REVIEW ARTICLE

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Ingestion of Caustic Substances

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Caustic substances injure tissue by means of a chemical reaction on direct physical contact. Often thought of as acids or bases, caustics broadly include desiccants, vesicants, and protoplasmic poisons. The term "corrosive" is often used interchangeably with "caustic," but corrosion implies a mechanical degradation, which does not always apply to caustics. This review provides an update on the epidemiology, pathophysiology, and clinical assessment of ingestions of caustic materials, with an emphasis on treatment approaches.

Caustics are present at home and in industry (Table 1). They cause injury after dermal, ocular, or gastrointestinal contact. In western countries, commonly ingested household caustics include lye (sodium or potassium hydroxide) found in drain cleaners and hair relaxers, bleach (sodium hypochlorite) or ammonia (ammonium hydroxide) found in cleaning products, and highly concentrated acids (e.g., hydrochloric acid) found in toilet bowl or swimming pool cleaners. In other countries, concentrated acids such as hydrochloric, nitric, and sulfuric acids are commonly found in homes.[1] An increase has been reported in caustic-induced injuries in children resulting from ingestion of the contents of laundry-detergent capsules (water-soluble membranes, commonly called pods, containing liquid detergent that is more concentrated than traditional liquid or powdered laundry detergents).[2] Pods are popular in developed countries and are particularly enticing to children because of their brightly colored packaging. When the pods are chewed, the contents are ejected in the pharynx, resulting in oropharyngeal and gastrointestinal injuries.[3-5] Injury-prevention groups are providing public education and advocating for improved packaging.

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HISTORY

Chevalier Jackson (1865–1958), the renowned otolaryngologist, is often called the "father of endoscopy." He recognized the public health implications of caustic ingestions and advocated for warning labels on bottles that contained caustics.[6] Subsequently, standards were instituted by the U.S. Federal Caustic Poison Act of 1927.[7] It was not until 1970, however, that the U.S. Poison Prevention Packaging Act mandated child-resistant containers for solutions containing caustics at a concentration of more than 10%, as listed in the Federal Hazardous Substances Act.[8,9] In 1973, this standard was reduced to 2% for household products. Currently, poison control centers in the United States advise storage of all dangerous household products "up and away" from sight and reach, as recommended by the Centers for Disease Control and Prevention (www.upandaway.org).

EPIDEMIOLOGY

Despite regulatory advances and educational initiatives, caustic-induced injuries in children still represent a serious public health concern in the United States.

Table 1. Common Caustic Substances and Their Uses.

Chemical	Common Uses
Classic alkalis	
Ammonium hydroxide	General cleaner and grease remover
Sodium hydroxide or potassium hydroxide	Drain opener, oven cleaner, hair relaxer, grease remover
Sodium hypochlorite	Bleach, swimming pool chlorinator
Classic acids	
Acetic acid	Food pickling, photographic stop bath
Hydrochloric acid	Toilet bowl cleaner, mold and mildew remover
Oxalic acid	Metal polish
Phosphoric acid	Rust remover
Selenous acid	Gun bluing agent
Sulfuric acid	Drain opener, large lead-acid batteries
Miscellaneous or unique caustics	
Cationic detergents (e.g., benzalkonium chloride)	Surface cleaner, preservative
Hydrofluoric acid	Rust and graffiti remover
Hydrogen peroxide	Surface and food cleaner
Phenol	Surface disinfectant
Zinc chloride	Soldering flux

Nearly 1000 children with caustic ingestions are hospitalized each year, for an average of 4 days, at direct hospital costs of more than $22 million.[10] Caustic exposures can be divided on the basis of intention. Exposures in children are best characterized as exploratory ingestions and typically involve small amounts. The unfortunate exceptions are the rare but dramatic alkali ingestions reported as manifestations of child abuse.[11,12] In contrast, adolescents and adults usually ingest larger volumes in deliberate attempts at self-harm. These intentional ingestions are usually more severe. A 1980 study of 214 caustic ingestions showed that 39% of children younger than 6 years of age were hospitalized, but only 8% required treatment. In contrast, 48% of adults were admitted, and 81% required treatment.[13] The 2018 annual report of the American Association of Poison Control Centers (AAPCC) noted that household cleaners ranked second among all exposures to poisons and foreign bodies, accounting for 9% of the total.[14] It is noteworthy that not all cleaning substances are caustic and that the AAPCC data reflect a focus on prehospital exposures. According to that annual report, a total of 103,387 exposures were in children 5 years of age or younger and 64,340 were in adults, although the numbers of exposures to caustics were not specified.

