



Original Contribution

Time to perforation for button batteries lodged in the esophagus☆☆☆

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ABSTRACT

Introduction: New strategies recently proposed to mitigate injury caused by lithium coin cell batteries lodged in the esophagus include prehospital administration of honey to coat the battery and prevent local hydroxide generation and in-hospital administration of sucralfate suspension (or honey). This study was undertaken to define the safe interval for administering coating agents by identifying the timing of onset of esophageal perforations. **Methods:** A retrospective study of 290 fatal or severe battery ingestions with esophageal lodgment was undertaken to identify cases with esophageal perforations.

Results: Esophageal perforations were identified in 189 cases (53 fatal, 136 severe; 95.2% in children ≤4 years). Implicated batteries were predominantly lithium (91.0%) and 92.0% were ≥20 mm diameter. Only 2% of perforations occurred in <24 h following ingestion, including 3 severe cases with perforations evident at 11–17 h, 12 h, and 18 h. Another 7.4% of perforations (11 cases) became evident 24 to 47 h post ingestion and 10.1% of perforations (15 cases) became evident 48 to 71 h post ingestion. By 3 days post ingestion, 26.8% of perforations were evident, 36.9% by 4 days, 46.3% by 5 days, and 66.4% by 9 days.

Conclusion: Esophageal perforation is unlikely in the 12 h after battery ingestion, therefore the administration of honey or sucralfate carries a low risk of extravasation from the esophagus. This first 12 h includes the period of peak electrolysis activity and battery damage, thus the risk of honey or sucralfate is low while the benefit is likely high.

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1. Introduction

The hazard of button batteries, especially lithium coin cells, lodged in the esophagus of a young child has been widely recognized for nearly a decade [1]. These lodged button cells pose a risk of serious, sometimes fatal complications, such as esophageal perforation, tracheoesophageal fistula, aortoesophageal fistula, vocal cord paralysis, esophageal stricture, spondylodiscitis, mediastinitis, pneumothorax and abscess formation. Most of these complications are delayed and are often seen days to weeks after battery removal.

While the quest for a safer battery remains elusive, a variety of therapeutic and even first-aid interventions have recently been proposed to mitigate injury. These mitigation strategies focus on the most important mechanism of injury, attempting to slow the generation of hydroxide at

the negative pole of the battery by limiting the electrolysis reaction occurring in tissue or fluid adjacent to the battery, or attempting to neutralize alkaline injury following battery removal. Three mitigation strategies have now been proposed, including 1) pre-hospital administration of honey to coat the battery and prevent hydrolysis and alkali generation, 2) in hospital, pre-endoscopy administration of sucralfate (Carafate®) [2], again to coat the battery, and 3) neutralization of accumulated tissue hydroxide through acetic acid irrigation at the time of endoscopic battery removal [3]. All of these approaches have now been shown to be effective experimentally, with results sufficiently convincing to justify their clinical implementation given the high risk of severe injury from batteries lodged in the esophagus and low risk of complications from the intervention. Yet the development of a clinical guideline for pre-hospital honey administration or in-hospital pre-operative sucralfate administration is missing one critical piece of information: how many hours post ingestion does the risk of esophageal perforation become significant? Once the patient reaches the time post ingestion when esophageal perforation may already be present, the administration of honey or sucralfate may no longer be benign. While we already know that the risk of esophageal perforation and serious complications rises dramatically when batteries lodge in the esophagus of a child for 2 h or more, the actual development of those complications

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is delayed for hours to months beyond the 2-hour risk window [1]. This study attempts to determine the earliest anticipated onset of esophageal perforations for the specific purpose of defining the safe interval for administration of oral coating or neutralizing agents.

