

Original Investigation

Evaluation and Management of Chronic Aspiration in Children With Normal Upper Airway Anatomy

Eelam Adil, MD, MBA; Hasan Al Shemari, MD; Amy Kacprowicz, BS; Jennifer Perez, MS, CCC-SLP; Kara Larson, MS, CCC-SLP; Kayla Hernandez, MS, CCC-SLP; Kosuke Kawai, ScD; Julia Cowenhoven, BS; David Urion, MD; Reza Rahbar, DMD, MD

IMPORTANCE Chronic airway aspiration is a challenging problem for physicians and caregivers and can cause significant pulmonary morbidity in pediatric patients. Our knowledge regarding the causes and optimal management of these patients is in its infancy.

OBJECTIVE To review our experience with the evaluation and management of pediatric patients with documented aspiration and normal upper airway anatomy.

DESIGN, SETTING, AND PARTICIPANTS In this retrospective medical record review, we studied pediatric patients for airway disorders at a pediatric tertiary referral center who were diagnosed as having aspiration on modified barium swallow study during a 10-year period (June 1, 2002, through September 31, 2012).

INTERVENTIONS Direct laryngoscopy and bronchoscopy performed with the patient under general anesthesia.

MAIN OUTCOMES AND MEASURES Demographics, comorbidities, management, and swallowing outcomes were analyzed.

RESULTS Forty-six patients met the inclusion criteria. The mean age at presentation was 1.56 years, and there was a male to female ratio of approximately 2:1. Eight patients (17%) were syndromic, 16 (35%) had developmental delay, and 12 (26%) had congenital heart disease. Fifteen patients (33%) underwent brain magnetic resonance imaging, and none had a brainstem or posterior fossa lesion that accounted for their aspiration. Patients were subdivided according to the consistency of the fluids that they aspirated: 25 (54%) aspirated thin liquids, 15 (33%) aspirated thickened liquids, and 6 (13%) aspirated purees. Of these patients, 21 (84%), 12 (80%), and 3 (50%) had resolution of their swallowing dysfunction with feeding and swallowing therapy, respectively. A total of 3 patients (7%) required a tracheostomy for their refractory aspiration.

CONCLUSIONS AND RELEVANCE We recommend feeding and swallowing therapy for children with normal upper airway anatomy. Brain magnetic resonance imaging should be considered for patients with suspected brainstem or posterior fossa lesion based on neurologic examination findings. Most patients who aspirate thin and thickened liquids will have resolution of their swallowing dysfunction within 1 year of beginning therapy.

JAMA Otolaryngol Head Neck Surg. 2015;141(11):1006-1011. doi:10.1001/jamaoto.2015.2266
Published online October 22, 2015.

+ CME Quiz at
jamanetworkcme.com and
CME Questions page 1036

Author Affiliations: Department of Otolaryngology and Communication Enhancement, Boston Children's Hospital, Boston, Massachusetts (Adil, Al Shemari, Kacprowicz, Perez, Larson, Hernandez, Kawai, Cowenhoven, Rahbar); Department of Otolaryngology, Harvard Medical School, Boston, Massachusetts (Adil, Rahbar); Department of Neurology, Boston Children's Hospital, Boston, Massachusetts (Urion); Clinical Research Center, Boston Children's Hospital, Boston, Massachusetts (Kawai).

Corresponding Author: Reza Rahbar, DMD, MD, Department of Otolaryngology and Communication Enhancement, Boston Children's Hospital, 300 Longwood Ave, Mailstop LO-367, Boston, MA 02115 (reza.rahbar@childrens.harvard.edu).

Aspiration—the inhalation of foreign material into the lower airway—has the potential to cause permanent damage to the developing lungs of infants and children. Aspiration in children includes oral feeds and secretions (direct aspiration) and reflux contents (indirect aspiration). Pulmonary aspiration is present in half of pediatric patients with unexplained or refractory respiratory symptoms, such as cough.¹ It can cause frequent hospitalizations and recurrent pneumonitis.