Caustic ingestions are also a worldwide public health problem. Young children in western and southern Africa are injured when caustic soda (sodium hydroxide) is stored in soft-drink and water bottles that are open and accessible.[15] The authors of a study in Iran reported that 68.3% of unintentional caustic ingestions by children occurred in the kitchen, and they emphasized the need for public education and safe chemical storage.[16] A study in Great Britain examined the toxic effects associated with direct ingestion of oven-cleaning products and ingestion of food contaminated by these products.[17] In a retrospective cross-sectional study of deliberate self-poisoning in Tunisia, the majority of patients were women 20 to 29 years old, and caustics were used in 5.5% of cases.[18] Similarly, women commonly use caustics to commit suicide in countries such as China, India, Pakistan, Bangladesh, and Sri Lanka.[19] In Taiwan, 48% of 273 adult suicide attempts involved industrial cleaners. Acid ingestion is more common in Asia than in western countries.[20] In Iran, hydrochloric acid accounts for almost 70% of caustic ingestions by adults.[21]

PATHOPHYSIOLOGY

The most common classification of caustic-induced injuries is dichotomous, with acids or alkalis defined according to pH. In general, acids with a pH of less than 2 and alkalis with a pH of more than 12 cause the most extensive injury. However, pH alone does not explain why caustics cause different degrees of injury. The titratable acid or alkaline reserve (TAR) quantifies the amount of acid or base ion that the body's physiologic response donates to injured tissues to return them to physiologic pH.[22] Most neutralization reactions are exothermic, and the heat released adds to the injury. Since the TAR is not known in clinical settings, a sound chemical risk assessment for most products can be based on the pH, concentration, volume ingested, and

duration of tissue contact, as well as the body-surface area affected if the skin is involved. Alkalis damage tissue by saponifying fats. The resultant liquefaction necrosis creates a gelatinous substance, allowing further penetration and extending tissue damage. In contrast, acids denature proteins through coagulation necrosis. The coagulum is thought to prevent the acid from reaching deeper tissues, thus limiting the damage. Despite this property, acid ingestions can cause severe injury and death.

Hydrofluoric acid causes injury not only by releasing hydrogen ions, which is typical of an acid, but also through direct cellular injury from the highly electronegative fluoride ions. The free fluoride binds rapidly available cations such as calcium and magnesium, resulting in life-threatening hypocalcemia and hypomagnesemia. Hyperkalemia also results from cell death. Further discussion of these systemic toxic effects is beyond the scope of this review.

CLINICAL EFFECTS

Clinical effects of caustic ingestions are divided into immediate, delayed, and remote manifestations. The organ systems most involved are the eyes, skin, airway, and gastrointestinal tract. Pain is often immediate, followed by loss of function. Common manifestations include swelling of the tongue and mouth, drooling, and vomiting. Bleeding can be severe if the injury involves erosion of a vessel. Swelling of the airway causes stridor, respiratory compromise, and changes in the voice. Perforation of the esophagus can lead to mediastinitis, and perforation of the stomach or bowel can lead to peritonitis. In the latter case, perforation is often not initially accompanied by classic peritoneal findings on physical examination.