2. Methods

This study is a retrospective analysis of 290 cases summarized in an ongoing, publicly-accessible, online national registry of battery ingestions maintained by the National Capital Poison Center, home of the National Battery Ingestion Hotline from 1982 to June 2018. The Hotline was established to collect case data for battery ingestions to inform triage and treatment guidelines, perform product surveillance, and define factors contributing to the growing hazard of button battery ingestions. These 290 cases include 59 fatal battery ingestions [4] and 231 severe outcomes [5] following esophageal lodgment. Cases included in this registry were reported either in the medical literature, by direct consultation to the National Battery Ingestion Hotline, or in the media, with many cases reported in multiple sources. Severe outcomes included cases with evidence of nonfatal perforation, fistulas, strictures, vocal cord paralysis, spondylodiscitis, airway compromise, or any other long term (>1 month) or permanent complication. Additional case data beyond that displayed online was accessed and abstracted for clinical and timing details. Esophageal perforations were considered present if any of the following complications or findings were described: tracheoesophageal fistula; esophageal-vascular fistula; pneumothorax; abscess; or a directly visualized perforation on endoscopy, post mortem exam, or imaging, even if “walled-off”. Cases without an esophageal perforation were excluded prior to data analysis.

Time to perforation was assessed through several different methods, including:

- 1) Analysis of time from ingestion to removal in cases where perforation was directly visualized at the time of battery removal.
- 2) Analysis of time from ingestion to perforation in cases where perforation was visualized on imaging, visualized at the time of battery removal, or present at death (as determined by post mortem examination).
- 3) Analysis of time from removal to perforation where perforation was visualized on imaging or present at death.

Where times were estimated (such as time of ingestion, time of removal, or time of imaging), the shortest possible intervals were determined and used in this analysis to avoid overestimating the minimum time to perforation.

This study was approved by the institutional review board following expedited review.

3. Results

Of the 290 cases reviewed, 59 were fatal battery ingestions and 231 had severe outcomes. Cases without a documented esophageal perforation (6 fatal cases and 95 severe outcome cases) were then excluded. Perforations were noted in 53 of the fatal battery ingestions and 136 severe outcome cases, thus 189 cases were included in this analysis.

Children 4 years of age and younger comprised 95.2% of cases, with 81.3% of cases occurring in children 2 years or younger (Table 1). Age ranged from 22 days to 10 years. One year olds alone comprised nearly half of all cases (43.9%).

Most batteries implicated in these severe and fatal cases were 20 mm diameter or greater (92.0% of cases with known diameter, Table 1). Lithium coin cell batteries were implicated in 91.0% of ingestions where the ingested battery chemistry was known.

Perforations were already visible at the time of battery removal in 44 cases (8 deaths; 36 severe cases). Perforations were not noted at the time of removal in 102 cases (20 fatal cases and 82 severe cases). The

Table 1

Characteristics of study cases and ingested button batteries.

	Fatalities	Severe cases	Total	Valid %	Cumulative %
Total battery ingestion cases reviewed	59	231	290		
Cases with perforation (included cases)	53	136	189		
Age (cases with perforation only)					
<1 year	6	31	37	19.8%	19.8%
1 year	22	60	82	43.9%	63.6%
2 year	15	18	33	17.6%	81.3%
3 year	2	15	17	9.1%	90.4%
4 year	6	3	9	4.8%	95.2%
5 year	1	5	6	3.2%	98.4%
6–10 years	0	3	3	1.6%	100.0%
Unknown	1	1	2		
Total	53	136	189	100.0%	
Battery chemistry					
Lithium	35	87	122	91.0%	
Other	3	9	12	9.0%	
Unknown	15	40	55		
Total	53	136	189	100.0%	
Battery diameter					
≥20 mm	36	91	127	92.0%	
<20 mm	3	8	11	8.0%	
Unknown	14	37	51		
Total	53	136	189	100.0%	

shortest time from ingestion to perforation (and removal) in these cases was 18 h (18 h was the shortest time in severe cases; 2 days was the shortest time in fatal cases). Time to removal (and perforation documentation) occurred from 2 to 14 days post ingestion for 8 fatal cases and from 18 h to 8 months post ingestion for 36 severe cases.

