Published in final edited form as:

Gastrointest Endosc Clin N Am. 2008 January ; 18(1): 73–ix. doi:10.1016/j.giec.2007.09.006.

Esophageal Dysmotility in patients with Eosinophilic Esophagitis

Samuel Nurko, MD MPH and Rachel Rosen, MD MPH

Center for Motility and Functional Gastrointestinal Disorders, Children's Hospital Boston

Summary

The understanding of esophageal motility alterations in patients with eosinophilic esophagitis is in its infancy despite the common presenting complaint of dysphagia. A diversity of motility disorders has been reported in patients with EE including achalasia, diffuse esophageal spasm, nutcracker esophagus and non-specific motility alterations including high amplitude esophageal body contractions, tertiary contractions, LES pressure abnormalities and other peristaltic problems. Some evidence suggests that treatment of EE will result in some improvements in motility. The advent of technology such as high resolution manometry and combined manometry with impedance may provide new insight into more subtle motility abnormalities.

One of the primary presenting symptoms in patients with eosinophilic esophagitis (EE) is dysphagia. Even though it is a very common symptom, its etiology is unclear. In some cases it is related to anatomic problems such as strictures. In most patients, however, there is no underlying anatomic problem raising the possibility that there may be an underlying esophageal motility disturbance. There is very limited information regarding esophageal motility patterns in patients with EE, but in recent years, small numbers of basic and clinical studies have begun to explore the cause for this dysphagia.

In this chapter, we will review the existing data focusing on motility alterations in patients with EE and its pathophysiological meaning.

Dysphagia

Intermittent dysphagia and food impactions are the most common presenting symptoms associated with EE in older children and adults. In a report of 103 children, 26% of patients presented with dysphagia (mean age 13 years) and 6.8% with food impaction (mean age 16 years) (1). Other pediatric series have found that food impaction was the initial presenting symptom in up to 20% of the patients(2). In adults, the main presenting symptom is dysphagia which has been reported in 29 to 100% of patients with EE (3).

Dysphagia in patients with EE is usually long standing, may be intermittent, and is resistant to therapy with acid blockade. It may be secondary to focal and diffuse esophageal narrowing consistent with esophageal strictures, rings or small caliber esophagus (4–6), the

Corresponding author: Samuel Nurko MD MPH, Director Center for Motility and Functional Gastrointestinal Disorders, Children's, Hospital Boston, Hunnewell – Ground, 300 Longwood Avenue, Boston, MA 02115, samuel.nurko@childrens.harvard.edu, phone; 617 355 6055, Fax 617-730-0043.

Rachel Rosen MD MPH, Hunnewell – Ground, 300 Longwood Avenue, Boston, MA 02115

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

presence of a Schatzki ring (SR) or if anatomic problems are excluded, to esophageal dysmotility, which is the main focus of the present chapter.

Etiopathogenesis of esophageal dysmotility

The etiopathogenesis of esophageal dysmotility is not well understood. It may be related to the eosinophilic infiltration of the esophageal mucosa and its interactions with the microenvironment. Studies in which full thickness biopsies of patients with EE documented eosinophilic infiltration in all esophageal layers (7–11).

The exact mechanisms by which eosinophilic infiltration may produce esophageal dysmotility is not certain but several speculations exist. First, co-culture of fibroblasts with eosinophils results in increased contraction of the fibroblasts which may result in abnormal motility (12). Second, eosinophil degranulation has been associated with axonal necrosis which may have an impact on esophageal motility (11,13,14). Third, eosinophil derived major basic protein binds muscarinic acetylcholine receptors (15,16) that can lead to smooth muscle contraction and subsequent dysmotility. Fourth, the gastric eosinophilia is associated with dysmotility though the direct cause is uncertain (17); some data suggests that the inflammatory cytokines IL-1 and IL-6 inhibit acetylcholinesterase release and result in esophageal dysmotility in animal models of esophagitis but their role in eosinophilic esophagitis in humans is unknown (18).

While endoscopic ultrasound data shows an increase esophageal wall thickness as well as expansion of the mucosa, submucosa and muscularis propria in patients with EE (19), recent data suggests that the expression of one of the most potent eosinophil chemoattractants, eotaxin-3, is upregulated only in the epithelial cells of the esophagus suggesting that esophageal mediated inflammation may begin in the epithelium and that the resultant damage to the submucosa may be a secondary effect (20). There may also be a potential role of activated eosinophils in fibroblast proliferation and/or collagen deposition, which could produce secondary fibrosis especially since eosinophils have been shown to have pro-fibrogenic properties (21). See Chapters 3, 11, 12 and 13.