Both delayed and remote complications occur in survivors of an acute episode. Ocular and dermal injuries have cosmetic and functional implications. Esophageal strictures occur over a period of weeks to months, leading to chronic pain and malnutrition. In one case series, 20% of children had strictures at 3 months of follow-up,[23] although most studies report a lower incidence. Some strictures progress to esophageal carcinoma, with latency measured in decades.[24-27]

ASSESSMENT AND PROGNOSTICATION

In clinically unstable patients, assessment starts with the patient's level of consciousness and an evaluation of the airway (Fig. 1). Once the airway has been cleared or stabilized, further assessment can proceed. Variables common to any clinical assessment of toxicologic risk are analyzed: intent, exact substance or category of substance, concentration, dose, timing, and coingestants. The presence of any symptoms such as vomiting, coughing, choking, or abdominal pain should be noted. Decontamination procedures performed before a patient's arrival at the emergency department, such as induced emesis, dilution, or irrigation, should also be noted. Developmental milestones must be assessed in cases of ingestions in children, to determine whether their age matches their ability to obtain access to a given product. For example, the pincer grasp is typically present by 9 months of age, whereas the ability to unscrew the lid of a bottle does not develop until approximately 2 years of age.

In most jurisdictions, prehospital personnel are instructed to bring product containers from the home to the hospital or to obtain the material safety data sheets if the ingestion occurred in the workplace. However, because of the risk of upper-airway compromise and gastrointestinal perforation, time-consuming efforts to identify the exact substance should be delegated to ancillary personnel or deferred until the patient has been completely evaluated and stabilized.

The remainder of the examination focuses on potential tissue injuries. With all ingestions in children and with ingestions in adults that involve vomiting, the face must be examined for signs of spills or splash injuries. Although it is somewhat intuitive that burns on the cheeks or lips or in the oropharynx are suggestive of lower gastrointestinal injury, this is inconsistent with published data. In fact, the absence of facial or oral findings is associated with endoscopic evidence of gastroesophageal injury in more than one third of children.[29] Similarly, because of hand-to-mouth behavior and the small amounts ingested by children, the presence of oropharyngeal injuries does not guarantee abnormal gastroesophageal endoscopic findings. However, in our