Time from ingestion to perforation, assessed through either imaging, direct visualization, or time of death (when perforation was diagnosed post mortem), was available in 149 cases (37 deaths, 112 severe cases). Only 2.0% of perforations (3 cases) were documented in the first 24 h after ingestion. All 3 of these were severe cases, with perforations evident at an estimated 11–17 h, 12 h, and 18 h post ingestion. Another 7.4% of perforations (11 cases) became evident 24 to 47 h post ingestion and 10.1% of perforations (15 cases) became evident 48 to 71 h post ingestion. Fig. 1 shows the time to evidence of perforation and cumulative percent of perforations, with 26.8% of perforations evident by 3 days post ingestion, 36.9% by 4 days, 46.3% by 5 days, 49.0% by 6 days, and 66.4% by 9 days post ingestion.

For 55 cases with batteries removed from the esophagus in <48 h from the time of ingestion, there was no correlation between time to removal and time to perforation ($R^2 = 0.007$, linear regression). Nearly all perforations (98%) of batteries removed in <48 h were diagnosed by 35 days post ingestion. Time from removal to perforation was known in 103 cases (excluding 75 cases with perforation detected at or prior to removal). Perforations were diagnosed by 3 days after removal in 49.5% of cases and by 48 days post removal in 98.1% of cases.

One hundred cases with tracheoesophageal fistulas (TEFs) or aortoesophageal fistulas (AEFs) and known time to perforation were analyzed to assess the interval to manifestation of these complications. Of the 100 cases, 79 had TEFs and 22 had AEFs (counts by fistula type include one patient with both). Fig. 2 shows that these complications can be quite delayed, with only 24.1% of TEFs and 9.1% of AEFs detected by 3 days post battery ingestion, and 58.2% of TEFs and 31.8% of AEFs detected by 7 days post ingestion. All AEFs developed within 27 days post ingestion, whereas TEFs continued to be diagnosed as late as 8 months after the ingestion. Virtually all of these late diagnoses (30 to 240 days) had earlier symptoms initially not attributed to ingested batteries or perforations, with those earlier symptoms developing 2 to 34 days post ingestion. Delayed detection was not as apparent with AEFs (Fig. 2), presumably because of the extremely high mortality rate

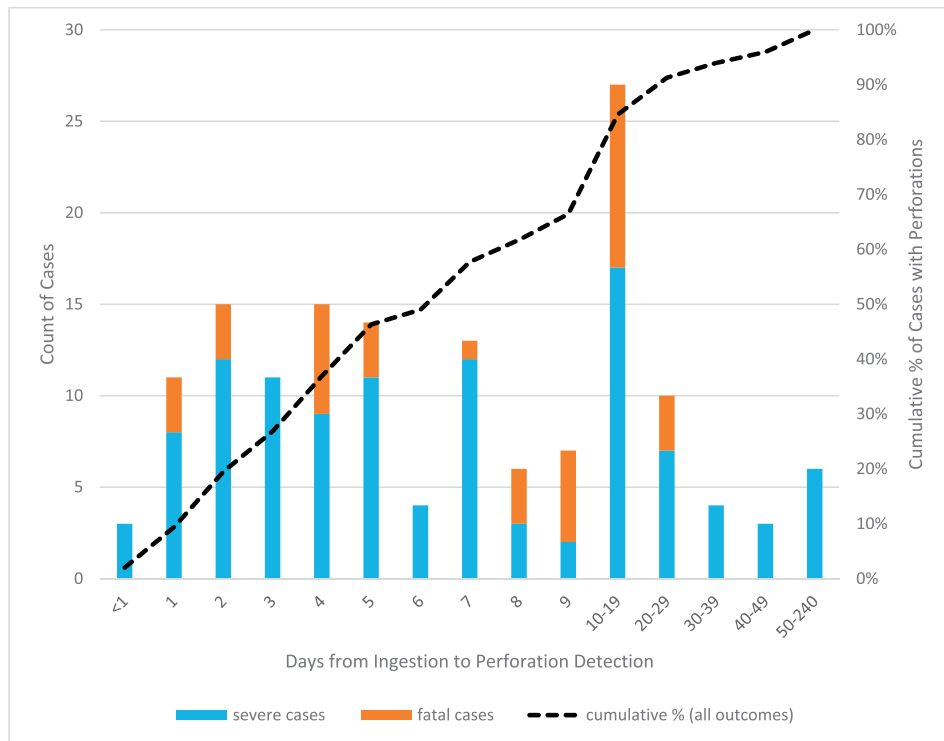


Fig. 1. Time from ingestion to perforation detection (by imaging, direct visualization or post mortem finding).

once AEFs develop (only 2 of 22 children with AEFs in our dataset survived).