The diagnosis and management of chronic aspiration in children represent a significant challenge for physicians. Chronic aspiration is generally believed to be a result of an anatomical abnormality, discoordinated swallow reflex, or both. Successful management begins with a thorough evaluation. After obtaining a complete history and performing a physical examination, it is important to determine the degree of aspiration. In the pediatric population, a modified barium swallow study (MBS) or fiberoptic endoscopic evaluation of swallowing (FEES) are viable options for diagnosing aspiration. If there is documented aspiration, then it is important to determine whether there is a contributing anatomical abnormality. An upper airway endoscopy, including direct laryngoscopy and bronchoscopy, should be performed. Vocal fold immobility, laryngeal cleft, and/or tracheoesophageal fistula can all contribute to recurrent aspiration and should be ruled out. All patients should be assessed from a gastroenterologic perspective to rule out any underlying gastroenterologic cause that may be contributing to aspiration, such as reflux or esophageal motility disorder. A pulmonary assessment is also valuable to determine the type and extent of pulmonary injury from aspiration.

When there is no upper airway anatomical abnormality contributing to the aspiration, caregivers often question the need for further evaluation, management options, duration of treatment, and outcomes. The aim of this study is to describe our management and evaluate our outcomes in pediatric patients with documented aspiration on an MBS and normal upper airway anatomy.

Methods

After obtaining approval from the Boston Children's Hospital Institutional Review Board, we performed a retrospective medical record review from June 1, 2002, through Septem-

ber 31, 2012, in a tertiary care pediatric hospital. Inclusion criteria included pediatric patients up to 18 years of age with documented aspiration on an MBS and normal upper airway anatomy as documented by direct laryngoscopy and bronchoscopy performed in the operating room with the patient under general anesthesia. Patients with any anatomical abnormalities, such as vocal fold immobility, laryngeal cleft, and/or tracheoesophageal fistula, were excluded. Those patients with esophageal motility disorders and eosinophilic esophagitis were also excluded. In addition, patients with incomplete feeding and swallow therapy data were excluded. Data regarding the patients' demographics, feeding and developmental history, medical comorbidities, further imaging, surgical procedures, aspiration consistency, and clinical outcomes were recorded and analyzed. Success of feeding and swallowing therapy was defined as a return to a regular diet. Analyses were performed with a statistical significance threshold of $P < .05$ using SAS statistical software, version 9.3 (SAS Institute Inc).

Results

Patient Demographics and Comorbidities

During the 10-year study period, 46 patients met our inclusion criteria. The mean age at presentation was 1.56 years (range, 6 weeks to 9 years). The male to female ratio was 1.9:1.

Many patients had at least 1 comorbidity that contributed to their aspiration (Table 1). Eight patients (17%) had a recognized syndrome, including DiGeorge syndrome, trisomy 21, Nail-Patella syndrome, Wolf-Hirschhorn syndrome, Rubenstein-Taybi syndrome, and X-linked intellectual disability. Sixteen patients (35%) had developmental delay, and 12 (26%) had congenital heart disease. Some patients had more than 1 comorbidity. As indicated in Table 2, no significant differences were found with regard to demographics and aspiration between patients with and without congenital heart disease.

Three patients (7%) had documented gastroesophageal reflux disease (GERD) according to 24-hour pH probe testing, and 33 (72%) had suspected GERD as diagnosed by a gastroenterologist. In 12 patients (26%), GERD was their only comorbidity. Six patients (13%) had no identifiable comorbidity.

Table 1. Patient Demographics, Comorbidities, and Outcomes Organized by Aspiration Consistency^a

Variable	Aspiration Consistency			Total (N = 46)
	Thin (n = 25)	Thick (n = 15)	Puree (n = 6)	
Mean age at presentation, y	1.6	1.1	1.3	... ^b
Mean duration of feeding therapy, y	0.78	1.03	1.72	...
Syndromic	2 (8)	4 (27)	2 (33)	8 (17)
DD	8 (32)	3 (20)	5 (83)	16 (35)
Congenital heart disease	7 (28)	4 (27)	1 (17)	12 (26)
GERD	18 (72)	12 (80)	6 (100)	36 (78)
Resolution of aspiration	21 (84)	12 (80)	3 (50)	...

