to be cationic. When the serum concentration of lithium ion climbs above 4 mEq/L, the anion gap may fall. The antimicrobial polymyxin B has cationic properties and can lower the anion gap as well. Hypercalcemia, hyperkalemia, and hypermagnesemia have often been cited as potential causes of a decreased anion gap, but these seem to be more theoretical with little clinical evidence to support this assumption [27,28]. Table 2 lists several recognized causes of a low or negative anion gap.

What Treatment Is Recommended in Patients Who Are Bromide Poisoned?

Identifying and removing the source of bromide exposure is critical. It may seem obvious, but several patients have had recurrent toxicity from re-exposure due to lack of initial identification of offending agent [4,19]. The first line of treatment in bromide poisoning is to "chloride load" the patient in an effort to try to retain chloride and enhance bromide clearance. Renal bromide clearance is dependent on the total serum and urinary halide concentration [2,6,16]. This is done most commonly by aggressive hydration with IV normal saline. There are no evidence-based recommendations regarding the amount of volume necessary, but a recommended goal is to have the urine output reach 2–4 ml/kg per hour. It is possible to orally load patients with 2–3 g of sodium chloride in conjunction with several liters of oral fluid in-

Table 2: Causes of a Low or Negative Anion Gap

Laboratory Error

- Factitiously Elevated Chloride
  - Elevated serum bromide (or any halide)
  - Hypertriglyceridemia
  - Nitrates
- Factitiously Low Sodium
  - Hypernatremia
  - Hypertriglyceridemia
  - Dysproteinemia
- Factitiously Elevated Bicarbonate
  - Cells not separated from serum rapidly

True Causes

- Hypoalbuminemia
- Elevated circulating immunoglobulins (e.g., multiple myeloma)
- Lithium toxicity
- Polymyxin B
- Hypercalcemia, hyperkalemia, hypermagnesemia (theoretical causes)

take [5,16]. Oral therapy may seem inappropriate for individual severe cases, but in mass poisonings such as in Angola this may be the most feasible means of treatment. Ammonium chloride can be used when "chloride loading" is indicated, but the sodium content of normal saline has the potential for harm, such as in a patient with hypernatremia [16].

Aggressive saline loading consistently reduces bromide's serum half-life from 12 days to about 3 days [3]. Patients can usually be managed with IV hydration alone. A few case reports have also documented the use of diuretic agents, such as furosemide and ethacrynic acid with mannitol, which may further increase the elimination of bromide [6,31]. However, this may occur at the expense of volume depletion and should be done very carefully, if at all.

Hemodialysis was first reported as a treatment for bromism in 1951. The half-life of bromide during hemodialysis is about 1–2 hours [3,32]. Hemodialysis should be reserved for patients who would not be able to tolerate the sodium or fluid load required to enhance urinary bromide elimination. Congestive heart failure, anuria, oliguria, and renal failure are conditions that would likely warrant hemodialysis for patients with severe symptomatic poisoning, with manifestations such as acute delirium, coma, or respiratory depression [3,13,32]. Significantly elevated bromide concentrations can take days to fall even with forced diuresis and chloride loading, therefore dialysis should be considered to improve symptoms rapidly and decrease need for intensive treatment and length of stay in the hospital [3,6,13].

Bromoderma can be treated with topical or oral steroids, as well as immunosuppressive agents such as cyclosporine [15]. There is no strong evidence available to recommend these treatments, and it seems more important to enhance elimination of bromide by mechanisms described earlier. The rash often resolves within 8–12 weeks, but may last as long as 5 months [2,15].

What Is a Toxic Serum Bromide Concentration?

Serum bromide concentration can be reported in different units: 1 mg/dL equals 0.125 mEq/L [22]. When bromides were used commonly as anti-epileptics, a large therapeutic range existed, from 80 to 200 mg/dL (10–25 mEq/L). Toxic concentrations are now considered to be >50 mg/dL or 6.3 mEq/L, and severe systemic toxicity can occur at concentrations >200 mg/dL or 25 mEq/L [2,3].

Signs and symptoms of bromide toxicity correlate poorly with serum concentration [1,2,19,31]. Several reports have noted serum bromide concentrations <40 mg/dL (5 mEq/L) causing significant symptoms, other factors such as chronicity of exposure, age, volume status, and renal function can alter the clinical effect for a given serum bromide concentration [4,9,19,31]. Serum bromide concentrations may not mirror CSF values, which likely correlate better with clinical neurological effects. In a classic paper in which CSF bromide concentrations were measured, rapid decline of serum bromide concentration was observed after dialysis, but the CSF bromide lagged behind for several days and was slow to equilibrate with the serum [32]. It can be assumed that this phenomenon likely occurs in patients who are chronically exposed to bromides [6,32].

What Is the Endpoint of Treatment?