Apart from the role of the eosinophil as the offender in esophageal motility alterations, mast cells may exert a negative effect on esophageal motility. Mast cells are located in the esophagus and are present in higher numbers in patients with EE and mast cell genes are upregulated in patients with EE (20) They also exert an effect on fibrosis by releasing proinflammatory mediators such as TNF alpha, TNF beta, tryptase and they can independently produce type IV collagen (22,23). Additionally, the activation of acetylcholine by histamine released from mast cells in the esophageal wall may cause contraction of the muscle fibers in the muscularis mucosa resulting in uncoordinated contractions or hypocontraction (24). See Chapters 12 and 13.

It is not clear if the motility abnormalities are specific to EE, or just secondary to non-specific eosinophilic infiltration (9,11,25). Much of the data available on the role of eosinophils in the dysmotility is derived from models of the esophagus that are non-allergic in origin or are derived from studies of eosinophils in different organ systems. Additional studies are critical in patients with eosinophilic esophagitis or in models with an allergic foundation.

Esophageal Motility abnormalities

Stationary Esophageal manometry

Esophageal motility has not been well characterized in patients with EE. The results of stationary manometry are varied and include findings ranging from normal peristalsis to

ineffective peristalsis (particularly after meals) including simultaneous contractions, and high amplitude esophageal body contractions, achalasia, diffuse esophageal spasms, tertiary contractions, aperistalsis, nonspecific motor disorders, nutcracker esophagus and high amplitude contractions particularly in the lower esophagus (26).

In the initial report by Attwood (26), 10 of 12 patients had abnormal esophageal peristalsis by stationary manometry; two had diffuse esophageal spasm (DES), two nutcracker esophagus, three had a mean amplitude of contractions that was < than the 2.5 percentile of normal, and 4 had contractions of short duration. All 12 patients had normal LES pressure and function (26). In a report from 1978, Landres et al described a patient with vigorous achalasia that had underlying severe eosinophilic infiltration of the esophageal mucosa. In that case the symptoms were probably related to the achalasia, but it suggested the possibility that EE may predispose to a motor esophageal disorder (8). Dobbins et al described one patient with EE that had esophageal spasm (27).

Since the initial reports there have been at least 22 published series or case reports in which the results of esophageal manometry have been reported, 19 adult and 3 pediatric studies (Table 1). Esophageal manometry has been reported in 144 patients, 115 adults and 29 children. The studies are summarized in Table 1.

Most of the abnormalities have been described in adults, although as can be seen in the Table, one third of children may also have peristaltic abnormalities during stationary manometry. Primary motility disorders were rare but found in 12 adult patients with EE: two had achalasia, 7 had DES and 3 had nutcracker esophagus. The remaining abnormalities were largely nonspecific and affected mainly the peristalsis. Of the 144 patients, 129 had a normal lower esophageal sphincter tone. The LES was hypotensive with normal relaxation in 12, hypertensive with normal relaxation in 3, and incomplete relaxation in 2 patients who had a diagnosis of achalasia. Non-specific peristaltic abnormalities (tertiary contractions, low amplitude, ineffective peristalsis) were reported in 42/144 patients (35 adults and 7 children), and high amplitude contractions were reported in 11 patients (all adults). Hence, abnormal esophageal manometry was found in 59 (41%) patients who underwent this procedure. No prospective large studies have been performed to determine if the manometric abnormalities result in abnormal esophageal transit or if the severity of histologic disease correlates with manometric abnormalities or the severity of dysphagia.

Some investigators suggest the existence of different phases in the development of esophageal motor abnormalities. Initially the motility is normal, and then motor alterations develop with hyperperistaltic or spastic abnormalities that eventually evolve into abnormal peristalsis with low amplitude simultaneous contractions (28). This evolution has been observed in other disorders affecting esophageal function like GERD or achalasia (28).

Studies with High resolution manometry

High resolution manometry offers some advantages over standard manometry; the catheters have increased numbers of recording sites and decreasing the spacing between them allowing the clinician to completely define the intraluminal pressures and reduce movement-related artifacts (29,30). The technology allows for seamless, dynamic representation of peristalsis at every axial position within and across the esophagus though the role of this increased data in clinical management is unclear (29,30). Recent studies showed that HRM predicts the presence of abnormal bolus transport more accurately than conventional manometry, and identified clinically important motor dysfunction that was not detected by standard manometry and radiography (31). In a recent study using HRM in 24 patients with EE (Table 2), Chen et al describe that the most common motility abnormality was elevation in peristaltic velocity; subsets of patients had failed esophageal peristalsis and impaired LES

junction relaxation, and one patient had a significantly elevated esophageal contractile pressure (32).

