



TESTING PLACEMENT OF GASTRIC FEEDING TUBES IN INFANTS

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Background Inadvertent positioning of a nasogastric tube in the lung can cause serious complications, so identifying methods to detect improperly inserted tubes is imperative. **Objectives** To compare the sensitivity, specificity, and negative and positive predictive values of 4 pH cut points (<4.0, <4.5, <5.0, and <5.5) in differentiating gastric and tracheal aspirates under various treatment conditions and to explore the utility of a pepsin assay for distinguishing between gastric and tracheal aspirates.

Methods Gastric and tracheal aspirates were collected from critically ill infants undergoing mechanical ventilation who had nasogastric or orogastric feeding tubes. Aspirates were tested with colorimetric pH indicators and a rapid pepsin assay. Information about treatment conditions was obtained from medical records.

Results Two hundred twelve gastric aspirates and 60 tracheal aspirates were collected from 212 patients. Sensitivity was highest and specificity was lowest at the gastric aspirate pH cut point of less than 5.5. Positive predictive values were 100% at all pH cut points less than 5.0. Negative predictive values were higher at the pH cut point of less than 5.0 than at cut points less than 4.5. A higher percentage of pepsin-positive readings was found in gastric aspirates (88.3%) than in tracheal aspirates (5.4%).

Conclusion For a desired positive predictive value of 100%, a pH cut point of less than 5.0 provides the best negative predictive values, regardless of gastric acid inhibitor administration and feeding status. The pepsin assay is promising as an additional marker to distinguish gastric from tracheal aspirates. (*American Journal of Critical Care*. 2017;26:466-473)

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Improperly positioned nasogastric tubes can result in serious and even fatal complications.¹ Therefore, it is critical that proper tube positioning be confirmed before the tube is used for feeding or medication delivery. A recent survey of 63 hospitals in the United States revealed that the most commonly used methods to verify tube placement in children were aspiration (21 hospitals) and auscultation (18 hospitals). Less common methods were pH measurement (10 hospitals), measurement of tube length (8 hospitals), and radiography (6 hospitals).²

A concern about these findings is the infrequent use of radiography (the “gold standard”) to confirm correct placement of new blind tube insertions. A properly obtained abdominal radiograph can show an incorrect tube placement; however, the tissues of very young children are more sensitive than those of adults to the deleterious effects of radiation.³ For this reason, clinicians are reluctant to use radiography to determine tube location in infants, especially those who frequently dislodge their tubes.^{4,5} Another concern from the survey is the frequent reliance on auscultation to confirm tube location, despite warnings from major practice organizations to avoid this method.⁶⁻⁸

Current consensus among pediatric nurse experts is that measuring the pH of aspirates from nasogastric tubes is the best available bedside method to verify tube location when combined with other measures, such as confirmation of tube length.⁹ However, the survey indicated that the pH method was used less often than aspiration and auscultation were used.² A possible reason for the infrequent use of pH testing in infants is confusion about the appropriate pH cut point to distinguish between gastric and respiratory placement of nasogastric tubes. Gastric pH is higher in children less than 1 year of age than in older children.^{10,11} In addition, infants often receive gastric acid inhibitors and frequent feedings, factors known to elevate gastric pH. The extent to which these conditions affect the efficacy of the pH method for determining tube placement in infants is unclear.

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The first aim of this study was to evaluate the utility of 4 pH cut points (under a variety of treatment conditions) for distinguishing between gastric and respiratory placement of a nasogastric tube in infants. The second aim was to determine the extent to which the presence of pepsin in aspirates could be used along with pH measurement to distinguish between gastric and respiratory placement of a nasogastric tube.

