

## REVIEW ARTICLE

Dan L. Longo, M.D., *Editor*

## Ingestion of Caustic Substances

Robert S. Hoffman, M.D., Michele M. Burns, M.D., M.P.H.,  
and Sophie Gosselin, M.D.

**C**AUSTIC 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.<sup>1</sup> 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).<sup>2</sup> 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.<sup>3-5</sup> Injury-prevention groups are providing public education and advocating for improved packaging.

From the Division of Medical Toxicology, Ronald O. Perelman Department of Emergency Medicine, New York University Grossman School of Medicine, New York (R.S.H.); the Division of Emergency Medicine, Program in Medical Toxicology, Boston Children's Hospital, Harvard Medical School, Boston (M.M.B.); and Centre Intégré de Santé et de Services Sociaux (CISSS) Montérégie-Centre Emergency Department, Hôpital Charles-Lemoyne, Greenfield Park, QC, the Department of Emergency Medicine, McGill University, Montreal, and Centre Antipoison du Québec, Quebec, QC — all in Canada (S.G.). Address reprint requests to Dr. Hoffman at 455 First Ave., Rm. 123, New York, NY 10016, or at robert.hoffman@nyumc.org.

N Engl J Med 2020;382:1739-48.

DOI: 10.1056/NEJMr1810769

Copyright © 2020 Massachusetts Medical Society.

## 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.<sup>6</sup> Subsequently, standards were instituted by the U.S. Federal Caustic Poison Act of 1927.<sup>7</sup> 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.<sup>8,9</sup> 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](http://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                                              |
|---------------------------------------------------|----------------------------------------------------------|
| <b>Classic alkalis</b>                            |                                                          |
| 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                        |
| <b>Classic acids</b>                              |                                                          |
| 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                  |
| <b>Miscellaneous or unique caustics</b>           |                                                          |
| 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.<sup>10</sup> 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.<sup>11,12</sup> 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.<sup>13</sup> 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.<sup>14</sup> 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.<sup>15</sup> 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.<sup>16</sup> 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.<sup>17</sup> 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.<sup>18</sup> Similarly, women commonly use caustics to commit suicide in countries such as China, India, Pakistan, Bangladesh, and Sri Lanka.<sup>19</sup> In Taiwan, 48% of 273 adult suicide attempts involved industrial cleaners. Acid ingestion is more common in Asia than in western countries.<sup>20</sup> In Iran, hydrochloric acid accounts for almost 70% of caustic ingestions by adults.<sup>21</sup>

#### 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.<sup>22</sup> 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. Alkaline 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.