Studies with combined esophageal impedance and manometry

Technological advances have allowed the pairing of impedance sensors and with pressure sensors in a single catheter. The addition of impedance provides insight into the transit of liquid, viscous and solid food in the esophagus, and its relation with esophageal peristalsis. The sensors provide information about the transit time of substances down the esophagus and can identify areas of the esophagus that retain ingested contents suggesting impaired motility. Studies in adults showed that manometric evidence demonstrating ineffective peristalsis may underestimate the true bolus clearance; thus the combined impedance with manometry may be a more sensitive technique to assess esophageal function, and to evaluate patients with dysphagia (33–35). The combined use of manometry and impedance has shown that approximately 97% of normal peristaltic swallows have normal bolus transit, but also that almost half of manometrically ineffective swallows have normal bolus transit suggesting that motility abnormalities may not be representative of true esophageal function (35). In children preliminary information has shown that effective bolus clearance by impedance is present in 75% of swallows that had ineffective peristalsis (34).

While no large studies have been completed in patients with EE, preliminary data from our center suggests that this new technology may help clarify the degree of esophageal dysfunction in patients with EE. Figures 1, 2 and 3 show a normal swallow with good clearance of the esophagus as detected by impedance (Fig 1), a swallow with evidence of esophageal spasm with normal esophageal clearance (Fig 2) and a swallow with abnormal peristalsis and poor esophageal clearance (Fig 3).

Studies with Prolonged esophageal manometry

The majority of patients with EE and dysphagia have normal esophageal stationary manometries. While this may be a limitation of the technology, other possibilities to explain the normal results include the study's short duration, its performance during fasting rather than meal periods and the lack of symptoms that typically occur during the short study duration. Prolonged esophageal manometry, conducted over 24 hours, allows the clinician to measure motility during meal periods and provides more opportunities to capture symptoms with the catheter in place (Table 2).

We performed 24 ambulatory pH/manometry measurements on 17 children with EE, and compared their findings to control patients and children with GERD (Table 2). All controls and children with GERD had a normal stationary manometry, while 41% of those with EE had nonspecific peristaltic abnormalities. Patients with EE had a significantly higher percent of ineffective peristalsis (Figure 4), high amplitude contractions (> 180 mmHg) (Figure 5) and isolated contractions compared to control patients in a 24 hour period (36). Importantly, abnormal esophageal peristaltic events correlated with dysphagia during the study. In our case series, there were no motility abnormalities in patients with documented peptic esophagitis suggesting that the inflammation alone was not responsible for the motor abnormalities (37).

Effect of treatment on esophageal motility abnormalities

It is not clear if non-specific motor abnormalities are responsible for the dysphagia and it has been suggested the abnormalities found during stationary manometry may be non-specific. Three case reports and one prospective study tried to establish if the motor abnormalities would disappear after successful treatment (Table 3). In one case report with a patient with

achalasia and EE, normal peristalsis returned after myotomy. Two other patients experience resolution of non-specific motor abnormalities after treatment with either systemic or swallowed steroids (28,38). In the only prospective study, Lucendo et al report the manometric abnormalities in 12 patients. Of those 9 had abnormal esophageal peristalsis before treatment: Six had a nonspecific esophageal motor disorder characterized by up to 80% of non-transmitted or very low amplitude waves in the distal esophagus, and 3 with high amplitude contractions in the distal esophagus. Of those 9 patients, an esophageal manometry was repeated in 7 patients after successful treatment with fluticasone; in all 7 patients, the esophageal motor problems and the dysphagia had improved. They found a significant increase in the number of normal peristaltic waves ($p=0.018$) as well as a significant decrease in non-transmitted and high amplitude waves (28). While the data is limited to a small number of individual cases, treatment of the EE does seem to improve manometric abnormalities and the associated symptom of dysphagia.

Other possible explanations for the dysphagia

It is often difficult to demonstrate if subtle motor abnormalities are responsible for symptoms; adult studies have shown that non-specific motor disorders do not consistently result in functional abnormalities (35). As mentioned before, patients with EE have a high incidence of esophageal narrowing and strictures which may represent diffuse thickening of the muscularis propria, or a functional constriction related to the marked infiltration of the myenteric plexus (11). It has also been postulated that the eosinophilic infiltrate leads to edema and inflammation, perhaps evolving over time to fibrosis. Straumann et al demonstrated architectural alteration and increased fibrous tissue in some patients with long-standing EE; the result is the narrow-bore esophagus (39). EUS studies have demonstrated the full-thickness nature of the condition. Chehade et al also demonstrated fibrosis in a significant proportion of children with EE, and they described that fibrosis was associated with the presence of dysphagia (40).

