Clinical Toxicology

CAUSTICS

Exposure to caustic agents may occur via the dermal, ocular, respiratory, and gastrointestinal routes with the most significant of these, by far, resulting from ingestion. Morbidity and mortality from exposures to caustics is a worldwide problem.

Caustics cause both histologic and clinical damage on contact with tissues. Table 1 lists common caustics and the commercial products that contain them. Many are available for home use, in both solid and liquid forms, with variations in viscosity, concentration, and pH. Usually, children are unintentionally exposed to household products. Adults may be exposed to household or industrial products that result from occupational exposure or are suicide attempts.

PATHOPHYSIOLOGY

A caustic is a xenobiotic that causes both functional and histologic damage on contact with tissue surfaces. Although there are many ways to categorize caustics, they are most typically classified as acids or alkalis. An acid is a proton donator and causes significant injury, generally at a pH below 3. An alkali is a proton acceptor and causes significant injury, generally at a pH above 11. The extent of injury is modulated by duration of contact; ability of the caustic to penetrate tissues; volume, pH, and concentration; the presence or absence of food in the stomach; and a property known as *titratable acid*/*alkaline reserve* (TAR). TAR quantifies the amount of neutralizing xenobiotic needed to bring the pH of a caustic to that of physiologic tissues. Neutralization of caustics takes place at the expense of the tissues, resulting in the release of thermal energy, producing burns. Generally, as the TAR of caustics increases, so does their ability to produce tissue damage. Some xenobiotics, such as zinc chloride and phenol, have a high TAR and are capable of producing severe burns even though their pH is near physiologic.

ALKALIS

Following exposure to an alkaline xenobiotic, dissociated hydroxide (OH^-) ions penetrate tissue surfaces producing what is histologically described as liquefactive necrosis. This process includes protein dissolution, collagen destruction, fat saponification, cell membrane emulsification, transmural thrombosis, and cell death.

The alkali, such as sodium hydroxide ("liquid lye"), then continues to penetrate until the OH^- concentration is sufficiently neutralized by the tissues.

Although federal regulations have lowered the maximal available house- hold

concentration of many caustics, there are two industrial strength products that seem to be readily available and therefore warrant special mention: ammonium hydroxide and sodium hypochlorite. Ammonia (ammonium hydroxide) products are weak bases—partially dissociated in water—that can cause significant esophageal burns, depending on the concentration and volume ingested. Household ammonium hydroxide ranges in concentration from 3% to 10%. Strictures have formed in patients who ingested 28% solutions. Sodium hypochlorite is the major component in most industrial and household bleaches. Large case series and reports have found that severe injuries occur only in patients with large-volume ingestions of concentrated products and that most other patients do well with supportive care.

Table 1:

TABLE 104–1. Sources of Common Caustics

Xenobiotic	Applications
Acetic acid	Permanent wave neutralizers, photographic stop bath
Ammonia (ammonium hydroxide)	Toilet bowl cleaners, metal cleaners and polishes, hair dyes and tints, antirust products, jewelry cleaners, floor strippers, glass cleaners, wax removers
Benzalkonium chloride	Detergents
Boric acid	Roach powders, water softeners, germicide
Formaldehyde, formic acid	Deodorizing tablets, plastic menders, fumigant, embalming agent
Hydrochloric acid (muriatic acid)	Metal and toilet bowl cleaners
Hydrofluoric acid	Antirust products, glass etching, microchip etching
Iodine	Antiseptics
Mercuric chloride ($HgCl_2$)	Preservative
Methylethyl ketone peroxide	Industrial synthetic agent
Oxalic acid	Disinfectants, household bleach, metal polish, antirust products, furniture refinisher

Phenol (creosol, creosote)	Antiseptics, preservatives
Phosphoric acid	Toilet bowl cleaners
Phosphorus	Matches, fireworks, rodenticides, methamphetamine synthesis
Potassium permanganate	Illicit abortifacient, antiseptic solution
Selenious acid	Gun bluing agent
Sodium hydroxide	Detergents, paint removers, drain cleaners and openers, oven cleaners
Sodium borates, carbonates, phosphates, and silicates	Detergents, electric dishwasher preparations, water softeners
Sodium hypochlorite	Bleaches, cleansers
Sulfuric acid	Automobile batteries, drain cleaners
Zinc chloride	Soldering flux

Ingestion of button batteries were once considered a unique caustic exposure. Composed of metal salts and a variety of alkaline xenobiotics, such as sodium and potassium hydroxide, leakage of battery contents was a legitimate concern. In recent years, however, new techniques used in the production of button batteries that effectively prevent leakage have shifted the concern following their ingestion from caustic to foreign-body exposure. Household detergents, such as laundry powders and dishwasher detergents, contain silicates, carbonates, and phosphates, and have the potential to induce caustic burns and strictures even when ingested unintentionally.