Background The pH Method

Fasting gastric pH levels are usually less than 4 within about a day after birth.¹² Several studies have shown that gastric acid-inhibiting drugs sometimes fail to maintain a pH greater than 4 in children because of inadequate dosages or administration schedules.¹³⁻¹⁵ Other researchers have reported that elevated gastric pH is not consistently maintained in recently fed children.¹⁶⁻¹⁹

A 2016 guideline⁸ prepared for the Ministry of Health, New South Wales, Australia, for confirming placement of nasogastric and orogastric tubes in infants and children recommends considering medical imaging to check tube placement if an aspirate’s pH is not 4.0 or less. The guideline states that medical imaging must *always* be used to confirm initial tube placement if an aspirate’s pH is greater than 5.0. (Note that the guideline also recommends using narrow-range pH paper that detects pH values from about 2 to 9 in minimum increments of 0.5.) Others have recommended a pH cut point of 5.0 or less to distinguish between gastric and respiratory aspirates in children.^{11,20,21} Unfortunately, making a clear distinction between readings in the narrow pH range of 4 to 6 can be very difficult when subjective colorimetric pH tests are used.

Pediatric nurse experts consider the pH method reasonable for bedside assessment of feeding tube location.

Gastric and tracheal aspirates were tested for pH and pepsin.

Pepsin Content in Nasogastric Tube Aspirates

Additional biological markers should be explored to supplement pH readings when establishing correct tube placement in infants. One potential marker is the gastric proteolytic enzyme pepsin.²² In a study²³ of gastric aspirates from 32 critically ill infants, researchers using a Western blot immunoassay with a sensitivity of 1 µg/mL for pepsin found a mean pepsin concentration of 111.9 (SD, 36.8) µg/mL. Researchers have also analyzed tracheal aspirates for pepsin in pediatric settings to detect aspiration of gastric contents.²⁴⁻²⁷

Specific Aims

Our study, conducted in a population of critically ill children less than 1 year of age with a nasally or orally inserted gastric feeding tube, had 2 aims.

Aim 1. To describe the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of 4 pH cut points (<4.0, <4.5, <5.0, and <5.5) for distinguishing between gastric and respiratory placement of feeding tubes in infants in 4 treatment categories:

- I. Absence of gastric acid inhibitor and absence of feeding within 2 hours before tube placement
- II. Presence of gastric acid inhibitor and absence of feeding within 2 hours before tube placement
- III. Absence of gastric acid inhibitor and presence of feeding within 2 hours before tube placement
- IV. Presence of gastric acid inhibitor and presence of feeding within 2 hours before tube placement

Aim 2. To determine the efficacy of a rapid pepsin assay in distinguishing between tracheal aspirates and gastric aspirates at 4 gastric pH cut points (>4.0, >4.5, >5.0, and >5.5).

Methods

Site and Sample

The study was conducted in a pediatric intensive care unit at the Children's Hospital of Michigan in Detroit. The sample (described in Table 1) consisted of 212 critically ill infants with a nasogastric or orogastric feeding tube who were receiving mechanical ventilation.

Data Collection Procedure

Before beginning the study, we obtained permission from the appropriate institutional review board for waived consents (protocol #1305012028). A research nurse collected samples from nasogastric feeding tubes early in the morning on Mondays,

Tuesdays, Wednesdays, and Thursdays near the time of routine radiography that revealed tube position. Bedside nurses saved tracheal aspirates obtained at the time of routine suctioning (without normal saline) for use in the study. Immediately after collection of the gastric and tracheal aspirates, a research nurse performed pH testing (described in next section). The aspirates were then mixed with 0.01-M citric acid (1 part citric acid to 3 parts specimen) for storage at 4°C until they were shipped (refrigerated) overnight on Thursday for early Friday delivery to a research laboratory for pepsin assay. Specimens were labeled either "gastric" or "tracheal" to allow appropriate dilution of the sample during the pepsin assay (described in next section). A research nurse reviewed the infants' medical records to determine age, gestational age, sex, weight, use of gastric acid inhibitors, feeding status, and radiographic evidence of tube location.

Measurements

pH. One of 2 research nurses tested 212 gastric aspirates and 60 tracheal aspirates first with plastic wide-range pH indicator strips that indicate pH values from 0 to 14 in increments of 1.0 pH unit (Hydriion 0-14, Micro Essential Laboratory Inc). If the wide-range pH strip indicated a pH of 5.0 or less, the nurse made a final pH reading by using a narrow-range pH indicator paper calibrated for pH values from 2.9 to 5.2 in increments of 0.3 to 0.4 pH units (Hydriion Microfine [MF-1604], Micro Essential Laboratory Inc). If the reading on the wide-range indicator strip was greater than pH 5.0, the nurse made the final pH reading with a narrow-range pH indicator paper calibrated for pH values from 4.9 to 6.9 in increments of 0.2 to 0.3 pH units (Hydriion Microfine [MF-1605], Micro Essential Laboratory Inc). We used only the results from the narrow-range pH paper (calibrated in units of 0.2 to 0.4) in the data analyses. We were unable to use a pH meter because the aspiration sample volumes were often low.