4. Discussion

The severity of button battery ingestions increased markedly around 2006 with the increased consumer use of 20 mm lithium coin cells. Data from 2015 to 2017 shows that the percent of battery ingestion cases with fatal or severe outcomes remains high compared to data from 1985 to 2006 [6], despite voluntary standards intended to limit a child's

access to product battery compartments, more secure manufacturer packaging for new batteries, extensive health professional education to minimize time from ingestion to removal, and exhaustive public education efforts to prevent battery ingestions [7]. Button battery ingestion is now widely recognized as a cause of serious injury in children, with 12.6% of children swallowing a lithium coin cell of 20 mm diameter or more experiencing a severe or fatal outcome [1]. Proposed technical changes to make lithium batteries safer remain elusive.

Two recent investigations suggest relatively safe clinical interventions that may lessen the injury caused by button cells lodged in the

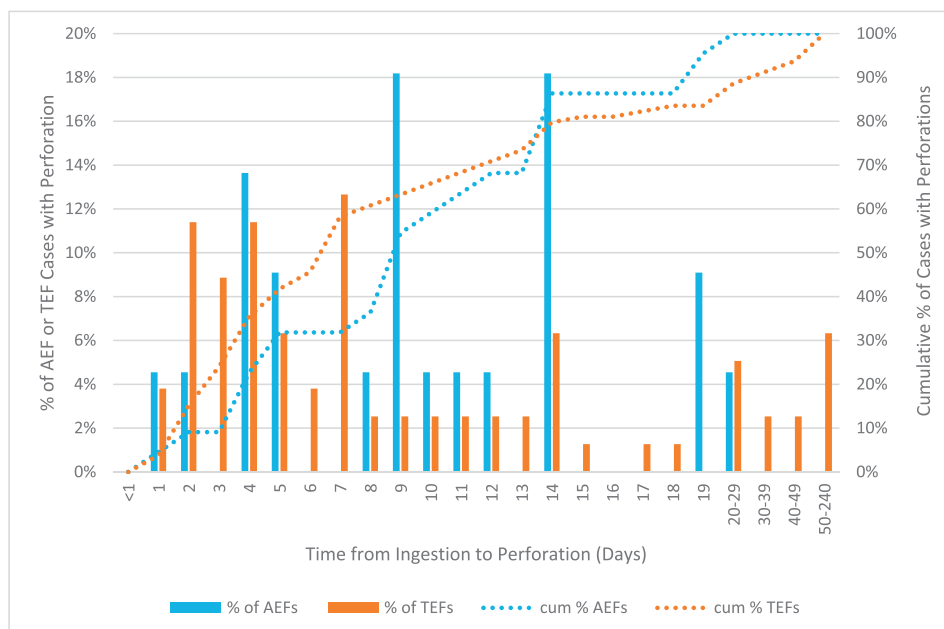


Fig. 2. Time from ingestion to perforation detection: aortoesophageal compared to tracheoesophageal fistula cases.

esophagus. The first, published by Jatana in 2016, dispelled prior myths that neutralization of an alkaline battery injury is unsafe because of feared thermal damage, and demonstrated a protective effect of irrigation of the injured esophagus with 0.25% acetic acid without a concomitant rise in temperature. This investigation led to modification of the National Capital Poison Center's guideline for battery ingestions to include endoscopic irrigation of the injured esophagus with 150 mL 0.25% acetic acid immediately following battery removal [8].