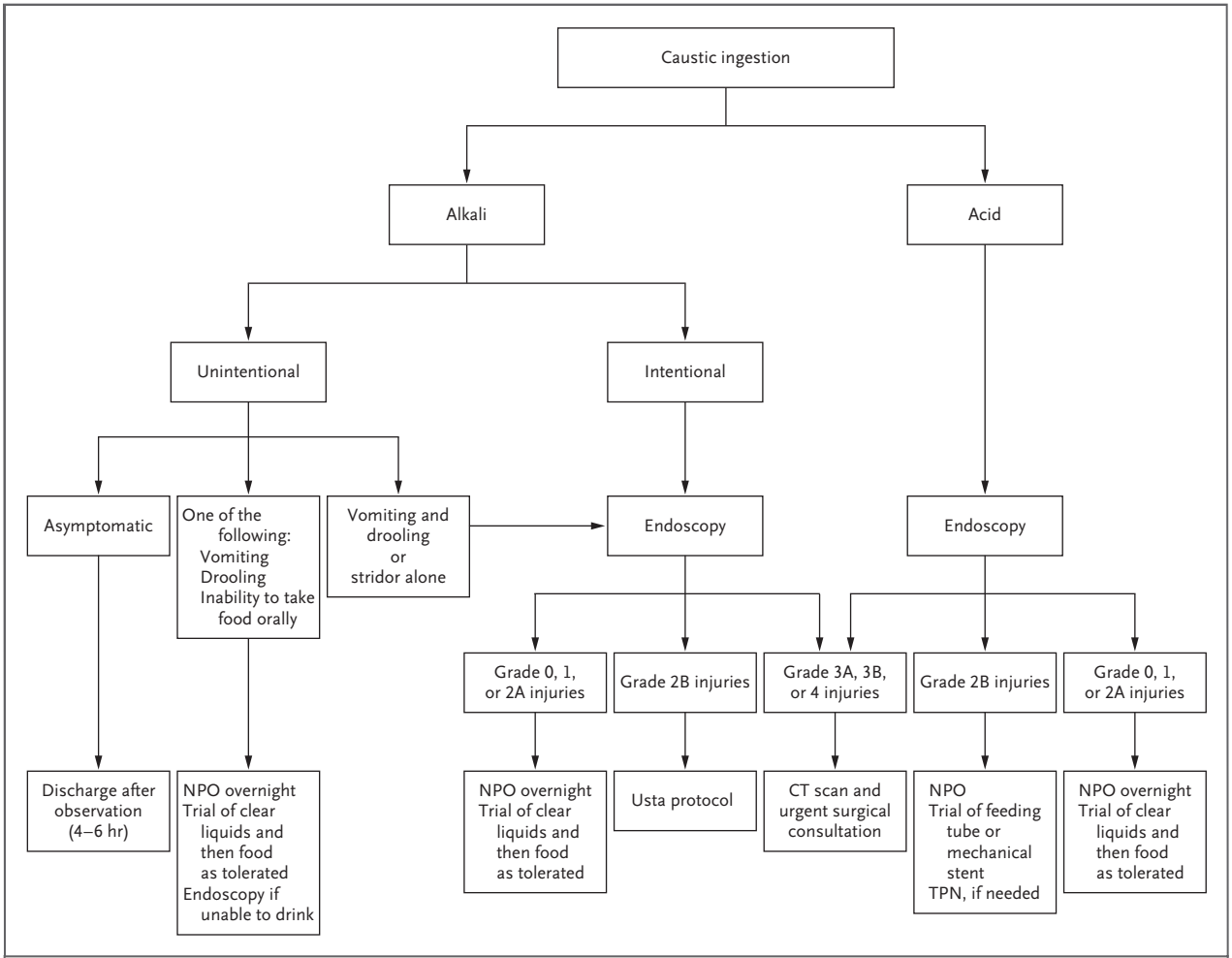

Figure 1. Algorithm for the Diagnosis and Management of Caustic Ingestions.

In all cases of caustic ingestion, the airway should be assessed initially and protected if necessary. If endoscopy is not rapidly available and severe injury is strongly suspected, obtain a contrast-enhanced computed tomographic (CT) study. The Usta protocol consists of methylprednisolone (1 g per 1.73 m^2 of body-surface area per day, given intravenously for 3 days) plus ranitidine (4 mg per kilogram of body weight per day in children or the standard adult dose in adults, given intravenously) plus ceftriaxone (100 mg per kilogram per day in children or the standard adult dose in adults, given intravenously).[28] NPO denotes nothing by mouth, and TPN total parenteral nutrition.

experience, when oropharyngeal findings are present in adults with intentional ingestions, there is a high likelihood of gastroesophageal injury.

Standard laboratory tests indicated in any critically ill patient are recommended for those with caustic ingestions but are unlikely to influence treatment. One possible exception is the presence of a metabolic acidosis. In the case of alkali ingestion, acidemia or hyperlactatemia is likely to be indicative of clinically significant tissue injury. Although this may also be true for acid ingestions, an acidemia also results from direct absorption of the acid and associated anion. This produces a non–anion-gap acidemia with hydrochloric acid and an elevated anion-gap acidemia with other acids. A chest radiograph with the patient in an upright position can show free air in the abdomen resulting from perforation, but with poor sensitivity and specificity.

At one time, esophagogastroduodenoscopy was routinely performed in a child with an exploratory alkali ingestion because of the per-

ceived inability to identify injury on the basis of signs and symptoms.[30] This practice is no longer necessary. In a landmark study by Crain and colleagues, only children with both vomiting and drooling or with stridor alone had clinically significant injuries.[31] Children with no symptoms or with only vomiting or drooling had no more than a grade 1 injury. In contrast, half the children with both vomiting and drooling or with stridor alone had grade 2 or more severe injuries. Strictures ultimately developed in 4% of the children, all of whom would have been correctly evaluated endoscopically with the use of a decision rule based on the presenting symptoms.[31] For children with only vomiting or drooling and those who refuse to drink, overnight observation is routine, and endoscopy is performed only if symptoms persist and the child remains unable to take oral fluids (Fig. 1). Decades of clinical work at poison control centers support this watchful observation period for asymptomatic or minimally symptomatic children with alkali ingestions, thereby allowing judicious resource allocation and reducing the procedural risks involved with mandatory endoscopy. Unfortunately, this approach applies neither to acid ingestions nor to adults with intentional caustic ingestions.