We compared the results of the colorimetric pH paper tests of gastric aspirate specimens with radiologist-interpreted radiographs obtained within 60 minutes of specimen collection. All of the feeding tubes were placed in the stomach.

Pepsin. We used a commercially available device (Peptest, RD Biomed Limited) to assess for pepsin in all of the gastric and tracheal aspirates that provided a sufficient volume of supernatant for the analysis. This device uses 2 highly specific monoclonal antibodies to human pepsin and has been reported to have a sensitivity of 88%, a specificity of 87%, and

Table 1
Description of sample

Variable	Description
Participants	212 critically ill children with a nasogastric or orogastric feeding tube who were receiving mechanical ventilation
Age, weeks	Range, 0.5-51.0; median, 12 (interquartile range, 4.25-24.0)
Gestational age, weeks	Range, 24-40; median, 37 (interquartile range, 34-40)
Sex	Female, 43.4% (n=92); male, 56.6% (n=120)
Weight, kg	Range, 1.5-11.3; median, 4.3 (interquartile range, 3.4-5.8)
Treatment category (n=212)	I: Acid inhibitor absent, recent feeding absent; 24.1% (n=51) II: Acid inhibitor present, recent feeding absent; 23.6% (n=50) III: Acid inhibitor absent, recent feeding present; 28.3% (n=60) IV: Acid inhibitor present, recent feeding present; 24.1% (n=51)
Gastric acid inhibitor (n=212)	Present: 47.6% (n=101) Absent: 52.4% (n=111)
Name of gastric acid inhibitor (n=101)	Ranitidine: 81.2% (n=82) Pantoprazole: 17.8% (n=18) Combination of ranitidine and pantoprazole: 1.0% (n=1)
Route of gastric acid inhibitor (n=101)	Enteral: 50.5% (n=51) Intravenous: 49.5% (n=50)
Fed in previous 2 hours (n=212)	Yes: 52.4% (n=111) No: 47.6% (n=101)
Feeding method (n=111)	Continuous feeding: 83.8% (n=93) Bolus feeding: 16.2% (n=18)
Type of feeding (n=111)	Formula: 73.9% (n=82) Breast milk: 23.4% (n=26) Combination of formula and breast milk: 0.9% (n=1) Oral rehydration solution (Pedialyte): 1.8% (n=2)
Gastric aspirates	212 independent aspirates tested initially with pH test strips calibrated in units of 1.0 and then with pH paper calibrated in units of 0.2-0.3 or 0.3-0.4; subset of 206 also assayed for pepsin Volume: range, 0.3-2.0 mL; median, 1.5 mL (interquartile range, 0.8-1.5 mL)
Tracheal aspirates	60 independent aspirates tested initially with pH test strips calibrated in units of 1.0 and then with pH paper calibrated in units of 0.2-0.3; subset of 37 also assayed for pepsin Volume: range, 0.10-1.5 mL; median, 0.3 mL (interquartile range, 0.1-0.5 mL)

a PPV of 97% for pepsin in sputum. Although not conducive to bedside use, the test can be performed on a countertop in a clinical setting within a 15-minute period. For the tracheal aspirates, we used the device's standard directions because the test was designed to detect very low levels of refluxed pepsin (16 ng/mL) in saliva and sputum. However, the sensitivity level of the commercially available device is not appropriate for use with gastric aspirates, which typically contain much larger amounts of pepsin. Therefore, before data collection, we consulted with the device manufacturer to modify the test for use in our study. We sent 6 gastric aspirates from critically ill infants to the manufacturer for analysis. On a suggestion from the manufacturer, we began the study with a 1:100 dilution of gastric aspirates with the designated migration buffer solution for infants 3 months of age or younger and an additional dilution of 1:25 for infants more than 3 months of age. However, because

specimens with the latter dilution often yielded negative readings, we decided to report findings solely from the 1:100 dilution for all gastric aspirates to provide uniformity in the gastric pepsin assays.

