Journée d'Automne

29 août 2013

OESOPHAGITE A EOSINOPHILES: COORDINATION MÉDECIN DE FAMILLE – SPÉCIALISTE

Sébastien Godat et Alain Schoepfer
Divison de Gastroentérologie et d'Hépatologie
CHUV, Lausanne

Questions

- Est-ce que c‘est une EoE?
- impaction alimentaire: dangereux ou pas?
- Quelle thérapie à choisir?
- Comment suivre?

Questions

- Est-ce que c‘est une EoE?
- impaction alimentaire: dangereux ou pas?
- Quelle thérapie à choisir?
- Comment suivre?

Definition

Eosinophilic esophagitis: Updated consensus recommendations for children and adults

JACI 2011;128:3-20

Chris A. Liacouras, MD, Glenn T. Furuta, MD, Ikuo Hirano, MD, Dan Atkins, MD, Stephen E. Attwood, MD, FRCS, FRCSI, MCh, Peter A. Bonis, MD, A. Wesley Burks, MD, Mirna Chehade, MD, Margaret H. Collins, MD, Evan S. Dellon, MD, MPH, Ranjan Dohil, MD, Gary W. Falk, MD, MS, Nirmala Gonsalves, MD, Sandeep K. Gupta, MD, David A. Katzka, MD, Alfredo J. Lucendo, MD, PhD, Jonathan E. Markowitz, MD, MSCE, Richard J. Noel, MD, Robert D. Odze, MD, FRCP, Philip E. Putnam, MD, FAAP, Joel E. Richter, MD, FACP, MACG, Yvonne Romero, MD, Eduardo Ruchelli, MD, Hugh A. Sampson, MD, Alain Schoepfer, MD, Nicholas J. Shaheen, MD, MPH, Scott H. Sicherer, MD, Stuart Spechler, MD, Jonathan M. Spergel, MD, PhD, Alex Straumann, MD, Barry K. Wershil, MD, Marc E. Rothenberg, MD, PhD,* and Seema S. Aceves, MD, PhD* *Aurora and Denver, Colo, Milwaukee, Wis, Cincinnati, Ohio, Rochester, Minn, Philadelphia, Pa, Basel and Lausanne, Switzerland, Chapel Hill and Durham, NC, Boston, Mass, Chicago, Ill, San Diego, Calif, New York, NY, Indianapolis, Ind, Tomelloso, Spain, Greenville, SC, and North Shields, United Kingdom*

Eosinophilic esophagitis represents a chronic, immune/antigen-mediated esophageal disease, characterized **clinically** by symptoms related to esophageal dysfunction and **histologically** by eosinophil predominant inflammation

clinically by **symptoms** related to esophageal dysfunction

Adults and Adolescents

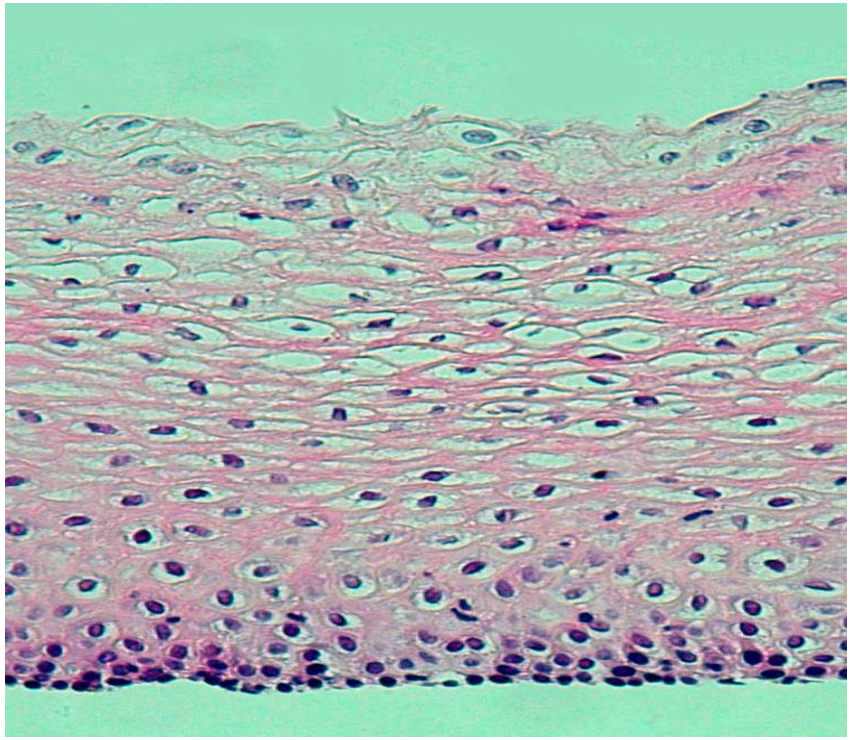
- Dysphagia for solids ≅100% (“slow-eaters” and “drinkers”)
- Long lasting food impaction (>35%; 148/414)
- Non-swallowing related retrosternal pain (>50%)