Endoscopy should be performed in the first 24 to 48 hours after ingestion, since wound softening increases the risk of perforation. Injuries should be graded with the use of standardized terminology as described by Zargar et al.[32] (Table 2 and Fig. 2). For patients who are too ill to undergo endoscopy, contrast-enhanced computed tomography (CT) is an acceptable diagnostic alternative.[33] Besides being both rapidly available in many institutions and noninvasive, contrast-enhanced CT provides the additional benefits of evaluating the serosal surface of the gastrointestinal tract and identifying subtle and early evidence of perforation.

Table 2. Common Classification of Caustic-Induced Gastrointestinal Injuries and Prognoses.

Grade	Findings	Prognosis
0	Normal	Complete recovery
1	Edema and erythema	Complete recovery
2A	Friability, hemorrhage, and superficial ulcerations	Stricture unlikely
2B	Deep ulcerations (either discrete or circumferential), in addition to friability, hemorrhage, and superficial ulcerations	High risk of stricture, low risk of perforation
3A	Small, scattered areas of necrosis	High risk of stricture, greater risk of perforation than with grade 2B injury
3B	Extensive necrosis	High risk of perforation and strictures
4	Perforation	Often fatal

TREATMENT

EMERGENCY MANAGEMENT

After caustic ingestion, a person's most immediate risk to life is loss of the airway, which can occur from direct contact during swallowing or emesis or from edema that extends locally from an injured esophagus. Because of the rapid progression of many injuries, particular attention should be paid to the inability to control oral secretions or a change in voice, indicating impending airway compromise. In one case series, 12% of children required intubation.[34] By comparison, a study of ingestions in adults showed that 50% of patients required intubation, with 21% of intubated patients considered to have difficult airways.[35] Because the safety of further evaluation with CT or endoscopy depends on airway security, we recommend placement of a definitive airway at the first sign of a change in voice, an inability to tolerate secretions, stridor, or other markers of potential airway compromise. Accepted guidelines for patients with difficult airways should be followed.[36]

Although it is tempting to focus on injuries to the aerodigestive tract after caustic ingestions, potential injuries to the skin and eyes that may result from splashes, spills, or emesis also need to be considered. Clothing should be removed and exposed, and the skin irrigated with copious amounts of water. Immediate irrigation of the eyes is indicated when ocular exposure is suspected, followed by advanced management in consultation with an ophthalmologist.[37] The standard toxicologic principles of gastrointestinal decontamination do not apply to patients with caustic ingestions, since clinical attempts to empty the stomach can potentially increase injury. In addition, activated charcoal does not adsorb caustics, and adherent particles of acti-