It is paramount that treatment continues until symptoms significantly improve. It has been recommended that treatment continue until bromide concentrations fall below 50 mg/dL (6.25 mEq/L) [22]. Most hospital laboratories are not able to measure serum bromide concentration, and it may take days to return from outside labs. This delay limits the value of using serum bromide concentrations to monitor the response to treatment. A falsely elevated chloride may be used cautiously as an indirect measure of falling bromide. If the same chloride assay is used, a declining chloride value likely represents serum bromide decline [9,24,31].

Serum bromide concentrations can rebound after aggressive elimination [6,32]. Bromide distributes into several intracellular compartments and after acute lowering of the serum concentration, redistribution back into the serum occurs. This effect likely contributes to the long half-life and extended effects poisoning can have [6].

The lag in CSF decline explains why delayed symptoms persist despite subtoxic serum bromide concentration [32]. Although symptoms may persist for weeks, complete recovery without any permanent sequelae is expected even in very severe cases [13,32]. Psychiatric symptoms not caused by a functional disorder should also resolve after complete treatment and recovery [4].

What about the Safety of Bromides during Pregnancy, and in Lactation? Could this Patient Have Been Poisoned during Pregnancy?

Bromide exposure during pregnancy had been suggested in case reports to cause fetal abnormalities, but is not clearly linked to birth defects. Transplacental accumulation of bromide resulting in infants born with clinical signs and symptoms of bromism has been reported. Most of these cases were linked to maternal ingestion of bromide-containing products during pregnancy, but one mother had an occupational exposure to bromide in photograph-developing chemicals [7,19].

Lactation also provides a potential route of exposure to the infant. High levels of bromide can appear in breast milk, and can linger from days to weeks after the mother's last exposure to bromide [33].

Our patient suffered from very similar symptoms described in cases of trans-placental bromide exposure, but the patient exhibited no signs of bromism at birth and further questioning revealed that the mother did not use the Cordial de Monell herself or any other medications. In addition, the mother stated that the patient had been feeding mostly by formula due to lack of production of breast milk.

CASE CONTINUATION

The patient was admitted to the pediatric ICU and treated with empiric antibiotics. During hospitalization, several other conditions were investigated further, such as inborn errors of metabolism and seizures. We advised fluid bolus with normal saline and aggressive, age-appropriate IV fluid administration, with close monitoring of electrolytes. Serum was sent for bromide analysis; it was known that results would not be available for several days.

Over the first two days in the hospital, the infant showed gradual but progressive improvement. She became more responsive and her muscle tone increased. By day 3, the parents felt that the child was nearly back to her normal mental status and was observed to have a strong cry and vigorous appetite. Blood, urine, and CSF cultures were all reported to be normal, and other workup provided no medical cause for this presentation. She was kept for observation until hospital day 5, then was discharged home. At a three-month follow-up, she had no return of similar symptoms and appeared to be developing normally.

One week after she was discharged the serum bromide results returned. Unfortunately, the samples submitted from hospital days 1 and 2 had inadequate volume; only 0.1 mL of plasma was available for a test that normally requires at least 1–2 mL. Serum from hospital day 3 showed a bromide concentration of 0.63 mg/dL (5.0 mEq/L). A review of the chart revealed no administration of medications that contained bromide. We believe this confirms bromide poisoning, as the patient had not received any Cordial de Monell for almost 4 days from when the sample was obtained, in which time the patient had been aggressively hydrated with chloride-containing IV fluids.

This exposure was reported to the FDA, who examined the remaining fluid from the bottle of Cordial de Monell that had been administered to the patient. Analysis revealed that the liquid contained potassium bromide at a concentration of 0.3 g/100 mL, which confirms the product label declaration. As indicated earlier, bromides are no longer legal in OTC preparations, and following an FDA investigation, the manufacturer issued an immediate recall of this product.

CONCLUSION

After an extensive literature review, this appears to be the first case documenting bromide toxicity in a patient exposed to the product called Cordial de Monell, which contains potassium bromide. We have identified this product on store shelves in areas of New York City. We believe this child suffered from excess therapeutic sedative exposure due to her size, age, and repeated exposure. Bromism is not nearly as common as it once was, but several forms of bromide are still readily available. This diagnosis should be included in the differential diagnosis of patients who present with sedative-hypnotic–type intoxication. Elevations in the reported serum chloride levels and a negative anion gap are helpful findings if present, but our case and others before confirm that the lack of these features do not rule out this poisoning. This case further illustrates the need for clinicians to be diligent in obtaining thorough medication, dietary, herbal supplement, social, occupational, and cultural histories from their patients. Aggressive hydration with chloride-containing solutions is the cornerstone of treatment, and in severe cases dialysis may be considered. Bromides are not gone, and bromism should not be forgotten.

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