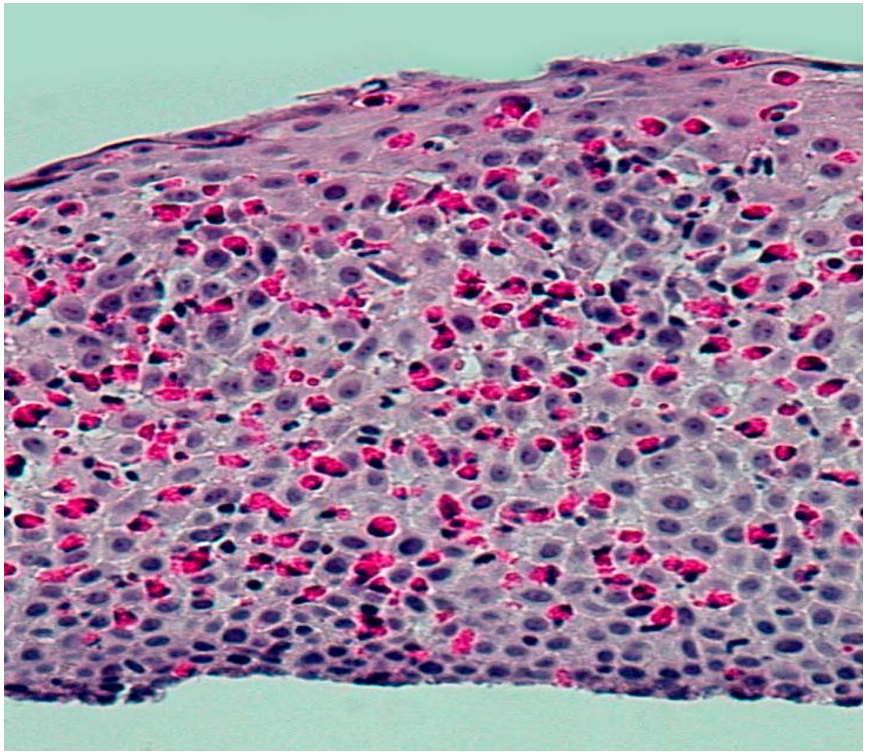
Children

- Food refusal
- Failure to thrive
- Vomiting, Regurgitation
- Chest Pain, abdominal Pain

1. Attwood SE et al. Dig Dis Sci 1993
2. Straumann A et al. SMW 1994
3. Furuta GE et al. Gastroenterol 2007
4. Liacouras CA et al. JACI 2011

Histologie





Peak eos count ≥ 15 eos/hpf

Esophageal eosinophilia: differential diagnosis

- GERD
- PPI responsive esophageal eosinophilia
- Eosinophilic gastroenteritis with esophageal involvement
- Drug hypersensitivity
- esophageal Crohn‘s disease
- invasive parasitosis (eg. Anisakis)

Proposals

PPI trial for 6-8 weeks

Re-endoscopy with Bx

EoE if ≥ 15 eos/hpf and DD excluded

Questions

- Est-ce que c‘est une EoE?
- impaction alimentaire: dangereux ou pas?
- Quelle thérapie à choisir?
- Comment suivre?

Consequences of food bolus impaction

Straumann A, et al. Clin Gastroenterol Hepatol 2008;6:598-600

697 confirmed EoE (SEED 2012)

35.2% (245/697**) long-lasting impactions** (necessity of bolus removal)

335 endoscopic interventions (1.4 per patient, range 1-5)

314x by flexible endoscopy

21x by rigid endoscopy

Perforations transmural:	9/335 ≅ 2.7%, 9/245 ≅ 3.7%
- Retching-induced:	5
- Procedure-induced (rigid):	4

….. and none of these patients was adequately treated

Straumann A, et al. Clin Gastro Hepatol 2008, up-dated

697 confirmed EoE (SEED 2012)

35.2% (245/697**) long-lasting impactions** (necessity of bolus removal)

335 endoscopic interventions (1.4 per patient, range 1-5)