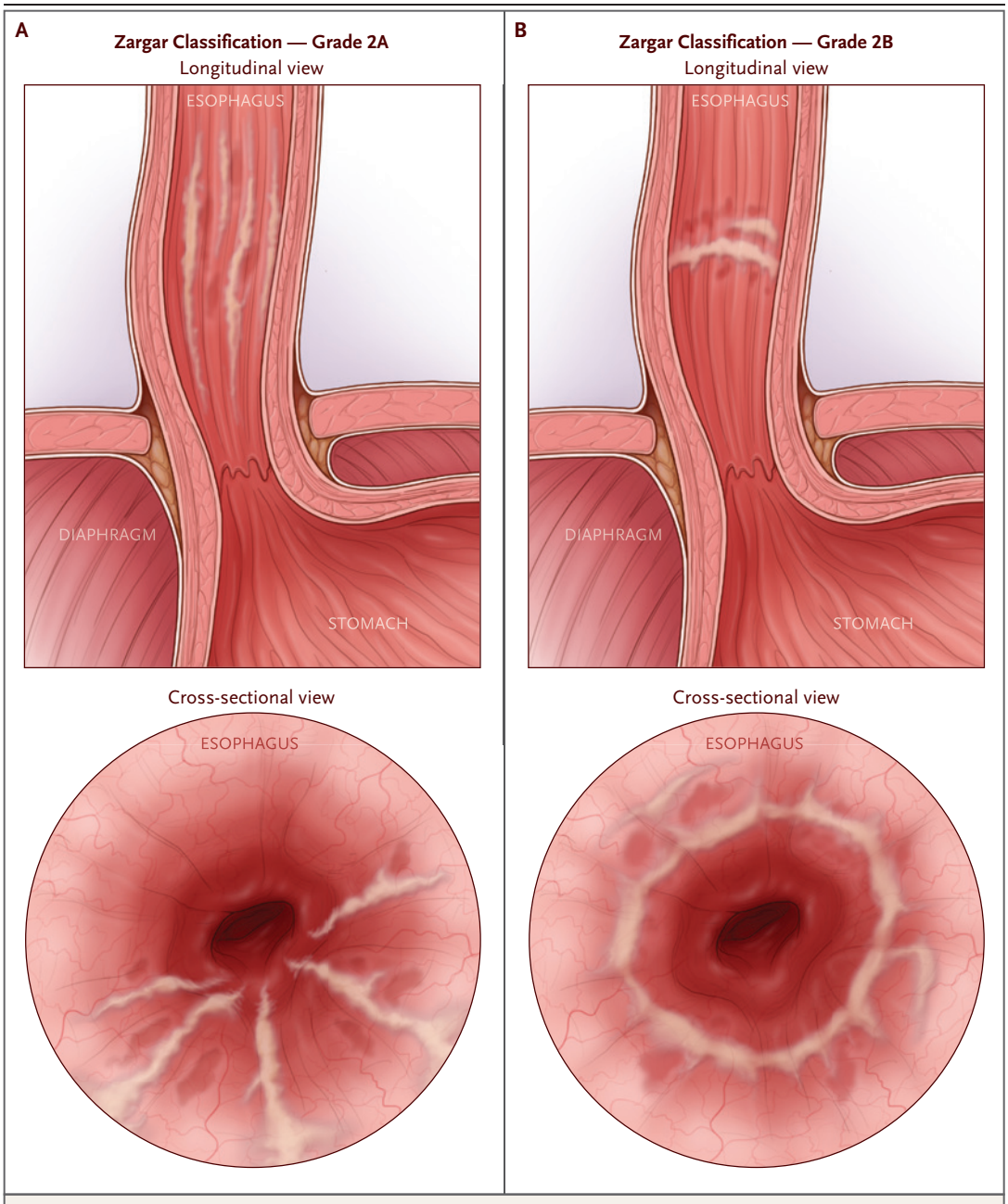

Figure 2. Common Endoscopic Findings after Caustic Ingestion.

Panel A shows linear vertical esophageal erosions that are characteristic of grade 2A burns, which are unlikely to result in stricture. Panel B shows circumferential esophageal erosions that are characteristic of grade 2B burns, which are associated with a high risk of stricture and a low risk of perforation.

vated charcoal will obscure endoscopic visualization. Although blind nasogastric-tube insertion has occasionally been recommended for acid ingestions[38] and is still performed by one third of international experts,[39] there is no evidence to support the efficacy or safety of this procedure.

Similarly, although dilution and neutralization are theoretically beneficial, thermal injury is possible from the heat of neutralization. Even if this risk might be overstated,[40,41] the clinical benefit of neutralization has never been shown. Further concerns over distention-induced injury

of damaged tissues caused by gas generated during neutralization and the risk of emesis prevent recommendations for neutralization at this time. A single exception would be the use of water immediately after ingestion (usually at home) to irrigate adherent materials in the oropharynx or esophagus if the patient can swallow, speak clearly, and breathe without difficulty. Early irrigation is likely to be most useful for ingestion of powdered caustics, which can prolong injury by adhering to tissues.