Abbreviations: DD, developmental delay; GERD, gastroesophageal reflux disease.

^a Data are presented as number (percentage) of patients unless otherwise indicated.

^b Ellipses indicate data not applicable.

Table 2. Comparisons Between Characteristics of Patients With and Without Congenital Heart Disease^a

Characteristic	Cardiovascular Disease (n = 12)	No Cardiovascular Disease (n = 34)	P Value ^b
Sex			
Female	2 (17)	13 (38)	.28
Male	10 (83)	21 (62)	
Age, y			
Mean (SD)	1.4 (1.1)	1.6 (2.5)	.31
Median (IQR)	1.2 (0.6-2.0)	0.8 (0.3-1.3)	
Feeding therapy duration, mo			
Mean (SD)	14.3 (11.1)	9.5 (6.9)	.19
Median (IQR)	12.8 (5.4-22.4)	7.0 (3.0-15.0)	
Aspiration consistency			
Thin	5 (42)	20 (59)	.56
Thick	5 (42)	10 (29)	
Puree	2 (17)	4 (12)	
Surgical intervention (gastrostomy, tracheostomy, laryngectomy, or fundoplication)	6 (50)	9 (26)	.14

Abbreviation: IQR, interquartile range.

^a Data are presented as number (percentage) of patients unless otherwise indicated.

^b P values are based on χ^2 or Fisher exact test for categorical variables and Wilcoxon rank sum test for continuous variables.

Neurologic Assessment

Nonsyndromic patients without a clear cause of their developmental delay and/or neuromuscular discoordination were referred to a pediatric neurologist. A total of 21 patients (46%) were referred, and 15 underwent brain magnetic resonance imaging (MRI) as part of their neurologic evaluation. The need for MRI was based on the history and examination findings and was determined by our pediatric neurologist (D.U.). In 10 patients, the MRI revealed varying degrees of brain atrophy, which was deemed nonspecific. The MRI findings were reported as normal for the remaining 5 patients. No significant differences were found in demographics, aspiration consistency, duration of feeding therapy, and need for surgical intervention between patients referred and not referred to a neurologist (Table 3).

Swallowing Therapy

All patients were treated with feeding and swallowing therapy, which was based on the severity of their aspiration. Of note, patients who aspirated thickened liquids also aspirated thin liquids, and those who aspirated purees also aspirated thickened liquids.

Patients who aspirated thin liquids alone required feeding therapy for a mean of 0.78 years (range, 0.25-2.5 years). Twenty-one patients who aspirated thin liquids (84%) had no aspiration on their last MBS. These successfully treated patients received feeding therapy for a mean of 0.64 years. One patient in this group had a gastrostomy tube placed because of failure to thrive, and it was subsequently removed after resolution of aspiration. Four patients who aspirated thin liquids continued to aspirate despite feeding therapy: 3 had severe developmental delay and 1 had tetralogy of Fallot. These patients all had gastrostomy tubes placed and were in feeding therapy for a mean of 1.25 years.

Fifteen patients (33%) aspirated thickened liquids (ie, nectar and/or honey thickened). The mean duration of feeding and swallowing therapy for these patients was 1.03 years (range, 0.5-1.6 years), and swallowing therapy was successful in 12 pa-

tients (80%). In the group of 12 patients who aspirated thickened liquids that resolved with feeding therapy, the mean duration of therapy was 0.92 years. The 3 patients in this group whose aspiration did not resolve with therapy were syndromic and required permanent gastrostomy tubes.

Six patients (13%) aspirated purees, and their mean duration of feeding and swallow therapy was 1.72 years (range, 1.1-2.75 years). Three patients (50%) who aspirated purees had resolution with therapy. Two of the patients who did not progress with therapy in this group were syndromic, and 1 had severe developmental delay.