ACIDS

In contrast to alkaline exposures, following exposure to an acid, hydrogen (H^+) ions desiccate epithelial cells, producing an eschar and resulting in what is histologically referred to as *coagulation necrosis*. This process leads to edema, erythema, mucosal sloughing, ulceration, and necrosis of tissues. Dissociated anions of the acid (Cl^-, SO_4^{2-}, PO_4^{3-}) also act as reducing agents further injuring tissue.

Ophthalmic exposure to acids results in coagulative necrosis that tends to prevent further penetration into deeper layers of the eye. In most series, following an acid ingestion, both the gastric and esophageal mucosa are equally affected. On occasion, the esophagus may be spared damage while severe injury is noted in the stomach. Skip lesions from acid ingestions may be a function of viscosity and contact time.

CLASSIFICATION AND PROGRESSION OF CAUSTIC INJURY

Esophageal burns, secondary to both alkali and acid exposures, are classified based on endoscopic visualization that employs a grading system similar to that used with burns of the skin. Grade I burns are generally described as hyperemia or edema of the mucosa without evidence of ulcer formation. Grade II burns include submucosal lesions,

ulcerations, and exudates. Some authors further divide grade II lesions into grade IIa, noncircumferential lesions, and grade IIb, nearcircumferential injuries. Grade III burns are defined as deep ulcers and necrosis into the periesophageal tissues.

Human case reports, postmortem studies, histologic inspection of surgical specimens, and experimental animal models reveal a consistent pattern of injury and repair following caustic injury. As wound healing of gastrointestinal tract tissue occurs, neovascularization and fibroblast proliferation take place, laying down new collagen and replacing the damaged tissue with granulation tissue. A similar pattern of repair occurs following caustic injuries of the eye.

Burns of the esophagus may persist for up to 8 weeks as remodeling takes place, and may be followed by esophageal shortening. If the initial injury penetrates deeply enough, there is progressive narrowing of the esophageal lumen. The dense scar formation presents clinically as a stricture. Strictures can evolve over a period of weeks to months, leading to dysphagia and significant nutritional deficits. Grade I burns carry no risk of stricture formation. Grade II circumferential burns lead to stricture formation in approximately 75% of cases. Grade III burns invariably progress to stricture formation and are also at a high risk of perforation.

DIAGNOSTIC TESTING

LABORATORY

All patients with presumed serious caustic exposure should have an evaluation of serum pH, blood type and cross-match, hemoglobin, coagulation parameters, electrolytes, and urinalysis. Elevated prothrombin time (PT) and partial thromboplastin times, as well as an arterial pH lower than 7.22 are associated with severe caustic injury.

Absorption of nonionized acid from the stomach mucosa may result in acidemia. Following ingestion of hydrochloric acid, hydrogen and chloride ions (both of which are accounted for in the measurement of the anion gap) dissociate in the serum resulting in a hyperchloremic normal anion gap metabolic acidosis. Although alkalis are not absorbed systemically, necrosis of tissue may result in a metabolic acidosis with an elevated lactate concentration.

RADIOLOGY

Chest and abdominal radiographs are useful in the initial stages of assessment to detect gross signs of esophageal or gastric perforation. Signs of alimentary tract perforation that may be present on plain radiographs. However, these studies have a limited sensitivity, and an absence of findings does not preclude perforation.

CT scanning is considerably more sensitive than radiography for detecting viscus perforation and should be obtained in patients with potentially serious caustic ingestions as soon as is feasible.

A contrast esophagram is useful for defining the extent of esophageal injury. Late after the

ingestion, it can detect stricture formation. In patients for whom there is a high suspicion for esophageal perforation and in whom adequate visualization of the upper gastrointestinal tract by endoscopy is not possible (grade IIb circumferential burns or grade III burns), an enteric contrast study can be obtained 24 hours after the ingestion. Extravasation of contrast outside of the gastrointestinal tract is diagnostic of perforation. Water-soluble contrast should be used when perforation is suspected as it is less irritating to mediastinal and peritoneal tissues if extravasated. However, barium contrast agents are more radiopaque than water-soluble agents and offer greater radiographic detail. Consequently, some authors recommend barium swallow if the water-soluble contrast study is nondiagnostic but demonstrates no leak. In addition, if there is risk of aspiration, barium is preferred because water-soluble contrast material can cause a severe chemical pneumonitis.