The dysphagia could also be related to mucosal plication. We recently described a series of 18 patient with Schatzki ring (SR) diagnosed by upper GI series. Eight of the patient with SR (44%) fulfilled criteria for EE including lack of response to acid blockade, normal pH probe monitoring of the distal esophagus, esophageal exudates and furrows and severe eosinophilic inflammation of the esophageal mucosa (41). However, these 8 children with EE did not have any endoscopic evidence of a SR despite an abnormal upper GI series. One hypothesis is that the ring appears and disappears as the longitudinal muscle of the esophagus contracts and relaxes below a redundant, overlying mucosa (42). Another hypothesis is that including mucosal edema and/or thickening of redundant, inflamed esophageal mucosa may result in the appearance of a SR.

Our previous work supports this speculation as endoscopic ultrasonographic evidence suggests that eosinophilic inflammation associated with EE extends beyond the squamous epithelium and into the esophageal submucosa and muscularis propria can be consistent with deep tissue edema and lack of tissue compliance (19). In a study in which high resolution ultrasound was used to compare esophageal tissue between 11 children with EE and 8 normal controls, we determined that children with EE developed significant esophageal wall expansion, with thickening of the total wall, mucosa, submucosa, and muscularis propria (19).

Adult data also suggests that the inflammation extends deep into the esophageal layers. Several case reports show evidence of eosinophils penetrating into all of the esophageal layers and even the paraesophageal connective tissue (9–11).

Conclusion

The etiopathogenesis of the dysphagia in patients with EE is probably multifactorial. Primary motility disorders like achalasia or diffuse esophageal spasms, as well as non-specific motility disorders including abnormal peristalsis, and high amplitude contractions, have been described. These abnormalities most likely result from the interactions between eosinophils and mast cells with the esophageal microenvironment. Even though some of the observed motility abnormalities improve after medical therapy, it is not clear if they are responsible for symptom improvement. Future studies are needed to determine the interrelationship between eosinophilic infiltration, abnormal motility testing and symptoms of dysphagia.

Acknowledgments

This work was supported in part by the Pappas Foundation, and NIH grant 1K23DK073713-01A1.

References

1. Noel RJ, Putnam PE, Collins MH, Assa'ad AH, Guajardo JR, Jameson SC, et al. Clinical and immunopathologic effects of swallowed fluticasone for eosinophilic esophagitis. *Clin Gastroenterol Hepatol* 2004;2(7):568–75. [PubMed: 15224281]
2. Khan S, Orenstein SR, Di Lorenzo C, Kocoshis S, Putnam PE, Sigurdsson L, et al. Eosinophilic Esophagitis. Strictures, Impactions, Dysphagia *Dig Dis Sci* 2003;48:22–29.
3. Sgouros SN, Bergele C, Mantides A. Eosinophilic esophagitis in adults: a systematic review. *Eur J Gastroenterol Hepatol* 2006;18(2):211–7. [PubMed: 16394804]
4. Walsh SV, Antonioli DA, Goldman H, Fox VL, Bousvaros A, Leichtner AM, et al. Allergic esophagitis in children: a clinicopathological entity. *Am J Surg Pathol* 1999;23(4):390–6. [PubMed: 10199468]
5. Teitelbaum JE, Fox VL, Twarog FJ, Nurko S, Antonioli D, Gleich G, et al. Eosinophilic esophagitis in children: immunopathological analysis and response to fluticasone propionate. *Gastroenterology* 2002;122(5):1216–25. [PubMed: 11984507]
6. Fox VL, Nurko S, Furuta GT. Eosinophilic esophagitis: it's not just kid's stuff. *Gastrointestinal Endoscopy* 2002;56:260–270. [PubMed: 12145607]
7. Nicholson AG, Li D, Pastorino U, Goldstraw P, Jeffery PK. Full thickness eosinophilia in oesophageal leiomyomatosis and idiopathic eosinophilic oesophagitis. A common allergic inflammatory profile? *J Pathol* 1997;183(2):233–6. [PubMed: 9390039]
8. Landres RT, Kuster GR, Strum W. Eosinophilic esophagitis in a patient with vigorous achalasia. *Gastroenterol* 1978;74:1298–1301.
9. Evrard S, Louis H, Kahaleh M, Zalcman M, Nagy N, El Nakadi I, et al. Idiopathic eosinophilic oesophagitis: atypical presentation of a rare disease. *Acta Gastroenterol Belg* 2004;67(2):232–5. [PubMed: 15285582]
10. Riou PJ, Nicholson AG, Pastorino U. Esophageal rupture in a patient with idiopathic eosinophilic esophagitis. *Ann Thorac Surg* 1996;62(6):1854–6. [PubMed: 8957408]
11. Stevoff C, Rao S, Parsons W, Kharilas P, Hirano I. EUS and histopathologic correlates in eosinophilic esophagitis. *Gastrointest Endosc* 2001;54:373–377. [PubMed: 11522985]
12. Zagai U, Skold CM, Trulson A, Venge P, Lundahl J. The effect of eosinophils on collagen gel contraction and implications for tissue remodeling. *Clin Exp Immunol* 2004;135(3):427–33. [PubMed: 15008974]
13. Dvorak AM, Onderdonk AB, McLeod RS, Monahan-Earley RA, Antonioli DA, Cullen J, et al. Ultrastructural identification of exocytosis of granules from human gut eosinophils in vivo. *Int Arch Allergy Immunol* 1993;102(1):33–45. [PubMed: 8400884]
14. Tottrup A, Fredens K, Funch-Jensen P, Aggestrup S, Dahl R. Eosinophil infiltration in primary esophageal achalasia. A possible pathogenic role *Dig Dis Sci* 1989;34(12):1894–9.