The second study tests a novel mitigation strategy for button battery ingestions, focusing on the use of honey in the prehospital setting, dosed at 10 mL (2 teaspoons) every 10 min, to coat the battery and prevent generation of hydroxide in adjacent tissue [2]. Honey is presumed to be effective for this purpose because of its high viscosity and low water content, a phenomenon known to beekeepers who strive for low water content (<18%) to prevent fermentation and maintain the quality of the honey. Studies with cadaveric porcine esophagi compared serial irrigations with honey, sucralfate or a saline control. These same investigators also conducted studies in anesthetized piglets with the negative pole of a lithium coin cell placed against the wall of the proximal esophagus, irrigated with either saline, sucralfate suspension, or honey every 10 min, then euthanized at 7 days for histologic examination of the esophagus. In both the in vitro and in vivo models, honey and sucralfate were more effective than the saline control, preventing delayed esophageal perforations and lessening the depth of necrotic tissue and destruction of the muscularis propria. Both honey and sucralfate are postulated to 1) provide a protective barrier, limiting the battery contact with surrounding water and tissue fluids required for electrolysis and local hydroxide generation, and 2) function as weak acids, neutralizing hydroxide that is generated. These authors propose use of honey in the home or prehospital setting and sucralfate in the health care facility prior to battery removal.

Much attention has been directed to the 2-hour window for removal of a battery from the esophagus before the risk of serious, even fatal, complications is determined. But these complications are usually delayed, thus 2 h is a risk window, not the time to perforation window.

4.1. Determining safe interval for intervention

Our data suggest that perforation may occur as early as 11 to 12 h post ingestion. Three cases had documented perforations in 11 to 18 h post ingestion, however only 2% of known perforations were documented <24 h post ingestion and only 9.4% were documented <48 h post ingestion. Thus administration of a coating agent such as honey or sucralfate carries a low risk of extravasation of the honey or sucralfate from the esophagus into the mediastinum or surrounding tissues, if given up to 12 h post ingestion.

4.2. Determining the effective interval for intervention

Since the majority of button batteries lodged in the esophagus with fatal or severe outcomes involve lithium coin cells, the mechanism of injury is attributed to electrical current-generated hydroxide in tissue. For lithium coin cells, leakage is not a factor in the mechanism of injury (there is no alkaline electrolyte in lithium button batteries). However, these batteries eventually stop generating a current, thus at some point, the battery becomes an inert foreign body, and there is no benefit from administration of a coating agent to prevent further hydroxide generation. While that interval has not been precisely defined, there are indications that it may range from as little as 6 to as much as 48 h post ingestion of a fresh 2032 lithium coin cell. Thus despite the limitations of these data, it's clear that at some point prior to 48 h after ingestion, the button battery stops generating hydroxide and becomes an inert foreign body. Once current generation has ceased, there is no anticipated benefit from a protective sucralfate or honey coating.

A number of prior studies suggest that electrolysis, the cause of the battery-induced injury, is most intense during the early post-ingestion

period, thus the 12-hour post-ingestion safe interval for mitigation with honey or sucralfate is likely also the most useful interval for intervention. Jatana reported a voltage drop from 3.3 V to between 0.88 and 1.22 V over a period of 24 to 48 h in cadaveric piglet esophagus bathed in saline, lower than the voltage required for electrolysis (1.23 V), thus demonstrating that damage stops occurring between 24 and 48 h [3]. Also using cadaveric pig esophagus bathed in artificial saliva, and CR 2032 lithium cells, Völker found tissue current increased from 1499 μ A upon initial battery contact with tissue to a peak of 3548 μ A 3.7 h into the exposure, dropping further to 1889 μ A 8 h into the exposure, then to 1129 μ A at 24 h and 811 μ A at 35 h [9]. While residual voltage remained at 2.24 V at 24 h, well over the threshold for electrolysis, the time versus current data peaked between 3 and 6 h and the strongest formation of gas bubbles (indicating electrolysis) was observed between 3.7 and 12 h, suggesting that the most intense injury occurred in this 3- to 12-hour range for this particular lithium coin cell. Völker's data do not extend beyond 24 h, thus the cut-off for electrolysis with this popular battery type cannot be established. Energizer laboratory data showed nearly full discharge of 2032 lithium cells in artificial saliva in 7 h, with a discharge rate in the range of 20 mA/h [10] and Tanaka found batteries implanted in the esophagus of dogs consumed 110 mA in 3 to 5 h, which if linearly discharged implies full discharge in just 6 to 10 h [11]. Of course children swallowing lithium coin cells may swallow batteries of different degrees of discharge ("freshness") and varying initial capacitance (even 20 mm lithium cells have dramatically varying initial capacitance based on differing battery specifications), and these batteries may have different amounts of tissue contact and surrounding fluid, all factors complicating the determination of a precise cut-off for injury.