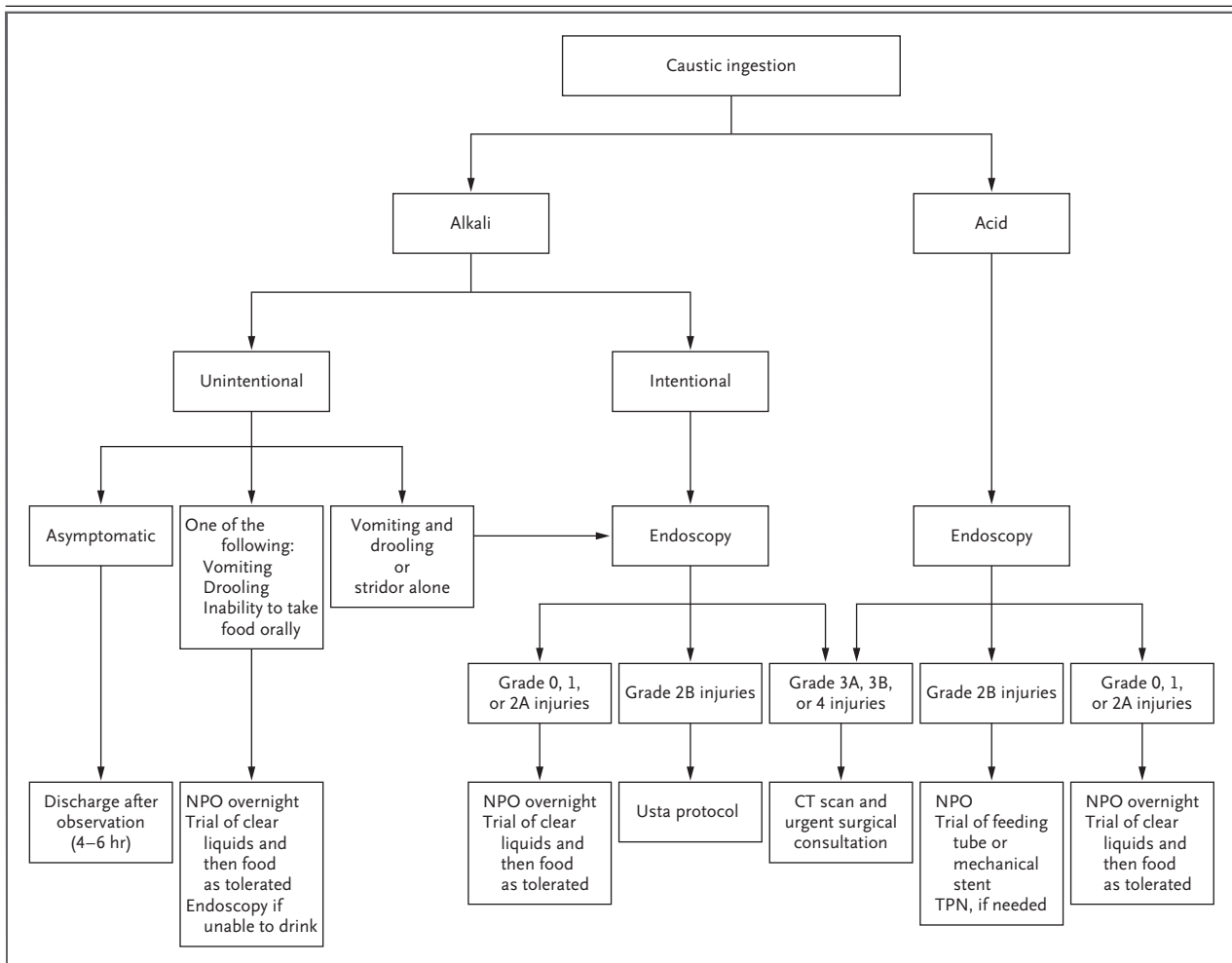
Both delayed and remote complications occur in survivors of an acute episode. Ocular and dermal injuries have cosmetic and functional implications. Esophageal strictures occur over a period of weeks to months, leading to chronic pain and malnutrition. In one case series, 20% of children had strictures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

#### 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.<sup>29</sup> 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<sup>2</sup> 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).<sup>28</sup> 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.<sup>30</sup> 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.<sup>31</sup> 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.<sup>31</sup> 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.<sup>32</sup> (Table 2 and Fig. 2). For patients who are too ill to undergo endoscopy, contrast-enhanced computed tomography (CT) is an acceptable diagnostic alternative.<sup>33</sup> 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.