15. Hogan SP, Mishra A, Brandt EB, Royalty MP, Pope SM, Zimmermann N, et al. A pathological function for eotaxin and eosinophils in eosinophilic gastrointestinal inflammation. *Nat Immunol* 2001;2(4):353–60. [PubMed: 11276207]
16. Gundel RH, Letts LG, Gleich GJ. Human eosinophil major basic protein induces airway constriction and airway hyperresponsiveness in primates. *J Clin Invest* 1991;87(4):1470–3. [PubMed: 2010556]
17. Martin ST, Collins CG, Fitzgibbon J, Lee G, Quigley EM, O’Sullivan GC. Gastric motor dysfunction: is eosinophilic mural gastritis a causative factor? *Eur J Gastroenterol Hepatol* 2005;17(9):983–6. [PubMed: 16093877]
18. Cao W, Cheng L, Behar J, Fiocchi C, Biancani P, Harnett KM. Proinflammatory cytokines alter/reduce esophageal circular muscle contraction in experimental cat esophagitis. *Am J Physiol Gastrointest Liver Physiol* 2004;287(6):G1131–9. [PubMed: 15271650]
19. Fox VL, Nurko S, Teitelbaum JE, Badizadegan K, Furuta GT. High-resolution EUS in children with eosinophilic “allergic” esophagitis. *Gastrointest Endosc* 2003;57(1):30–6. [PubMed: 12518127]
20. Blanchard C, Wang N, Stringer KF, Mishra A, Fulkerson PC, Abonia JP, et al. Eotaxin-3 and a uniquely conserved gene-expression profile in eosinophilic esophagitis. *J Clin Invest* 2006;116(2):536–47. [PubMed: 16453027]
21. Levi-Schaffer F, Garbuzenko E, Rubin A, Reich R, Pickholz D, Gillery P, et al. Human eosinophils regulate human lung- and skin-derived fibroblast properties in vitro: a role for transforming growth factor beta (TGF-beta). *Proc Natl Acad Sci U S A* 1999;96(17):9660–5. [PubMed: 10449750]
22. Ruger B, Dunbar PR, Hasan Q, Sawada H, Kittelberger R, Greenhill N, et al. Human mast cells produce type VIII collagen in vivo. *Int J Exp Pathol* 1994;75(6):397–404. [PubMed: 7734329]
23. Xu X, Rivkind A, Pikarsky A, Pappo O, Bischoff SC, Levi-Schaffer F. Mast cells and eosinophils have a potential profibrogenic role in Crohn disease. *Scand J Gastroenterol* 2004;39(5):440–7. [PubMed: 15180181]
24. Mann NS, Leung JW. Pathogenesis of esophageal rings in eosinophilic esophagitis. *Med Hypotheses* 2005;64(3):520–3. [PubMed: 15617859]
25. D’Alteroche L, Bourlier P, Picon L, Viguier J, Metman EH, Machet MC, et al. Myotomy for esophageal muscular hypertrophy with eosinophil infiltration of the esophagus associated with toxocariasis revealed by esophageal motor disorder. *Gastroenterol Clin Biol* 1998;22(5):541–5. [PubMed: 9762293]
26. Attwood SE, Smyrk TC, DeMeester TR, Jones JB. Esophageal eosinophilia with dysphagia. A distinct clinicopathologic syndrome. *Dig Dis Sci* 1993;38:109–116. [PubMed: 8420741]
27. Dobbins JW, Sheahan D, Behar J. Eosinophilic gastroenteritis with esophageal involvement. *Gastroenterol* 1977;72:1312–1316.
28. Lucendo AJ. Motor disturbances participate in the pathogenesis of eosinophilic oesophagitis, beyond the fibrous remodeling of the oesophagus. *Aliment Pharmacol Ther* 2006;24(8):1264–7. [PubMed: 17014589]
29. Ghosh SK, Pandolfino JE, Zhang Q, Jarosz A, Shah N, Kahrilas PJ. Quantifying esophageal peristalsis with high-resolution manometry: a study of 75 asymptomatic volunteers. *Am J Physiol Gastrointest Liver Physiol* 2006;290(5):G988–97. [PubMed: 16410365]
30. Pandolfino JE, Ghosh SK, Zhang Q, Jarosz A, Shah N, Kahrilas PJ. Quantifying EGJ morphology and relaxation with high-resolution manometry: a study of 75 asymptomatic volunteers. *Am J Physiol Gastrointest Liver Physiol* 2006;290(5):G1033–40. [PubMed: 16455788]
31. Fox M, Hebbard G, Janiak P, Brasseur JG, Ghosh S, Thumshirn M, et al. High-resolution manometry predicts the success of oesophageal bolus transport and identifies clinically important abnormalities not detected by conventional manometry. *Neurogastroenterol Motil* 2004;16(5):533–42. 32. [PubMed: 15500509]
32. Chen J, Ghosh S, Pandolfino J, Kharilas PJ, Hirano I. Esophageal dysmotility in eosinophilic esophagitis: Analysis using high resolution esophageal manometry. *Gastroenterology* 2007;132(Supplement):A-6.