According to the device manufacturer, test specimens are stable for 5 days when maintained at 4°C (as indicated earlier, all of the samples reached the research laboratory within this period of time). The principal investigator performed all of the assays as outlined in the manufacturer's protocol. A volume of specimen ranging from 0.2 to 0.5 mL was added to a centrifuge tube and centrifuged at 4000 revolutions per minute for 5 minutes. A portion of the supernatant was then mixed with migration buffer and vortexed for 10 seconds. For tracheal aspirates, 80 µL of supernatant was added to 240 µL of migration buffer solution; for gastric aspirates, 10 µL of supernatant was added to 990 µL of migration buffer solution. Eighty microliters of the resulting solution was

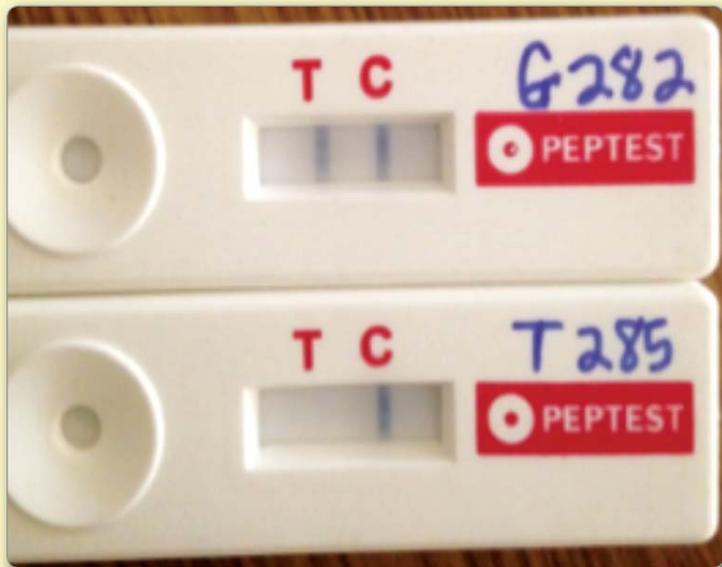


Figure 1 Examples of positive (top) and negative (bottom) test results for pepsin (PepTest, RD Biomed Ltd).

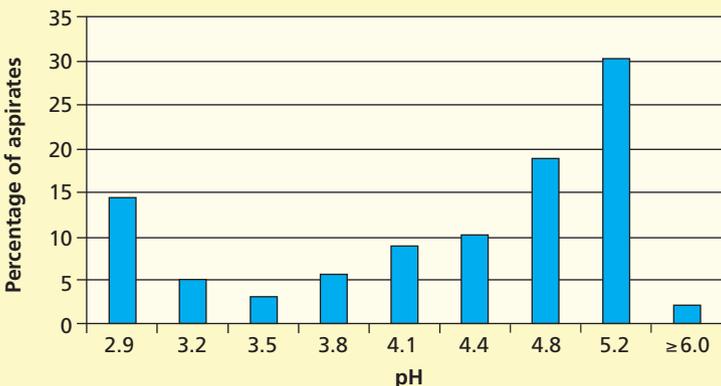


Figure 2 Distribution of the pH of 212 gastric aspirates.