Surgical Intervention

Aspiration-related surgical intervention was required for some patients (Table 4). Gastrostomy insertion was performed on 13 patients (28%), 3 of whom ultimately had their gastrostomy tubes removed after successful feeding therapy. Three patients (7%) required a tracheostomy. All of these patients had recurrent pneumonia and neuromuscular disorders (2 patients with cerebral palsy and 1 with severe hypotonia). Of these 3 patients, 1 patient aspirated thickened liquids, and 2 aspirated purees. Three patients (7%) underwent a Nissen fundoplication. These patients all had neuromuscular disorders (2 with hypotonia and 1 with cerebral palsy).

Discussion

Chronic aspiration can cause substantial infectious and inflammatory pulmonary morbidity. The extent of lung injury that results from chronic pulmonary aspiration depends on the frequency and quantity of aspiration, composition, and pH of aspirated material and efficiency of the lung clearance response. The consequences of injuries may include bronchospasm, atelectasis, pulmonary edema, pneumonia, and/or bronchiectasis.^{2,3}

Aspiration can occur as a result of anatomical abnormalities of the upper aerodigestive tract and/or aberrant physi-

Table 3. Characteristics of 21 Patients Referred to a Neurologist for Evaluation^a

Characteristic	Referred to Neurologist (n = 21)	No Referral (n = 25)	P Value ^b
Sex			
Female	7 (33)	8 (32)	.92
Male	14 (67)	17 (68)	
Age, y			
Mean (SD)	1.9 (2.5)	1.2 (1.8)	.24
Median (IQR)	1.0 (0.7-1.6)	0.7 (0.3-1.6)	
Feeding therapy duration, mo			
Mean (SD)	13.1 (8.2)	8.8 (8.1)	.06
Median (IQR)	13.7 (7.0-17.0)	6.0 (3.0-14.0)	
Aspiration consistency			
Thin	9 (43)	16 (64)	.27
Thick	8 (38)	7 (28)	
Puree	4 (19)	2 (8)	
Surgical intervention (gastrostomy, tracheostomy, laryngectomy, or fundoplication)	7 (33)	8 (32)	.92

Abbreviation: IQR, interquartile range.

^a Data are presented as number (percentage) of patients unless otherwise indicated.

^b P values are based on χ^2 or Fisher exact test for categorical variables and Wilcoxon rank sum test for continuous variables.

ologic features.^{4,5} In a child with documented aspiration, we commonly assess vocal fold motion in the office with flexible laryngoscopy. Direct laryngoscopy and bronchoscopy performed in the operating room with the patient under general anesthesia are also performed to evaluate for anatomical abnormalities, including laryngeal cleft and/or tracheoesophageal fistula.

In a child with normal upper aerodigestive tract anatomy, neuromuscular discoordination may contribute to aspiration. Swallowing normally occurs in 4 phases through a series of voluntary and involuntary responses to food boluses. Feeding and swallowing difficulties may exist because of immaturity and discoordination of the oral and pharyngeal muscles.⁶ These patients also may have a weak gag mechanism or ineffective cough that predisposes them to acute and chronic aspiration.⁷

In our study, we found that 46 patients with documented aspiration on an MBS had normal upper airway anatomy confirmed by a complete examination on rigid endoscopy. To our knowledge, this finding has not been evaluated in the literature. Patients who aspirated thin liquids had the highest rate of success (84%) with feeding and swallowing therapy. A mean of 7.68 months of feeding and swallowing therapy were necessary before resolution of aspiration. The 4 patients who did not progress despite therapy had significant comorbidities that contributed to their aspiration. We found that a history of congenital heart disease or unclear cause of aspiration that prompted referral to a neurologist was not associated with aspiration consistency or increased duration of feeding therapy.