## TREATMENT

### EMERGENCY MANAGEMENT

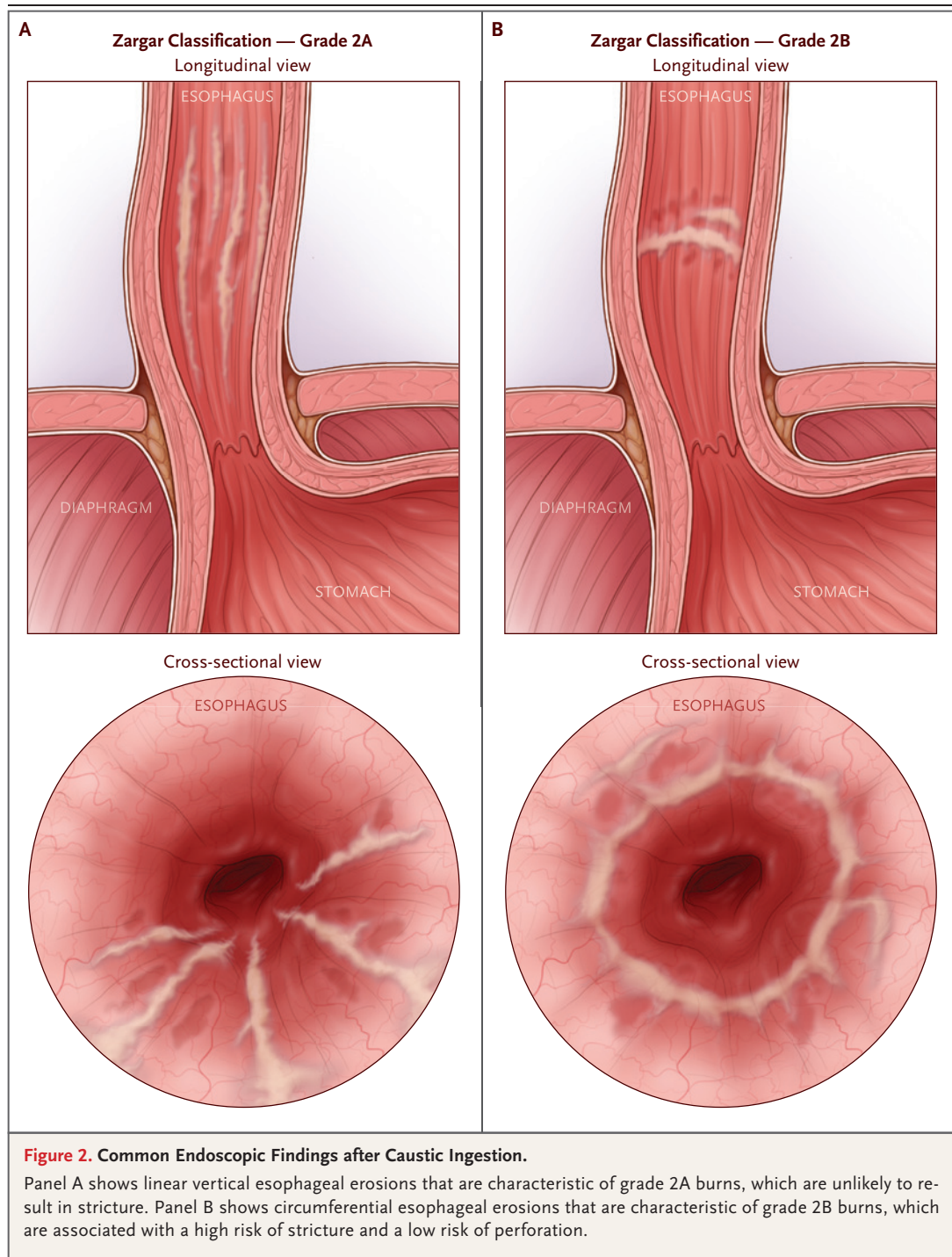
After caustic ingestion, a person's most immediate risk to life is loss of the airway, which can occur from direct contact during swallowing or emesis or from edema that extends locally from an injured esophagus. Because of the rapid pro-

**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                                                                   |

gression 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.<sup>34</sup> 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.<sup>35</sup> 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.<sup>36</sup>

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.<sup>37</sup> 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-



vated charcoal will obscure endoscopic visualization. Although blind nasogastric-tube insertion has occasionally been recommended for acid ingestions<sup>38</sup> and is still performed by one third of international experts,<sup>39</sup> 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,<sup>40,41</sup> 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.<sup>42</sup> A decision to perform surgical débridement is based on evidence of full-thickness tissue injury, perforation, or hemodynamic instability.<sup>43</sup>