As with thermal cutaneous burns, assessment and maintenance of fluid and electrolyte balance are essential. Strict monitoring of hemodynamics is recommended, since many patients are unable to take oral fluids and insensible fluid losses are associated with extracellular fluid shifts in response to tissue injury. Parenteral analgesics are often required for the severe pain of oropharyngeal injuries. There is no evidence to support routine use of therapies or investigations in all patients, although the use of proton-pump inhibitors and antibiotic agents is common.[42] A decision to perform surgical débridement is based on evidence of full-thickness tissue injury, perforation, or hemodynamic instability.[43]

GLUCOCORTICOID THERAPY

Early investigations showed that glucocorticoids impair wound healing and scar formation. Recognizing that a stricture is an esophageal scar, Rosenberg and coworkers administered cortisone in rabbits with sodium hydroxide–induced esophageal injuries. Although many treated animals succumbed to infection, the survivors had a reduction in stricture severity.[44] In a subsequent experiment, animals treated with both cortisone and penicillin survived longer and had less severe strictures.[45] Largely on the basis of these data, many patients with alkaline esophageal injuries received prolonged courses of high-dose glucocorticoids and antibiotics. Reported benefits were anecdotal at best, whereas the complications of prolonged immunosuppression were well documented.[46,47] After nearly 40 years of this practice, the routine use of prolonged glucocorticoid therapy was called into question when a landmark controlled trial failed to show a benefit in children with alkaline injuries.[47] Unfortunately, this trial included patients with all grades of injury and was underpowered to detect a clinical benefit. A similarly designed and powered study that included children with acid ingestions and those with alkali ingestions failed to show a benefit of prolonged glucocorticoid therapy in either group.[48] Although several analyses of pooled data attempted to delineate a subpopulation of patients who might benefit from prolonged glucocorticoid administration,[49-51] no such population was identified, and the use of glucocorticoid therapy fell out of favor.

Since then, however, an interest in glucocorticoids has been rekindled. Usta and colleagues randomly assigned children with grade 2B esophageal injuries to 3 days of methylprednisolone (1 g per 1.73 m^2 of body-surface area per day) or placebo, plus 1 week of ceftriaxone and ranitidine.[28] When analyzed either visually with endoscopy or functionally by means of barium swallow, a significant benefit was reported in the methylprednisolone group. The methylprednisolone-treated children also had a shorter duration of parenteral nutrition. No complications were noted. The unique design of this study suggests that patients with grade 2B injuries, who have a high risk of progression to stricture and a low risk of perforation, are most likely to benefit from — and least likely to be harmed by — the wound-softening effects of glucocorticoid therapy (Table 2). In addition, the shortened course of therapy is expected to mitigate the complications associated with immunosuppression. This approach is supported by a survey of international experts, 54% of whom would administer glucocorticoids in at least a subgroup of patients.[39] It should be noted, however, that one consensus conference recommended that glucocorticoids not be used.[43] Although we recognize that further research is needed, it is our opinion that the relatively benign regimen of 3 days of methylprednisolone therapy is reasonable in patients with grade 2B alkaline esophageal injuries. This recommendation is in agreement with a recent pediatric guideline[52] (Fig. 1).

OTHER PHARMACOTHERAPY

Only two other pharmacotherapies for ingestion of caustics are supported by sufficient clinical data: sucralfate and mitomycin C. In a single case report, the administration of sucralfate was associated with atypically rapid healing.[53] A subsequent animal model showed that sucralfate had favorable healing properties as compared with placebo.[54] These effects were further sup-

ported when 15 patients with caustic-related esophageal injuries were randomly assigned to receive standard therapy (glucocorticoids, a proton-pump inhibitor, and antibiotics) with or without high-dose sucralfate therapy.[55] Concerns over randomization and concealment of group assignments complicated the interpretation of the data; however, the sucralfate group had significantly fewer symptomatic strictures (0 in 8 patients, vs. 6 in 7 patients who did not receive sucralfate).