Eighty percent of patients who aspirated thickened liquids had resolution of their aspiration with feeding and swallowing therapy after a mean of 11.04 months. Those who continued with a modified diet had significant comorbidities. Feeding and swallowing therapy results in patients who aspirated pureed consistencies were variable, with a 50% resolution rate. This information is important for caregivers who often question how long therapy is necessary.

Table 4. Number of Aspiration-Related Procedures Assorted by Aspiration Consistency

Aspiration Consistency	Gastrostomy Tubes	Nissen Fundoplications	Tracheostomies
Thin	5	0	0
Thick	4	1	1
Puree	4	2	2
Total	13	3	3

GERD was a common comorbidity in our cohort of patients. Reflux may lead to respiratory symptoms even without frank aspiration.⁸ These symptoms may be due to reflex bronchospasm caused by gastric acid irritation of esophageal mucosa rather than entry of gastric content into the airways.⁹ Therefore, in patients with recurrent respiratory symptoms of unclear origin, the possibility of GERD as an underlying cause should be considered.

In our study, 36 patients (78%) had confirmed or suspected GERD. Three of these patients required a Nissen fundoplication. The incidence of GERD in our population was likely overestimated because most conditions were diagnosed based on symptoms and response to antireflux therapy alone. Multichannel intraluminal impedance testing with pH has become the criterion standard for diagnosis of reflux because it measures the height of refluxate and detects nonacidic reflux, both of which are missed by standard pH probe alone,¹⁰ and results of this test influence clinical decision making.¹¹ Future studies on this topic could examine the effect of antireflux therapy alone on aspiration in children with GERD confirmed by multichannel intraluminal impedance testing with pH with normal airway anatomy and no other comorbidities.

The goals of managing chronic aspiration with or without dysphagia are to foster safe and pleasant feeding, support normal growth, and prevent respiratory complications. The treatment plan must be practical and tolerated by the infant or child and the caregiver. The plan should be developed in

collaboration with pediatric otolaryngologists, pediatricians, speech language pathologists (SLPs), gastroenterologists, pulmonologists, and neurologists trained in neurodevelopmental disabilities.

Children with suspected aspiration at our institution undergo a clinical feeding evaluation by an SLP to assess the child's feeding and swallowing skills. This process begins with a directed history to obtain relevant contributing factors, including family and social history, medical diagnoses, and developmental history. The patient's feeding and swallowing history is also elicited with a focus on the child's current feeding regimen, parental concerns during feeding, and nutritional status.

Next, a thorough oral examination and oral motor skills assessment are performed. Sensory and behaviorally based feeding responses are also considered. The child is then provided with his/her normal diet through their normal delivery method, and swallowing skills and airway protection during swallowing are assessed. During this phase of the evaluation, new foods, changes in positioning, feeding equipment, and/or therapeutic strategies may be implemented as indicated. Specific approaches to therapeutic intervention can vary significantly depending on patient age and birth history, underlying medical and genetic diagnoses, nutritional status, and underlying anatomy and physiologic features of the oral and pharyngeal swallowing mechanism.

If swallowing impairment is suspected because of clinical observation of signs and/or symptoms of aspiration, and these signs and/or symptoms do not improve with therapeutic intervention, instrumental assessment of swallow function may be considered. Coughing and choking during or after feeds may be signs of aspiration and warrant an instrumental assessment. Other concerning signs and symptoms include congestion, wet vocal quality, wheezing, oxygen desaturation, cyanosis, throat clearing, and red or watery eyes during or after feeds.

An MBS is the most common method of instrumental assessment at our institution. Its disadvantage is that it involves radiation exposure. In addition, FEES is a valuable assessment tool for aspiration, but this testing is often not feasible in very young patients and patients with significant neurologic impairment. In our study, most patients were 1 to 2 years of age, which is a difficult group to test using FEES. Regardless of the testing method, it is important to recognize that swallowing requires a complex interplay between voluntary and involuntary muscles from the lips to the esophagus. We find that many children have abnormalities of their swallowing function above the level of the larynx, which may be overlooked during testing, but are important to consider in the treatment of these patients.