#### 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.<sup>44</sup> In a subsequent experiment, animals treated with both cortisone and penicillin survived longer and had less severe strictures.<sup>45</sup> 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.<sup>46,47</sup> 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.<sup>47</sup> Unfortunately, this trial included patients with all grades of injury and was underpowered to detect a clinical benefit. A similarly designed and pow-

ered study that included children with acid ingestions and those with alkali ingestions failed to show a benefit of prolonged glucocorticoid therapy in either group.<sup>48</sup> Although several analyses of pooled data attempted to delineate a subpopulation of patients who might benefit from prolonged glucocorticoid administration,<sup>49-51</sup> 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<sup>2</sup> of body-surface area per day) or placebo, plus 1 week of ceftriaxone and ranitidine.<sup>28</sup> 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.<sup>39</sup> It should be noted, however, that one consensus conference recommended that glucocorticoids not be used.<sup>43</sup> 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<sup>52</sup> (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.<sup>53</sup> A subsequent animal model showed that sucralfate had favorable healing properties as compared with placebo.<sup>54</sup> 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.<sup>55</sup> 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.<sup>56</sup> In a randomized, blinded trial, 40 patients with caustic-induced strictures were given either endoscopically administered mitomycin C or placebo, with subsequent mechanical dilation.<sup>57</sup> 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.<sup>58</sup> The beneficial effects of mitomycin C were also shown in children with long strictures that were refractory to standard approaches.<sup>59</sup> 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,<sup>22,60</sup> 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.<sup>61,62</sup> 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.<sup>39</sup> Alternatively, the use of biodegradable stents, placed during either endoscopy or laparoscopy, shows promise for relieving dysphagia and limiting stricture formation.<sup>63-65</sup> 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.<sup>66</sup> 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.

No potential conflict of interest relevant to this article was reported.