Mitomycin C provides an alternative approach, minimizing the clinical effects of strictures by making them more amenable to mechanical dilation. Mitomycin C induces fibroblast apoptosis, reducing scarring.[56] In a randomized, blinded trial, 40 patients with caustic-induced strictures were given either endoscopically administered mitomycin C or placebo, with subsequent mechanical dilation.[57] Patients treated with mitomycin C had a significant reduction in symptoms and required fewer dilations than the placebo group. The same authors reported impressive results in an open-label study involving patients with particularly long strictures.[58] The beneficial effects of mitomycin C were also shown in children with long strictures that were refractory to standard approaches.[59] Although these trials reveal no evidence of acute toxic effects associated with mitomycin C and are therefore encouraging, one unanswered question is whether mitomycin C increases the long-term risk of malignant transformation because of its ability to damage DNA.

STENTS AND MECHANICAL SUPPORT

The blind insertion of nasogastric tubes is contraindicated in patients with alkaline ingestions because of both the futility of gastrointestinal decontamination, since tissue injury occurs in minutes,[22,60] and the likelihood of inducing trauma, bleeding, or perforation. However, the insertion of a nasogastric tube under direct endoscopic visualization offers several theoretical benefits. First, the tube may behave like a mechanical stent to ensure luminal patency, thereby limiting the formation or severity of subsequent strictures.[61,62] In addition, if the stomach and duodenum are intact, the patient can be fed enterally, as opposed to receiving total parenteral nutrition. Seventy-two percent of experts noted that they would insert a nasogastric tube on the basis of endoscopic findings.[39] Alternatively, the use of biodegradable stents, placed during either endoscopy or laparoscopy, shows promise for relieving dysphagia and limiting stricture formation.[63-65] Unfortunately, neither the use of nasogastric tubes nor the use of biodegradable stents has been studied in controlled trials.

DISPOSITION

Children with exploratory ingestions who do not meet the criteria for endoscopy and children with negative endoscopies can be discharged after a short period of observation, typically 6 hours. Admission for a minimum of 24 hours is advisable for all other patients in order to assess their ability to tolerate oral nutrition. All patients with intentional ingestions require psychiatric evaluation. Patients with grade 1 or 2A lesions confirmed by endoscopy can be started on a clear-liquid diet. Oral feeding must usually be withheld from patients with grade 2B injuries for variable periods of time. Patients with grade 3 injuries are best cared for in monitored care units because of the likelihood of infection, perforation, and fluid and electrolyte abnormalities. Feeding should progress orally as tolerated, with the use of parenteral nutrition or distal feeding tubes when severe injuries preclude oral feeding.

LONG-TERM PROGNOSIS AND FOLLOW-UP

Asymptomatic children and patients with minimal injuries (grade 1 or 2A) do not require any specific follow-up. Patients with grade 2B or more severe injuries require periodic evaluation for the development of strictures. Strictures typically develop in the first 2 months but have been reported as early as 21 days after ingestion. Patients with grade 2B or 3 injuries are at increased risk for subsequent malignant transformation of the esophageal epithelium to adenocarcinoma or squamous-cell carcinoma.[66] This risk justifies yearly evaluations in such patients and all those in whom strictures develop, regardless of functional status. Adequate approaches to these evaluations are poorly defined, but direct visualization with endoscopy is recommended so that biopsies of suspicious lesions can be performed.

FUTURE DIRECTIONS

Ingestions of caustic substances are a relatively uncommon but serious concern in the United States. For many other nations, however, they remain a consequential public health problem associated with substantial morbidity and mortality. Future efforts should focus on primary prevention of injury through public health interventions such as implementing safe packaging and storage, taking existing prognostic data on children with minimal or asymptomatic ingestions of alkaline caustics and replicating the data in children with similar ingestions of acids, replicating the effects of short-course glucocorticoids, and improving understanding of mitigation measures such as mitomycin C and mechanical stenting.

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Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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