If there is documentation of laryngeal penetration or aspiration on MBS, recommendations are made regarding bolus delivery method, patient positioning, nipple flow rate, pacing, need for thickening, and/or diet modification based on the degree of aspiration. Infants are typically positioned semireclined or side-lying. Toddlers and older children are typically positioned upright. For children who aspirate and require thickened liquids, the SLP will provide individualized recommen-

dations for thickening products and recipes based on the thickness they require, the type of liquid they are drinking (eg, formula, breast milk, milk, water, or juice), and the age of the patient. Decisions regarding thickening are also discussed with the patient's physician. A child who aspirates on all consistencies is considered unsafe for an oral diet and admitted immediately for initiation of nonoral supplementation.

On the basis of each child's need and area of deficit, frequency and duration of feeding and swallowing therapy are determined by the SLP. Feeding and swallowing therapy techniques may include upgrading or downgrading diet, changing method of bolus delivery (ie, bottle to cup drinking), changing bolus flow rate, patient position, and pacing. Upgrading would be advancing diet to be less restrictive and closer to normal diet (eg, upgrading from nectar-thick to thin liquids), and downgrading would be making the diet more restrictive (eg, downgrading from thin liquids to nectar-thick liquids).

A follow-up therapy session is typically scheduled 1 to 4 weeks after the initial diagnosis of aspiration is made on instrumental assessment. Review of current feeding status, thickening agent, parent adherence, and monitoring of clinical signs and symptoms of aspiration are assessed. Need for change in thickening agent due to patient refusal, intolerance, or accessibility can be addressed. Discussion may take place regarding the appropriate interval for additional MBSs in conjunction with a primary otolaryngologist, pending clinical improvements or suspected decline in swallowing. Because of concern regarding radiation exposure, we typically do not perform a subsequent MBS for at least 6 months. Follow-up therapy sessions are scheduled based on the progress the patient makes toward advancing to an unrestricted diet.

Neurologic assessment was undertaken in this population of patients when the anatomical findings appeared insufficient to explain the degree of aspiration, including instances in which there were no findings of significance or in which the child was known or appeared to have a neurologic disorder. In our study, almost half were referred to a neurologist, and there were no differences in demographics or aspiration quality between this group and those who were not referred. Neurologic assessment began with an office assessment, which included a detailed history of feeding and other oromotor developmental features, a detailed family history, and a neurologic examination especially targeted toward issues of motor coordination and brainstem function. Historical elements considered particularly relevant included any history of early difficulties latching to breast or bottle, nasal regurgitation during feeding, excessive drooling in older infants and toddlers, and any difficulties with speech intelligibility in toddlers. In the latter instance, particular care in looking for the speech deformations characteristic of apraxic disorders was undertaken (usually reflected by primary care physicians not being able to understand the child and the speech deformations being "irregularly irregular").

In instances in which there was a suspicion of brainstem dysfunction based on neurologic examination, MRI of the brain was performed. This study was designed to focus particular attention on brainstem and posterior fossa, looking for any con-

genital structural abnormalities of the brainstem (Moebius plus syndromes or other dysgenetic anomalies) or a Chiari malformation. Given the particular interest in the brainstem, we have found fast imaging using steady-state acquisition to be very helpful. This sequence uses a T2 steady-state mechanism to provide high signal-to-noise ratio images, with a strong signal from fluid tissues while suppressing background tissue signal. This sequence, in turn, produces high contrast for the tiny structures of the small brainstem of these patients. Coupled with other, more commonly used pulse sequences, images with high accuracy can be obtained in short time frames. In the cohort of patients included in this study, 10 had nonspecific brain atrophy, and none had lesions of the brainstem or posterior fossa to account for their aspiration.