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

## REFERENCES

1. Zargar SA, Kochhar R, Nagi B, Mehta S, Mehta SK. Ingestion of corrosive acids: spectrum of injury to upper gastrointestinal tract and natural history. *Gastroenterology* 1989;97:702-7.
2. Scharman EJ. Liquid "laundry pods": a missed global toxicsurveillance opportunity. *Clin Toxicol (Phila)* 2012;50:725-6.
3. Health hazards associated with laundry detergent pods — United States, May–June 2012. *MMWR Morb Mortal Wkly Rep* 2012;61:825-9.
4. Davis MG, Casavant MJ, Spiller HA, Chounthirath T, Smith GA. Pediatric exposures to laundry and dishwasher detergents in the United States: 2013-2014. *Pediatrics* 2016;137(5):e20154529.
5. Valdez AL, Casavant MJ, Spiller HA, Chounthirath T, Xiang H, Smith GA. Pediatric exposure to laundry detergent pods. *Pediatrics* 2014;134:1127-35.
6. Boyd AD. Chevalier Jackson: the father of American bronchoesophagoscopy. *Ann Thorac Surg* 1994;57:502-5.
7. The Federal Caustic Poison Act. Hearing on S 2320. 69th Congress, Second session (1927).
8. The Poison Prevention Packaging Act of 1970. 15 U.S.C. § 1471 (1970).
9. Federal Hazardous Substances Act. 15 U.S.C. §§1261–1278 (1970).
10. Johnson CM, Brigger MT. The public health impact of pediatric caustic ingestion injuries. *Arch Otolaryngol Head Neck Surg* 2012;138:1111-5.
11. Dine MS, McGovern ME. Intentional poisoning of children — an overlooked category of child abuse: report of seven cases and review of the literature. *Pediatrics* 1982;70:32-5.
12. Friedman EM. Caustic ingestions and foreign body aspirations: an overlooked form of child abuse. *Ann Otol Rhinol Laryngol* 1987;96:709-12.
13. Hawkins DB, Demeter MJ, Barnett TE. Caustic ingestion: controversies in management — a review of 214 cases. *Laryngoscope* 1980;90:98-109.
14. Gummin DD, Mowry JB, Spyker DA, et al. 2018 Annual report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 36th annual report. *Clin Toxicol (Phila)* 2019;57:1220-413.
15. Botwe BO, Anim-Sampong S, Sarkodie BD, Antwi WK, Obeng-Nkansah J, Ashong GG. Caustic soda ingestion in children under-5 years presenting for fluoroscopic examinations in an Academic Hospital in Ghana. *BMC Res Notes* 2015;8:684.
16. Dehghani SM, Bahmanyar M, Javaherizadeh H. Caustic ingestion in children in south of Iran: a two-year single center study. *Middle East J Dig Dis* 2018;10:31-4.
17. Day RC, Bradberry SM, Sandilands EA, Thomas SHL, Thompson JP, Vale JA. Toxicity resulting from exposure to oven cleaners as reported to the UK National Poisons Information Service (NPIS) from 2009 to 2015. *Clin Toxicol (Phila)* 2017;55: 645-51.
18. Gharbaoui M, Ben Khelil M, Harzallah H, Benzarti A, Zhioua M, Hamdoun M. Pattern of suicide by self-poisoning in Northern Tunisia: an eleven-year study (2005-2015). *J Forensic Leg Med* 2019;61: 1-4.
19. Najafi F, Hasanzadeh J, Moradinazar M, Faramarzi H, Nematollahi A. An epidemiological survey of the suicide incidence trends in the southwest Iran: 2004-2009. *Int J Health Policy Manag* 2013;1: 219-22.
20. Cheng HT, Cheng CL, Lin CH, et al. Caustic ingestion in adults: the role of endoscopic classification in predicting outcome. *BMC Gastroenterol* 2008;8:31.
21. Alipour Faz A, Arsan F, Peyvandi H, et al. Epidemiologic features and outcomes of caustic ingestions; a 10-year cross-sectional study. *Emerg (Tehran)* 2017;5(1): e56.
22. Hoffman RS, Howland MA, Kamerow HN, Goldfrank LR. Comparison of titratable acid/alkaline reserve and pH in potentially caustic household products. *J Toxicol Clin Toxicol* 1989;27:241-6.
23. Honar N, Haghighat M, Mahmoodi S, Javaherizadeh H, Kalvandi G, Salimi M. Caustic ingestion in children in south of Iran: retrospective study from Shiraz — Iran. *Rev Gastroenterol Peru* 2017;37:22-5.
24. Adam JS, Birck HG. Pediatric caustic ingestion. *Ann Otol Rhinol Laryngol* 1982;91:656-8.
25. Cowan T, Foster R, Isbister GK. Acute esophageal injury and strictures following corrosive ingestions in a 27-year cohort. *Am J Emerg Med* 2017;35:488-92.
26. García Merino F, Martínez Caro A, García Vallés C. Caustic burns of the esophagus in childhood: our 14 years' experience. *An Esp Pediatr* 1988;29:293-7. (In Spanish.)
27. Wasserman RL, Ginsburg CM. Caustic substance injuries. *J Pediatr* 1985;107: 169-74.
28. Usta M, Erkan T, Cokugras FC, et al. High doses of methylprednisolone in the management of caustic esophageal burns. *Pediatrics* 2014;133:E1518-E1524.
29. Previtera C, Giusti F, Guglielmi M. Predictive value of visible lesions (cheeks, lips, oropharynx) in suspected caustic ingestion: may endoscopy reasonably be omitted in completely negative pediatric patients? *Pediatr Emerg Care* 1990;6: 176-8.
30. Gaudreault P, Parent M, McGuigan MA, Chicoine L, Lovejoy FH Jr. Predictability of esophageal injury from signs and symptoms: a study of caustic ingestion in 378 children. *Pediatrics* 1983;71: 767-70.
31. Crain EF, Gershel JC, Mezey AP. Caustic ingestion: symptoms as predictors of esophageal injury. *Am J Dis Child* 1984; 138:863-5.
32. Zargar SA, Kochhar R, Mehta S, Mehta SK. The role of fiberoptic endoscopy in the management of corrosive ingestion and modified endoscopic classification of burns. *Gastrointest Endosc* 1991;37: 165-9.
33. Ryu HH, Jeung KW, Lee BK, et al. Caustic injury: can CT grading system enable prediction of esophageal stricture? *Clin Toxicol (Phila)* 2010;48:137-42.
34. Cowan D, Ho B, Sykes KJ, Wei JL. Pediatric oral burns: a ten-year review of patient characteristics, etiologies and treatment outcomes. *Int J Pediatr Otorhinolaryngol* 2013;77:1325-8.