314x by flexible endosco

Perforations transmural: 3.7%

- Retching-induced
- Procedure-induced (rig

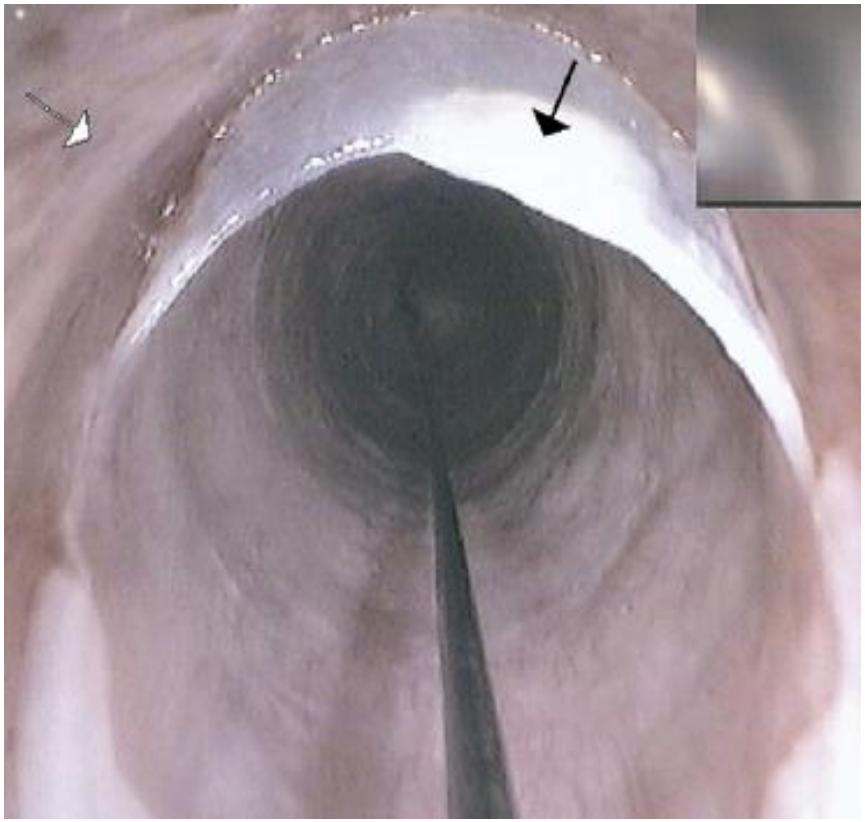
Rigid endoscopy:

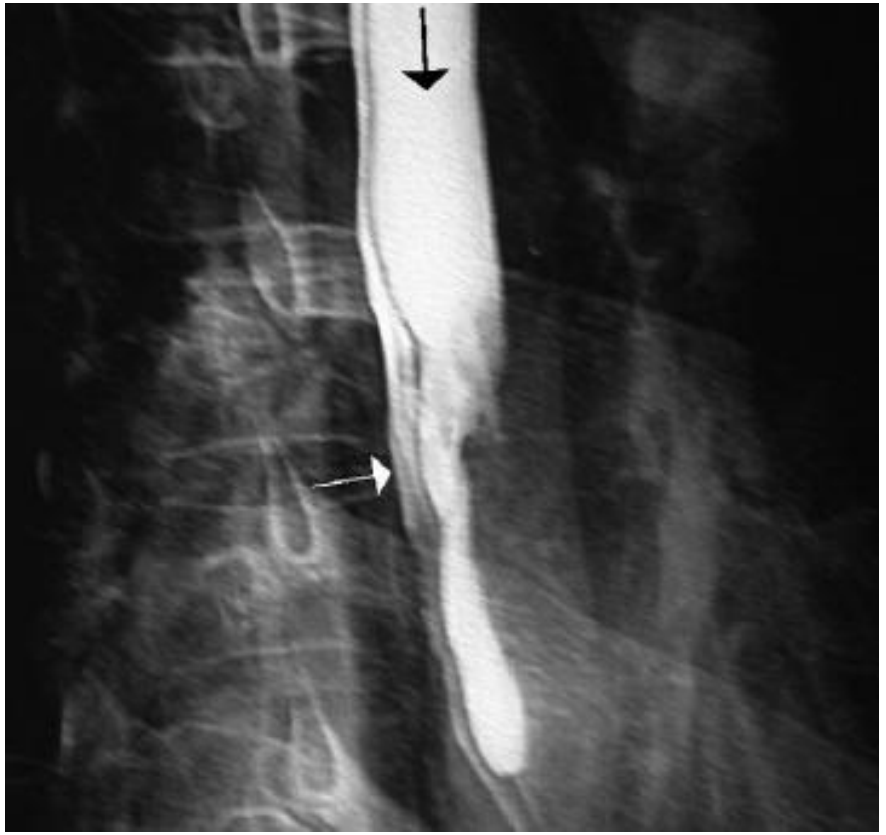
Perforation risk
4/21 = 19%

….. and none of these patients was adequately treated

Straumann A, et al. Clin Gastro Hepatol 2008, up-dated

Consequences of food bolus impaction



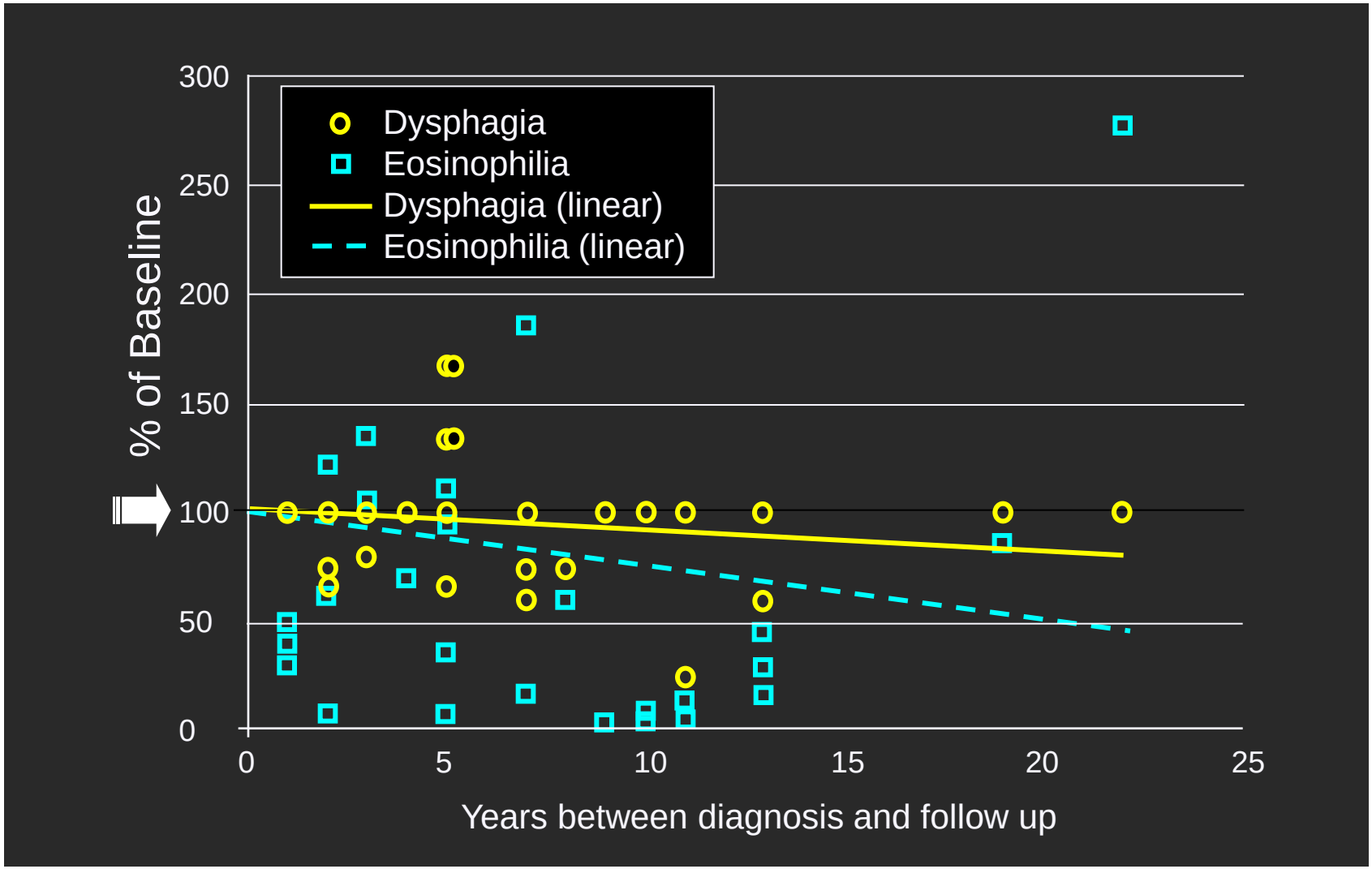


Straumann A, et al. Clin Gastroenterol Hepatol 2008;6:598-600

What happens without therapy?