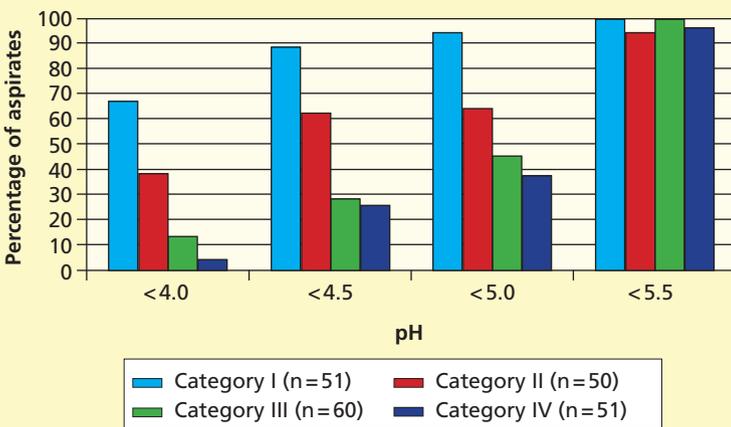


Figure 3 Percentage of pH readings according to treatment category (presence or absence of gastric acid inhibitors and feeding within 2 hours before sampling). Category I, absence of gastric acid inhibitors and absence of recent feedings; category II, presence of acid inhibitors and absence of recent feedings; category III, absence of acid inhibitors and presence of recent feedings; category IV, presence of acid inhibitors and presence of recent feedings.

then added to the well of the test device. After 15 minutes, the principal investigator made a visual reading of the results. Results were subjectively specified as positive (2 lines visible) or negative (only the control line visible; Figure 1). Sufficient supernatant was available for analysis in 206 of the 212 gastric aspirate specimens. About 38% of the 60 tracheal specimens could not be assayed because their thick consistency precluded obtaining a sufficient volume of supernatant.

Data Analysis

Aim 1. We computed the sensitivity, specificity, PPV, and NPV of each of the 4 pH cut points for each gastric acid inhibitor and feeding category. Area under the curve was also reported for each category. A power analysis indicated that for the pH cut point of less than 5.5, a sample size of 50 per group would achieve 96% power, given a predicted sensitivity of 95%.

Aim 2. The proportion of pepsin-positive aspirates from each tube placement site (gastric and tracheal) was compared with χ^2 tests using 4 gastric pH cut points (pH >4.0, >4.5, >5.0, and >5.5).

Results

Descriptive Data

Gastric Aspirates. The median pH of the 212 gastric aspirates was 4.8 (interquartile range, 3.8-5.2); the distribution of the 212 gastric pH readings is depicted in Figure 2. As shown in Figure 3, gastric pH was lowest in infants not receiving gastric acid inhibitors or recent feedings (category I) and highest in those receiving acid inhibitors and recent feedings (category IV). We found no significant relationship between gastric pH and the type or route of gastric acid inhibitor or the type or route of feeding. Of the 206 gastric specimens tested for pepsin, 88.3% were positive for pepsin.

Tracheal Aspirates. The pH range of the tracheal aspirates was 5.1 to 6.9 (6.9 was the upper limit of the pH paper used for the measurement). As can be seen in Figure 4, the vast majority (81.7%) of pH readings were at the upper calibration level (6.9) of the pH paper. One of the aspirates was interpreted as having a pH of 5.1 on the narrow-range pH indicator strip, although the reading for the same sample on the wide-range pH indicator strip was 6.0; pepsin was not measured in this aspirate. Of the 60 tracheal aspirates, pepsin assays were possible in only 37 because of the inability to obtain a supernatant from thick secretions. Two (5.4%) of the 37 tracheal aspirates tested for pepsin were positive for pepsin. The pH values of these 2 aspirates were 6.0 and 6.9 as measured by narrow-range pH paper (and 6 and 7, respectively, as measured by wide-range pH strips).

Aim 1

In all categories, sensitivity was highest and specificity was lowest at a pH cut point of less than 5.5. PPVs were 100% in all categories at pH cut points of less than 4.0, less than 4.5, and less than 5.0. However, PPVs ranged from 85.0% in category I patients to 98.4% in category III patients at the pH cut point of less than 5.5. In all categories, NPVs were highest at the pH cut point of less than 5.5 and lowest at the cut point of less than 4.0 (Table 2).

Aim 2

As shown in Table 3, the percentages of pepsin-positive readings were significantly higher in gastric than in tracheal aspirates at all pH cut points (>4.0, >4.5, >5.0, and >5.5).

The strongest comparison between gastric and tracheal aspirates was in gastric aspirates with pH values greater than 4.0; 84.1% of these aspirates were positive for pepsin, as compared with 5.4% of tracheal secretions. The weakest comparison was in gastric aspirates with pH values greater than 5.5; 60% of these samples were positive for pepsin.