35. Struck MF, Beilicke A, Hoffmeister A, et al. Acute emergency care and airway management of caustic ingestion in adults: single center observational study. *Scand J Trauma Resusc Emerg Med* 2016;24:45.
36. Frerk C, Mitchell VS, McNarry AF, et al. Difficult Airway Society 2015 guidelines for management of unanticipated difficult intubation in adults. *Br J Anaesth* 2015;115:827-48.
37. Sharma N, Kaur M, Agarwal T, Sangwan VS, Vajpayee RB. Treatment of acute ocular chemical burns. *Surv Ophthalmol* 2018;63:214-35.
38. Penner GE. Acid ingestion: toxicology and treatment. *Ann Emerg Med* 1980;9:374-9.
39. Kluger Y, Ishay OB, Sartelli M, et al. Caustic ingestion management: World Society of Emergency Surgery preliminary survey of expert opinion. *World J Emerg Surg* 2015;10:48.
40. Homan CS, Singer AJ, Henry MC, Thode HC Jr. Thermal effects of neutralization therapy and water dilution for acute alkali exposure in canines. *Acad Emerg Med* 1997;4:27-32.
41. Homan CS, Singer AJ, Thomajan C, Henry MC, Thode HC Jr. Thermal characteristics of neutralization therapy and water dilution for strong acid ingestion: an in-vivo canine model. *Acad Emerg Med* 1998;5:286-92.
42. Niedzielski A, Schwartz SG, Partycka-Pietrzyk K, Mielnik-Niedzielska G. Caustic agents ingestion in children: a 51-year retrospective cohort study. *Ear Nose Throat J* 2020;99:52-7.
43. Bonavina L, Chirica M, Skrobic O, et al. Foregut caustic injuries: results of the World Society of Emergency Surgery consensus conference. *World J Emerg Surg* 2015;10:44.
44. Rosenberg N, Kunderman PJ, Vroman L, Moolten SE. Prevention of experimental lye strictures of the esophagus by cortisone. *AMA Arch Surg* 1951;63:147-51.
45. Rosenberg N, Kunderman PJ, Vroman L, Moolten SE. Prevention of experimental esophageal stricture by cortisone. II. Control of suppurative complications by penicillin. *AMA Arch Surg* 1953;66:593-8.
46. Rontal E, Meyerhoff W, Duvall AJ III. Metastatic abscess as a complication of retrograde esophageal dilatation. *Ann Otol Rhinol Laryngol* 1973;82:643-8.
47. Anderson KD, Rouse TM, Randolph JG. A controlled trial of corticosteroids in children with corrosive injury of the esophagus. *N Engl J Med* 1990;323:637-40.
48. Tuncer R, Soyupak S, Sen N, et al. Does steroid treatment prevent caustic esophageal stricture? A prospective study. *Ann Med Sci* 2000;9:56-8.
49. Fulton JA, Hoffman RS. Steroids in second degree caustic burns of the esophagus: a systematic pooled analysis of fifty years of human data: 1956-2006. *Clin Toxicol (Phila)* 2007;45:402-8.
50. Howell JM, Dalsey WC, Hartsell FW, Butzin CA. Steroids for the treatment of corrosive esophageal injury: a statistical analysis of past studies. *Am J Emerg Med* 1992;10:421-5.
51. Pelclová D, Navrátil T. Do corticosteroids prevent oesophageal stricture after corrosive ingestion? *Toxicol Rev* 2005;24:125-9.