33. Nguyen NQ, Tippet M, Smout AJ, Holloway RH. Relationship between pressure wave amplitude and esophageal bolus clearance assessed by combined manometry and multichannel intraluminal impedance measurement. *Am J Gastroenterol* 2006;101(11):2476–84. [PubMed: 17029613]
34. Rosen R, Nurko S. Do abnormalities in peristalsis result in abnormal esophageal clearance? Use of esophageal function testing (EFT) a novel technology to evaluate dysphagia in children. *Gastroenterology* 2006;130(suppl 2):A-192–193.
35. Tutuian R, Castell DO. Combined multichannel intraluminal impedance and manometry clarifies esophageal function abnormalities: study in 350 patients. *Am J Gastroenterol* 2004;99(6):1011–9. [PubMed: 15180718]
36. Nurko SS, Fox VL, Furuta GT. Esophageal motor abnormalities in patients with eosinophilic esophagitis. A study using prolonged esophageal pH/manometry. *Neurogastro Mot* 2006;18:751.
37. Chitkara D, Fortunato C, Nurko S. Esophageal Motor Activity in Children with Gastro-esophageal Reflux Disease and Esophagitis. *J Pediatr Gastroenterol Nutr* 2005;40:70–75. [PubMed: 15625430]
38. Hempel SL, Elliott DE. Chest pain in an aspirin-sensitive asthmatic patient. Eosinophilic esophagitis causing esophageal dysmotility. *Chest* 1996;110:1117–1120. [PubMed: 8874281]
39. Straumann A, Spichtin H, Bucher KA, Herr P, Simon H. Natural history of primary eosinophilic esophagitis: A follow-up of 30 adult patients for up to 11.5. *Gastroenterol* 2003;125:1660–1669.
40. Chehade M, Sampson H, Morotti R, Magid M. Esophageal Subepithelial Fibrosis in Children with Eosinophilic Esophagitis. *JPGN*. 2007 In Press.
41. Nurko S, Teitelbaum JE, Husain K, Buonomo C, Fox VL, Antonioli D, et al. Association of Schatzki Ring with Eosinophilic Esophagitis in Children. *J Pediatr Gastroenterol Nutr* 2004;38:436–441. [PubMed: 15085025]
42. Chandrasanan AC, Lester PD, Johnson S, Sudarsanam D, Dunn D. Esophagogastric Ring: Why and when we see it, and What it implies: A radiologic-pathologic correlation. *Southern Medical Journal* 1992;85(10):946–952. [PubMed: 1411732]
43. Feczko P, Halpert R, Zonca M. Radiographic abnormalities in eosinophilic esophagitis. *Gastrointestinal Radiol* 1985;10:321–324.
44. Vitellas KM, Bennett WF, Bova JG, Johnston JC, Caldwell JH, Mayle JE. Idiopathic eosinophilic esophagitis. *Radiology* 1993;186(3):789–93. [PubMed: 8430189]
45. Borda F, Jimenez FJ, Martinez- Penuela JM, Echarri A, Martin-Granizo I. Eosinophilic esophagitis: an underdiagnosed entity? *Rev Esp Enferm Dig* 1996;88:701–4. [PubMed: 8983310]
46. Arora AS, Perrault J, Smyrk TC. Topical corticosteroid treatment of dysphagia due to eosinophilic esophagitis in adults. *Mayo Clin Proc* 2003;78(7):830–5. [PubMed: 12839078]
47. Croese J, Fairley SK, Masson JW, Chong AK, Whitaker DA, Kanowski PA, et al. Clinical and endoscopic features of eosinophilic esophagitis in adults. *Gastrointest Endosc* 2003;58:516–22. [PubMed: 14520283]
48. Vasilopoulos S, Murphy P, Auerbach A, Massey BT, Shaker R, Stewart E, et al. The small-caliber esophagus: an unappreciated cause of dysphagia for solids in patients with eosinophilic esophagitis. *Gastrointest Endosc* 2002;55(1):99–106. [PubMed: 11756928]
49. Kaplan M, Mutlu EA, Jakate S, Bruninga K, Losurdo J, Losurdo J, et al. Endoscopy in eosinophilic esophagitis: “feline” esophagus and perforation risk. *Clin Gastroenterol Hepatol* 2003;1(6):433–7. [PubMed: 15017642]
50. Straumann A, Spichtin HP, Grize L, Bucher KA, Beglinger C, Simon HU. Natural history of primary eosinophilic esophagitis: a follow-up of 30 adult patients for up to 11.5 years. *Gastroenterology* 2003;125(6):1660–9. [PubMed: 14724818]
51. Cantu P, Velio P, Prada A, Penagini R. Ringed oesophagus and idiopathic eosinophilic oesophagitis in adults: an association in two cases. *Dig Liver Dis* 2005;37(2):129–34. [PubMed: 15733527]
52. Remedios M, Campbell C, Jones DM, Kerlin P. Eosinophilic esophagitis in adults: clinical, endoscopic, histologic findings, and response to treatment with fluticasone propionate. *Gastrointest Endosc* 2006;63(1):3–12. [PubMed: 16377308]
53. Furuta K, Adachi K, Kowari K, Mishima Y, Imaoka H, Kadota C, et al. A Japanese case of eosinophilic esophagitis. *J Gastroenterol* 2006;41(7):706–10. [PubMed: 16933010]