Discussion

Current enteral feeding practice recommendations include pH testing as 1 method to assess tube placement in pediatric/neonatal patients when radiographic verification is not available. Abdominal radiography is recommended when other methods do not confirm tube location.⁴

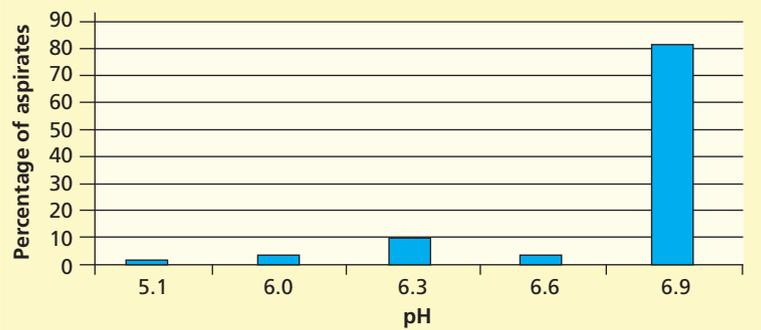


Figure 4 Distribution of the pH of 60 tracheal aspirates (6.9 was the upper range of the pH paper).

Aim 1

None of the pH cut points evaluated in our study achieved 100% accuracy when compared with radiographic evidence of tube location. However, clinicians can use information from this study to decide when the pH method is most likely to be effective; for example, it worked very well in infants in category I (no gastric acid inhibitor administration or recent feeding) and reasonably well in infants in category II (administration of gastric acid inhibitor but no recent feeding). As expected, pH testing was least accurate in infants who had received feedings within the previous 2 hours (categories III and IV). Using a pH cut point of less than 5.5 would result in the lowest number of required radiographs if one were willing to accept PPVs of less than 100%.

PPVs were 100% for 3 of the 4 pH cut points (<4.0, <4.5, and <5.0) in all 4 treatment categories. Assuming that a PPV of 100% is desirable, using a

Table 2

Sensitivity, specificity, positive predictive value, negative predictive value, and area under the curve according to pH cut point and treatment category for distinguishing between gastric and tracheal aspirates^a

Category	AUC	pH<4.0				pH<4.5				pH<5.0				pH<5.5			
		Sens	Spec	PPV	NPV	Sens	Spec	PPV	NPV	Sens	Spec	PPV	NPV	Sens	Spec	PPV	NPV
I Acid inhibitor absent, recent feeding absent	0.99	66.7	100.0	100.0	77.9	88.2	100.0	100.0	90.9	94.1	100.0	100.0	95.2	100.0	98.3	85.0	100.0
II Acid inhibitor present, recent feeding absent	0.98	34.0	100.0	100.0	64.5	56.0	100.0	100.0	73.2	70.0	100.0	100.0	80.0	94.0	98.3	97.9	95.2
III Acid inhibitor absent, recent feeding present	0.99	13.3	100.0	100.0	53.6	28.3	100.0	100.0	58.2	60.0	100.0	100.0	71.4	100.0	98.3	98.4	100.0
IV Acid inhibitor present, recent feeding present	0.99	3.9	100.0	100.0	55.0	25.5	100.0	100.0	61.2	47.1	100.0	100.0	69.0	96.1	98.3	98.0	96.7

Abbreviations: AUC, area under the curve; NPV, negative predictive value; PPV, positive predictive value; Sens, sensitivity; Spec, specificity.

^a All values for Sens, Spec, PPV, and NPV are percentages.

Table 3
Percentages of pepsin-positive readings in gastric and tracheal aspirates according to gastric pH cut point

Gastric aspirate pH cut point ^a	Pepsin-positive readings, % (n)		χ^2	P
	Gastric aspirates ^b	Tracheal aspirates		
>4.0	84.1 (122 of 145)	5.4 (2 of 37)	84.2	<.001
>4.5	81.7 (85 of 104)	5.4 (2 of 37)	67.3	<.001
>5.0	76.6 (49 of 64)	5.4 (2 of 37)	47.5	<.001
>5.5	60.0 (3 of 5)	5.4 (2 of 37)	12.2	<.001

^a In order to perform χ^2 tests, it was necessary to use the pH categories presented in this table (>4.0, >4.5, >5.0 and >5.5) as opposed to the pH categories defined in the aims (<4.0, <4.5, <5.0 and <5.5) because no tracheal samples tested for pepsin were present in the categories of <4.0, <4.5, and <5.0.