52. Thomson M, Tringali A, Dumonceau JM, et al. Paediatric gastrointestinal endoscopy: European Society for Paediatric Gastroenterology Hepatology and Nutrition and European Society of Gastrointestinal Endoscopy guidelines. *J Pediatr Gastroenterol Nutr* 2017;64:133-53.
53. Reddy AN, Budhreja M. Sucralfate therapy for lye-induced esophagitis. *Am J Gastroenterol* 1988;83:71-3.
54. Temir ZG, Karkiner A, Karaca I, Ortaç R, Özdamar A. The effectiveness of sucralfate against stricture formation in experimental corrosive esophageal burns. *Surg Today* 2005;35:617-22.
55. Gümürdülü Y, Karakoç E, Kara B, Taşdoğan BE, Parsak CK, Sakman G. The efficiency of sucralfate in corrosive esophagitis: a randomized, prospective study. *Turk J Gastroenterol* 2010;21:7-11.
56. Sun Y, Ge Y, Fu Y, et al. Mitomycin C induces fibroblasts apoptosis and reduces epidural fibrosis by regulating miR-200b and its targeting of RhoE. *Eur J Pharmacol* 2015;765:198-208.
57. El-Asmar KM, Hassan MA, Abdelkader HM, Hamza AF. Topical mitomycin C application is effective in management of localized caustic esophageal stricture: a double-blinded, randomized, placebo-controlled trial. *J Pediatr Surg* 2013;48:1621-7.
58. El-Asmar KM, Hassan MA, Abdelkader HM, Hamza AF. Topical mitomycin C can effectively alleviate dysphagia in children with long-segment caustic esophageal strictures. *Dis Esophagus* 2015;28:422-7.
59. Ghobrial CM, Eskander AE. Prospective study of the effect of topical application of mitomycin C in refractory pediatric caustic esophageal strictures. *Surg Endosc* 2018;32:4932-8.
60. Mattos GM, Lopes DD, Mamede RC, Ricz H, Mello-Filho FV, Neto JB. Effects of time of contact and concentration of caustic agent on generation of injuries. *Laryngoscope* 2006;116:456-60.
61. Wijnburg FA, Beukers MM, Heymans HS, Bartelsman JF, den Hartog Jager FC. Nasogastric intubation as sole treatment of caustic esophageal lesions. *Ann Otol Rhinol Laryngol* 1985;94:337-41.
62. Wijnburg FA, Heymans HS, Urbanus NA. Caustic esophageal lesions in childhood: prevention of stricture formation. *J Pediatr Surg* 1989;24:171-3.
63. Repici A, Vleggaar FP, Hassan C, et al. Efficacy and safety of biodegradable stents for refractory benign esophageal strictures: the BEST (Biodegradable Esophageal Stent) study. *Gastrointest Endosc* 2010;72:927-34.
64. Saito Y, Tanaka T, Andoh A, et al. Usefulness of biodegradable stents constructed of poly-L-lactic acid monofilaments in patients with benign esophageal stenosis. *World J Gastroenterol* 2007;13:3977-80.
65. Wang RW, Zhou JH, Jiang YG, et al. Prevention of stricture with intraluminal stenting through laparotomy after corrosive esophageal burns. *Eur J Cardiothorac Surg* 2006;30:207-11.
66. Appelqvist P, Salmo M. Lye corrosion carcinoma of the esophagus: a review of 63 cases. *Cancer* 1980;45:2655-8.

Copyright © 2020 Massachusetts Medical Society.