One of the limitations of this study is the relatively small number of patients, which limited our ability to perform parametric statistical analyses. Although we identified many patients with normal upper airway anatomy who aspirated during the study period, most were excluded because of incomplete feeding and swallowing therapy data because they

elect to undergo their therapy closer to home. In total, this group of patients represents approximately 10% of our total pediatric aspiration population. Future studies will examine those patients with abnormal direct laryngoscopy and bronchoscopy findings and their outcomes.

Conclusions

The investigation and treatment of swallowing problems in children are challenging. Early diagnosis and intervention, including feeding and swallowing therapy, are extremely important to support optimal growth and to prevent pulmonary complications. Most pediatric patients who aspirate thin and thickened liquids will have resolution of their aspiration with appropriate feeding and swallowing therapy within 7.68 and 11.04 months, respectively. Syndromic children and those with significant neurologic comorbidities are less likely to progress with therapy and require gastrostomy tube placement.

ARTICLE INFORMATION

Submitted for Publication: February 1, 2015; final revision received August 12, 2015; accepted August 25, 2015.

Published Online: October 22, 2015.
doi:10.1001/jamaoto.2015.2266.

Author Contributions: Drs Adil and Al Shemari contributed equally to this work. Drs Adil and Rahbar had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Adil, Perez, Hernandez, Urion, Rahbar.

Acquisition, analysis, or interpretation of data: Adil, Al Shemari, Kacprowicz, Perez, Larson, Hernandez, Kawai, Cowenhoven, Rahbar.

Drafting of the manuscript: Adil, Al Shemari, Kacprowicz, Perez, Cowenhoven, Urion, Rahbar.

Critical revision of the manuscript for important intellectual content: Adil, Perez, Larson, Hernandez, Kawai, Rahbar.

Statistical analysis: Adil, Kawai, Cowenhoven.

Administrative, technical, or material support: Adil, Al Shemari, Kacprowicz, Larson, Hernandez.

Study supervision: Adil, Perez, Rahbar.

Conflict of Interest Disclosures: None reported.

REFERENCES

1. Ravelli AM, Panarotto MB, Verdoni L, Consolati V, Bolognini S. Pulmonary aspiration shown by scintigraphy in gastroesophageal reflux-related respiratory disease. *Chest*. 2006;130(5):1520-1526.
2. Kirsch CM, Sanders A. Aspiration pneumonia. Medical management. *Otolaryngol Clin North Am*. 1988;21(4):677-689.
3. Blitzer A. Evaluation and management of chronic aspiration. *N Y State J Med*. 1987;87(3):154-160.
4. de Benedictis FM, Carnielli VP, de Benedictis D. Aspiration lung disease. *Pediatr Clin North Am*. 2009;56(1):173-190, xi.
5. Boesch RP, Daines C, Willging JP, et al. Advances in the diagnosis and management of chronic pulmonary aspiration in children. *Eur Respir J*. 2006;28(4):847-861.
6. Platzer ACG. Gastroesophageal reflux and aspiration syndromes. In: Chernick V, Boat TF, Wilmott RW, Bush A, eds. *Kendig's Disorders of the Respiratory Tract in Children*. 7th ed. Philadelphia, PA: Saunders Elsevier; 2006:592-609.
7. Colombo JL. Pulmonary aspiration. In: Hilman BC, ed. *Pediatric Respiratory Disease: Diagnosis and Treatment*. Philadelphia: WB Saunders Co; 1993: 429-436.
8. Gaudes GS. Pulmonary manifestations of gastroesophageal reflux disease. *Ann Thorac Med*. 2009;4(3):115-123.
9. Rifley WJ, Little AG. Gastroesophageal reflux and respiratory disease. *Pulmon Crit Care Update*. 1990; 5:2-5.
10. Rosen R, Nurko S. The importance of multichannel intraluminal impedance in the evaluation of children with persistent respiratory symptoms. *Am J Gastroenterol*. 2004;99(12):2452-2458.
11. Rosen R, Hart K, Nurko S. Does reflux monitoring with multichannel intraluminal impedance change clinical decision making? *J Pediatr Gastroenterol Nutr*. 2011;52(4):404-407.