^b Sixty-one of the 206 gastric aspirates tested for pepsin had pH values less than 4.0.

pH cut point of less than 5.0 provided the most reasonable NPVs to distinguish between gastric and respiratory aspirates in all patient categories, as compared with the lower pH cut points of less than 4.0 and less than 4.5. This finding supports the recommendation in the 2016 Australian guideline⁸ to always obtain appropriate medical imaging to confirm initial placement if an aspirate's pH is higher than 5.0.

Finding a tracheal aspirate pH value of 5.1 was unexpected, especially given that previous investigators have not reported tracheal pH values of less than 6.0 in children.¹¹ One possible explanation is a faulty interpretation of the narrow-range pH paper, given that a reading made on the same specimen with a wide-range pH test strip by the

same research nurse was 6.0. This case raises a potentially serious problem with using subjective colorimetric pH tests to make distinctions between values within a narrow range.

Aim 2

We had expected to find 100% pepsin-positive gastric secretions and a very low percentage of pepsin-positive tracheal secretions. We were therefore surprised to find that 11.7% of the gastric specimens were negative for pepsin. The most likely explanation is that we used an excessive dilution (1:100) for the gastric specimens. We were not surprised to find pepsin in 2 of the tracheal aspirates because pepsin has been found in tracheal secretions in previous pediatric studies, most likely indicating aspiration of gastric contents.²⁷ Although the comparisons

between percentages of pepsin-positive gastric aspirates and percentages of pepsin-positive tracheal secretions were statistically significant at all of the pH cut points, the comparisons lack clinical significance.

Strengths and Limitations

A strength of the study was our ability to test a relatively large number of gastric and tracheal aspirates for pH and pepsin content under a variety of conditions near the time of radiographic evidence of tube location. The pilot testing of a rapid pepsin assay to help distinguish between gastric and respiratory aspirates provides potentially useful data for future study. A limitation was our inability to validate the subjective colorimetric pH test results with a pH meter because of small aspirate volumes (although we attempted to minimize this problem by limiting pH testing to 2 research nurses). Another limitation was our probable use of an inappropriate dilution of the gastric contents for the pepsin assays.

Conclusion

Aspirate pH is a reasonable bedside indicator of gastric feeding tube placement when radiography is not readily accessible. Assuming that a PPV of 100% is desired, our findings indicate that a pH cut point of less than 5.0 (as measured by pH papers calibrated in units ranging from 0.2 to 0.4) provides the best NPVs in all gastric acid inhibitor and feeding categories. Given the subjective nature of colorimetric pH tests, we concur with the 2016 Australian guideline⁸ that recommends considering radiographic confirmation for aspirate pH values greater than 4.0 and requiring it for aspirate pH values greater than 5.0. The pepsin assay described in this investigation may be promising as an additional marker to distinguish between gastric and tracheal aspirates. However, the study needs to be replicated with a weaker dilution of gastric aspirates to determine the pepsin assay's actual benefit.

FINANCIAL DISCLOSURES

This study was supported by an Impact Grant from the American Association of Critical Care Nurses (2014-2016).

SEE ALSO

For more about pH test strips, visit the *Critical Care Nurse* website, www.ccnonline.org, and read the article by Metheny et al, "Effect of pH Test-Strip Characteristics on Accuracy of Readings" (June 2017).

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An aspirate pH cut point of <5.0 was the best for distinguishing gastric from respiratory tube placement.

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This article has been designated for CE contact hour(s). The evaluation demonstrates your knowledge of the following objectives:

1. Describe the effect of gastric acid inhibitors and/or recent feedings on the gastric pH of critically ill infants.
2. Describe typical pH values of tracheal aspirates from critically ill infants.
3. Describe the typical presence of pepsin in gastric and tracheal aspirates from critically ill infants.

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