54. Gonsalves N, Policarpio-Nicolas M, Zhang Q, Rao MS, Hirano I. Histopathologic variability and endoscopic correlates in adults with eosinophilic esophagitis. *Gastrointest Endosc* 2006;64(3): 313–9. [PubMed: 16923475]
55. Lucendo AJ, Castillo P, Martin-Chavarri S, Carrion G, Pajares R, Pascual JM, et al. Manometric findings in adult eosinophilic oesophagitis: a study of 12 cases. *Eur J Gastroenterol Hepatol* 2007;19(5):417–24. [PubMed: 17413294]
56. Orenstein SR, Shalaby TM, Di Lorenzo C, Putnam PE, Sigurdsson L, Kocochis S. The spectrum of pediatric eosinophilic esophagitis beyond infancy: a clinical series of 30 children. *Am J Gastroenterol* 2000;95(6):1422–30. [PubMed: 10894574]
57. Cheung KM, Oliver MR, Cameron DJ, Catto-Smith AG, Chow CW. Esophageal eosinophilia in children with dysphagia. *J Pediatr Gastroenterol Nutr* 2003;37(4):498–503. [PubMed: 14508223]
58. Luis AL, Rinon C, Encinas JL, Prieto G, Molina M, Sarria J, et al. Non stenotic food impaction due to eosinophilic esophagitis: a potential surgical emergency. *Eur J Pediatr Surg* 2006;16(6): 399–402. [PubMed: 17211786]

Figure 1. Normal esophageal peristalsis with good esophageal clearance as evidenced by a drop in impedance followed by a subsequent return to baseline in all of the impedance channels.

Figure 2.

A high amplitude contraction in the distal esophagus with normal esophageal clearance as evidenced by drop in impedance followed by a subsequent return to baseline in all of the impedance channels.

Figure 3.
Simultaneous, non-peristaltic esophageal contractions with no impedance changes in the esophagus indicating poor esophageal clearance.

Figure 4.
Tracing from a 24 hour manometry showing absent mid-esophageal peristalsis with a simultaneous symptom of dysphagia.

Figure 5.
Tracing from a 24 hour manometry showing high amplitude distal contractions.

Table 1
Summary of studies in which stationary esophageal manometry was performed in adults and children with EE
DES- diffuse esophageal spasms; NEMD- Nonspecific motility disorders.