CT has great sensitivity at detecting extraluminal air in the mediastinum or peritoneal cavity as a sign of perforation. In addition, CT can visualize the esophagus and stomach distal to severe caustic burns that cannot be safely seen using endoscopy or an esophagram. CT may therefore replace enteric contrast radiography for detection of perforation in the acute stage (within 24 hours) of a caustic ingestion.

ENDOSCOPY

Endoscopy should be performed within 12 hours and generally not later than 24 hours postingestion. Numerous case series demonstrate that the procedure is safe during this period. Early endoscopy serves multiple purposes in that it allows patients with minimal or no evidence of gastrointestinal injury to be discharged. It also offers a rapid means of obtaining diagnostic and prognostic information while shortening the period of time that patients forego nutritional support, permitting more precise treatment regimens. The use of endoscopic assessment from the 2nd or 3rd day postingestion is discouraged and should be avoided between 5 days and 2 weeks postingestion as it is at this time that wound strength is least and the risk of perforation is greatest.

The choice of rigid versus flexible endoscopy is dependent on the comfort and experience of the endoscopist.

MANAGEMENT
- ACUTE MANAGEMENT

As in the case of any patient presenting with a toxicologic emergency, the healthcare provider must adhere to universal precautions. Initial stabilization should include airway inspection and protection, basic resuscitation principles, and decontamination. Examination of the oropharynx for signs of injury, drooling, and vomitus, as well as careful auscultation of the neck and chest for stridor, may reveal signs of airway edema that should prompt immediate airway protection. Careful and constant attention to signs and symptoms of respiratory distress and airway edema, such as a change in voice, are essential and should prompt intubation as airway edema may rapidly progress over minutes to hours.
A delay in prophylactic airway protection may make subsequent attempts at intubation or bag-valve-mask ventilation difficult or impossible.

Direct visual inspection of the vocal cords with a fiberoptic laryngoscope may also reveal signs of impending airway compromise. Patients necessitating intubation are best served by direct visualization of the airway either via direct laryngoscopy or fiberoptic endoscope, as perforation of edematous tissues of the pharynx and larynx is a grave complication that may occur during blind nasotracheal intubation attempts.
Following control of the airway, large-bore intravenous access should be secured and volume resuscitation initiated.

DECONTAMINATION, DILUTION, AND NEUTRALIZATION

Decontamination should begin with careful, copious irrigation of the patient's skin and eyes when indicated to remove any residual caustic and to prevent contamination of other patients and staff.

Gastrointestinal decontamination is usually limited in patients with a caustic ingestion. Induced emesis is contraindicated, as it may cause reintroduction of the caustic to the upper gastrointestinal tract and airway. Activated charcoal is also contraindicated, as it will interfere with tissue evaluation by endoscopy and preclude a subsequent management plan. Additionally, most caustics are not adsorbed to activated charcoal.

Gastric emptying via cautious placement of a narrow nasogastric tube with gentle suction may be attempted to remove the remaining acid in the stomach only in patients with large life-threatening intentional ingestions of acid who present within 30 minutes.

Therefore, preventing absorption of some portion of the ingested acid may have potential benefit in reducing systemic toxicity. Although the procedure has the potential to induce injury, a risk-to-benefit analysis favors gastric emptying following a presumed lethal ingestion.

In contrast, gastric emptying should be avoided with alkaline and unknown caustic ingestions as blind passage of a nasogastric tube carries the risk of perforation of damaged tissues; a risk that outweighs the benefit.

Exceptions to the general rules of gastrointestinal decontamination of caustic agents exist in the management of zinc chloride ($ZnCl_2$) and mercuric chloride ($HgCl_2$). Both are caustics with severe systemic toxicity. Ingestion of these xenobiotics causes life-threatening illness from cationic metal exposure.

The local caustic effects, though of great concern, are less consequential than the manifestations of systemic absorption. Therefore, prevention of systemic absorption should be addressed primarily, followed by the direct assessment and management of the local effects of these xenobiotics. Initial management to prevent systemic absorption includes aggressive decontamination with gentle nasogastric tube aspiration and administration of activated charcoal. In vitro data exist to suggest adequate charcoal adsorption of Hg^{2+} ion.

The use of dilutional therapy has been examined using in vitro, ex vivo, and in vivo models in an attempt to assess its efficacy in caustic ingestions. An early in vitro model demonstrated a dramatic increase in temperature when either water or milk was added.

Another in vitro model found less consequential increases in temperature despite large volumes of diluent. Results of both studies suggested that dilutional therapy was of limited benefit.