Our analysis supports use of honey or sucralfate intervention up to 12 h after ingestion of a lithium coin cell. During that interval, there is little risk of honey or sucralfate extravasation from a perforated esophagus and there is maximal benefit as a fresh lithium coin cell is likely causing the peak damage (maximum electrolysis is observed during this period).

4.3. Guideline revision

The National Capital Poison Center's Battery Ingestion Triage and Treatment Guideline has been modified to recommend honey for button battery ingestions in children. The revised guidelines [8] state:

Administer honey immediately and while en route to the ED, if:

- A lithium coin cell may have been ingested (if battery type is unknown, assume it is a lithium coin cell unless it is a hearing aid battery);*
- The child is 12 months of age or older (because honey is not safe in children younger than one year);*
- The battery was swallowed within the prior 12 h;*
- The child is able to swallow; and*
- Honey is immediately available.*

How to dose honey:

- Give 10 mL (2 teaspoons) of honey by mouth every 10 min, up to 6 doses.*
- Use commercial honey if available, rather than specialized or artisanal honey (to avoid inadvertent use of large amounts of honey produced from potentially toxic flowers).*
- Honey is NOT a substitute for immediate removal of a battery lodged in the esophagus. Honey slows the development of battery injury but won't stop it from occurring. Do not delay going to an ER [8].*

The battery ingestion guidelines were also revised to address the administration of coating agents in the emergency department during the

hopefully brief period between x-ray diagnosis of an esophageal battery and battery removal. The revised guidelines state:

If possible, and if the child is able to swallow, administer sucralfate (Carafate® suspension, 1 g/10 mL). Give 10 mL PO every 10 minutes, up to 3 doses, from the time of x-ray determination that a battery is lodged in the esophagus until sedation is given for endoscopy. Honey has comparable efficacy and may be substituted for sucralfate suspension in children 12 months of age or older, dosed as outlined above. Do not give sucralfate or honey if the battery was possibly in the esophagus for more than 12 hours. Sucralfate or honey administration is not a substitute for emergent battery removal as these agents slow but do not eliminate tissue damage. Do not delay battery removal because a patient has eaten recently or because a patient was given honey or sucralfate (Carafate®) by mouth [8].

4.4. Limitations of this investigation

The accuracy of the study results are limited by deficiencies in comprehensive documentation of chronologic data (time of ingestion, time of removal, time of imaging, time of death) recorded in published cases and inaccuracies in histories rendered by phone (by providers or by parents) to the National Battery Ingestion Hotline. This limitation is mitigated by review of medical records when made available, and by use of the shortest possible time from ingestion to removal or imaging in order to avoid overestimating the interval to perforation. The study is also limited by the absence of a clinical signal of the precise time that perforation has occurred, with perforation possibly progressing as a continuum from microscopic to detectable, and with the diagnosis of perforation likely delayed some unknown time from occurrence to detection.

5. Conclusion

Esophageal perforation is unlikely in the first 12 h after battery ingestion. Therefore, the administration of a coating agent such as honey

or sucralfate suspension carries a low risk of extravasation from the esophagus into the mediastinum or surrounding tissues. This first 12 h post ingestion includes the period of peak electrolysis activity and battery damage, thus the risk of honey or sucralfate suspension administration is low while the potential benefit is likely high. Clinicians should feel confident that honey and sucralfate suspension can be safely administered in the first 12 h after a suspected battery ingestion. However, these interventions slow but do not eliminate battery injury, thus their use does not justify a delay in removal of an esophageal battery.

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