Name/Year (Ref)	n	LES				Esophageal peristalsis				Other diagnosis		
		Normal	Hypo- tensive	Hyper- tensive	Abnorma l relaxation	Normal	High amplitude	Abnormal peristalsis NSMD	Type of abnormal peristalsis	Achalasia	DES	Nutcracker
Dobbins 1977 (27)	1	1					1				1	
Landres 1978 (8)	1			1	1		1		Simultaneous contractions	1		
Feczko 1985 (43)		1						1	Simultaneous contractions			
Attwood 1993 (26)	12	12				1		7	3 low amplitude; 4 short duration		2	2
Vitellas 1993 (44)	13	12		1		12	1				1	
Borda 1994 (45)	1	1						1	Absent peristalsis			
Hempel 1996 (38)	1		1								1	
Arora 2003 (46)	6	6				4	1	1				1
Croese 2003 (47)	13	13				8		5				
Stevoff 2004 (11)	1		1					1	Aperistalsis upper and middle esophagus, simultaneous lower esophagus			
Vasilopoulos 2002 (48)	4	4				4						
Kaplan 2005 (49)	5	5				4					1	
Straumann 2003 (50)	3	3				3						
Evrard 2004 (9)	1			1	1					1		
Cantu 2005 (51)	2	2				1		1	Absence of peristalsis middle esophagus			
Remedios 2006 (52)	23	15	8			19	3	1	aperistalsis			
Furuta 2006 (53)	1						1	1	Ineffective peristalsis, simultaneous contractions			
Gonsalves 2006 (54)	15	15				5		9			1	
Lucendo 2007 (55)	12	10	2			2	3	7	6 severe Interrupted peristalsis, low amplitude			

Adults											
Name/year (Ref)	n	LES				Esophageal peristalsis				Other diagnosis	
		Normal	Hypo-tensive	Hyper-tensive	Abnormal I relaxation	Normal	High amplitude	Abnormal peristalsis NSMD	Type of abnormal peristalsis	Achalasia	Nutcracker
Total (Adults)	115	100	12	3	2	63	11	35	contractions; 1 simultaneous	2	3
Children											
Name/year (Ref)	n	LES				Esophageal peristalsis				Other diagnosis	
		Normal	Hypo-tensive	Hyper-tensive	Abnormal relaxation	Normal	High amplitude	Abnormal peristalsis	Type of abnormal peristalsis	Achalasia	Nutcracker
Orenstein 2000 (56)	1	1				1					
Cheung 2003 (57)	11	11				11					
Nurko 2005 (36)	17	17				10		7	Ineffective peristalsis, low amplitude		
Total (Children)	29	29				22		7			
All patients											
Name/year (Ref)	n	LES				Esophageal peristalsis				Other diagnosis	
		Normal	Hypo-tensive	Hyper-tensive	Abnormal relaxation	Normal	High amplitude	Abnormal peristalsis	Type of abnormal peristalsis	Achalasia	Nutcracker
TOTAL (Adults and Children)	144	129	12	3	2	85	11	42		2	3

Table 2

Summary of prolonged and high resolution manometry studies

24 hour prolonged pH/manometry	n	Age	
Luis 2006 (58)	13	Median age: 12 (7.6–14.4 years)	Normal LES. 10% had high amplitude contractions in the distal esophagus. All patients had an increased mean duration (> 7 sec) of the esophageal contractions as compared to controls.
Nurko 2006(36)	17	Mean age: 9.7 ± 1.1 years	High number of high amplitude contractions. Significant decrease in complete peristaltic waves, as well as a significant increase in ineffective peristalsis, both during fasting and during meals as compared to controls. High correlation between symptoms with ineffective peristalsis.
HIGH RESOLUTION MANOMETRY	n	Age	
Chen 2007 (32)	24	Mean age: 42 (14–80 years)	Elevation in esophageal peristaltic velocity. Subsets of patients had failed esophageal peristalsis and impaired esophago-gastric junction relaxation, and one patient had a significantly elevated esophageal contractile pressure.

Table 3

Studies in which esophageal manometry was performed before and after treatment for EE.

		Before treatment	Treatment	After treatment
Name/year (Ref)	n	Peristalsis		Peristalsis
Landres 1978 (8)	1	Vigorous achalasia	Myotomy	Normal peristalsis Normal LES pressure
Hempel 1996 (38)	1	Low LES DES	Systemic steroids	Low LES Normal peristalsis
Lucendo 2006 (28)	1	Absent distal 2/3 Low amplitude simultaneous waves	Fluticasone	80% normal
Lucendo 2007 (55)	12	6 severe abnormal peristalsis 1 mildly abnormal peristalsis 3 high amplitude contractions	Fluticasone	7 patients with abnormal baseline manometry had a repeat test. In all there was significant improvement in number of peristaltic waves.