Additionally, the usefulness of dilution appeared to be inversely related to the length of time from exposure, with minimal efficacy noted in as little as 30 minutes.

The extrapolation of these variable results to humans with caustic ingestions is limited, and suggests that histologic damage can only be attenuated by milk or water when administered within the first seconds to minutes following ingestion.

Caution should be used in advising patients or family members about the use of dilutional agents. A child who refuses to swallow or take oral liquids should never be forced to do so. In general, dilutional therapy should be limited to patients within the first few minutes after ingestion who have no airway compromise, who are not complaining of significant pharyngeal, chest, or abdominal pain, who are not vomiting, and who are alert. Dilutional therapy should be avoided in patients with nausea, drooling, stridor, or abdominal distension as it may stimulate vomiting and result in reintroduction of the caustic into the upper gastrointestinal tract.

Attempts at neutralization of ingested caustics should likewise be avoided. This technique has the potential to worsen tissue damage by forming gas and generating an exothermic reaction.

SURGICAL MANAGEMENT

The decision to perform surgery in patients with caustic ingestions is obvious in the presence of either endoscopic or diagnostic imaging evidence of perforation, severe abdominal rigidity, or persistent hypotension. Hypotension is a grave finding and often indicates perforation or significant blood loss. Additionally, elevated prothrombin time (PT) and partial thromboplastin times, as well as an arterial pH lower than 7.22, are associated with severe caustic injury.

- SUBACUTE MANAGEMENT

The extent of tissue injury dictates the subsequent management and disposition of patients with caustic ingestions.

Grade I Esophageal Injuries Patients with isolated grade I injuries of the esophagus do not develop strictures and are not at increased risk of carcinoma. Their diet can be resumed as tolerated. No further therapy is required. These patients can be discharged from the hospital as long as they are able to eat and drink and their psychiatric status is stable.

Grade IIa Esophageal Injuries If endoscopy reveals grade IIa lesions of the esophagus

and sparing of the stomach, a soft diet can be resumed as tolerated, or a nasogastric tube can be passed under direct visualization. If oral intake is contraindicated because of the risk of perforation, feeding via gastrostomy, jejunostomy, or total parenteral nutrition should be instituted as rapidly as possible.

Grades IIb and III Esophageal Injuries Patients with grades IIb and III lesions must be followed for the complications of perforation, infection, and stricture development. Strictures are a debilitating complication of both acid and alkaline ingestions that can evolve over a period of weeks or months.

Although steroid therapy is theorized to arrest the process of inflammatory repair and potentially prevent stricture formation, there is some evidence that grade III burns, in particular, will progress to stricture formation regardless of therapy. In addition to stricture formation, patients with grade III burns are also at high risk for other complications, including fistula formation, infection, and perforation with associated mediastinitis and peritonitis. The use of corticosteroids in the management of grade III burns may mask infection and make the friable, necrotic esophageal tissue more prone to perforation. For these reasons, steroid therapy is not a recommended therapy for grade III esophageal burns. When required in these patients for other indications such as caustic- induced airway inflammation, short-term steroids should be administered in conjunction with antibiotics.

A variety of other management strategies have been used in an attempt to prevent strictures and esophageal obstruction. In both animal models and in human case series, intraluminal stents and nasogastric tubes made of silicone rubber tubing can successfully maintain the patency of the esophageal lumen. These tubes are left in place for 3 weeks and are often used with concomitant corticosteroid and antibiotic therapy

Additionally, multiple therapies have been studied in various animal models in an attempt to identify agents that either inhibit synthesis or stimulate breakdown of collagen and thereby prevent stricture formation. □-Amino propionitrile (BAPN), penicillamine, *N*-acetylcysteine (NAC), halofuginone, vitamin E, and colchicine are some of these agents.

- CHRONIC TREATMENT OF STRICTURES

Commonly, the management of esophageal strictures includes early endoscopic dilation for which a variety of types of dilators are available. Contrast CT can be used to determine maximal esophageal wall thickness, which can then be used to predict response, as well as the number of sessions required to achieve adequate dilation. Multiple dilations are often necessary.

Measurement of maximal wall thickness may be also be useful in determining long-term follow up, type of nutritional support, and the potential need for surgical repair as an alternative to dilations. It may also provide an indication for those who should undergo dilations under fluoroscopy to limit the risk of perforation.

The risk of perforation from esophageal dilation is decreased if the initial procedure is

delayed beyond 4 weeks postingestion, when healing, remodeling, and potential stricture formation in the esophagus have already taken place.

Patients with stricture formation require long-term endoscopic follow up for the presence of neoplastic changes of the esophagus that may occur with a delay of several decades.