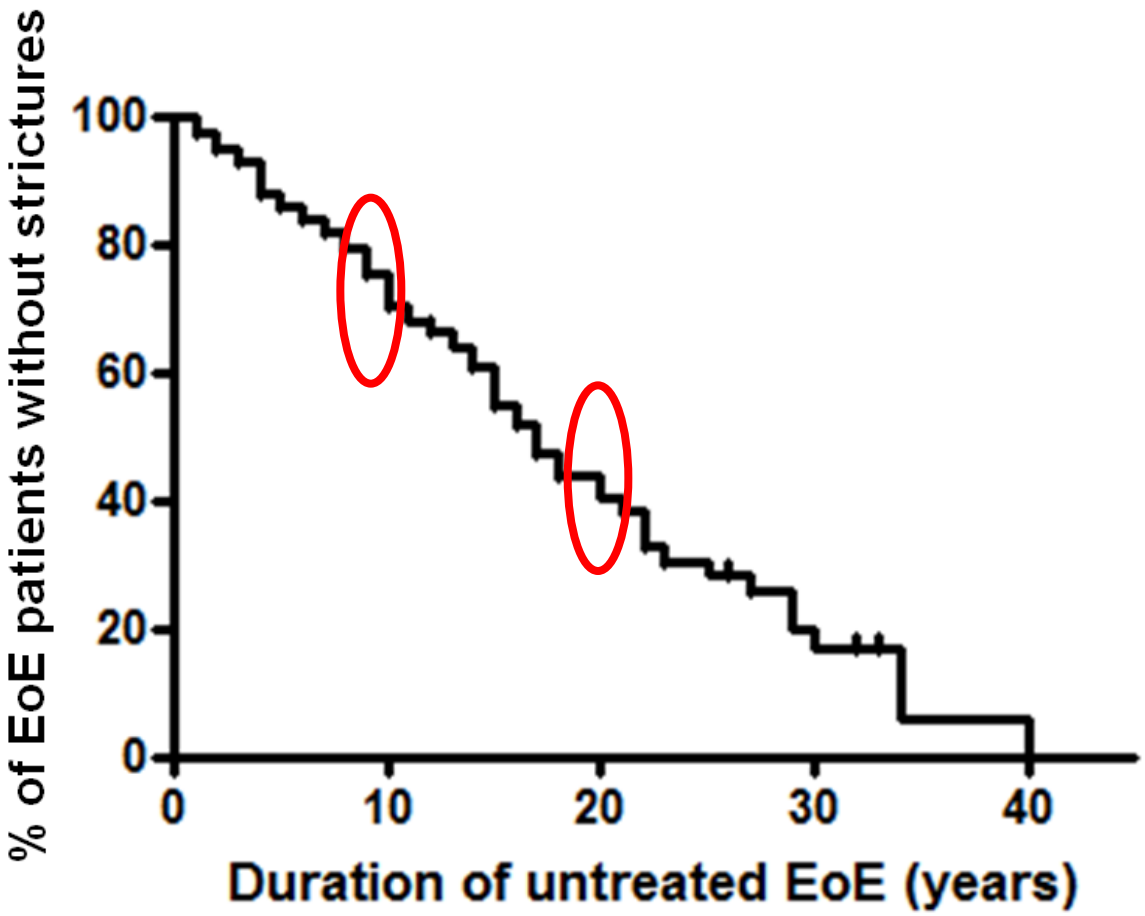
Intensity of Dysphagia and Inflammation over Time

30 Adults followed for a mean of 7.2 years



Straumann A, et al. Gasroenterol 2003;125:1660-69.

Stricture risk over time (n=200)



Schoepfer AM, Safroneeva E, et al, Gastroenterology, 2013

Conclusions

Untreated EoE leads to stricture formation

Strictures are associated with food impactions

Food impaction => perforation risk

EoE should be treated to avoid remodeling

Questions

- Est-ce que c‘est une EoE?
- impaction alimentaire: dangereux ou pas?
- Quelle thérapie à choisir?
- Quels intervals pour le suivi?

Therapeutic Options 2013: DDD

Drugs
- Corticosteroids systemically (e.g. prednisone)
- Corticosteroids topically (e.g. budesonide, fluticasone)
- Anti-Allergens (Leukotriene-Antagonists, CRTH2-Blocker)
- Biologicals (e.g. anti-IL5, anti-IL13)
- Immunosuppressant's (e.g. azathioprine, 6-mercaptopurine)

Diet
- Elemental Diet
- Elimination Diet (individually, allergy-testing based)
- Six-Food Elimination Diet

Dilation

Swallowed budesonide for EoE treatment

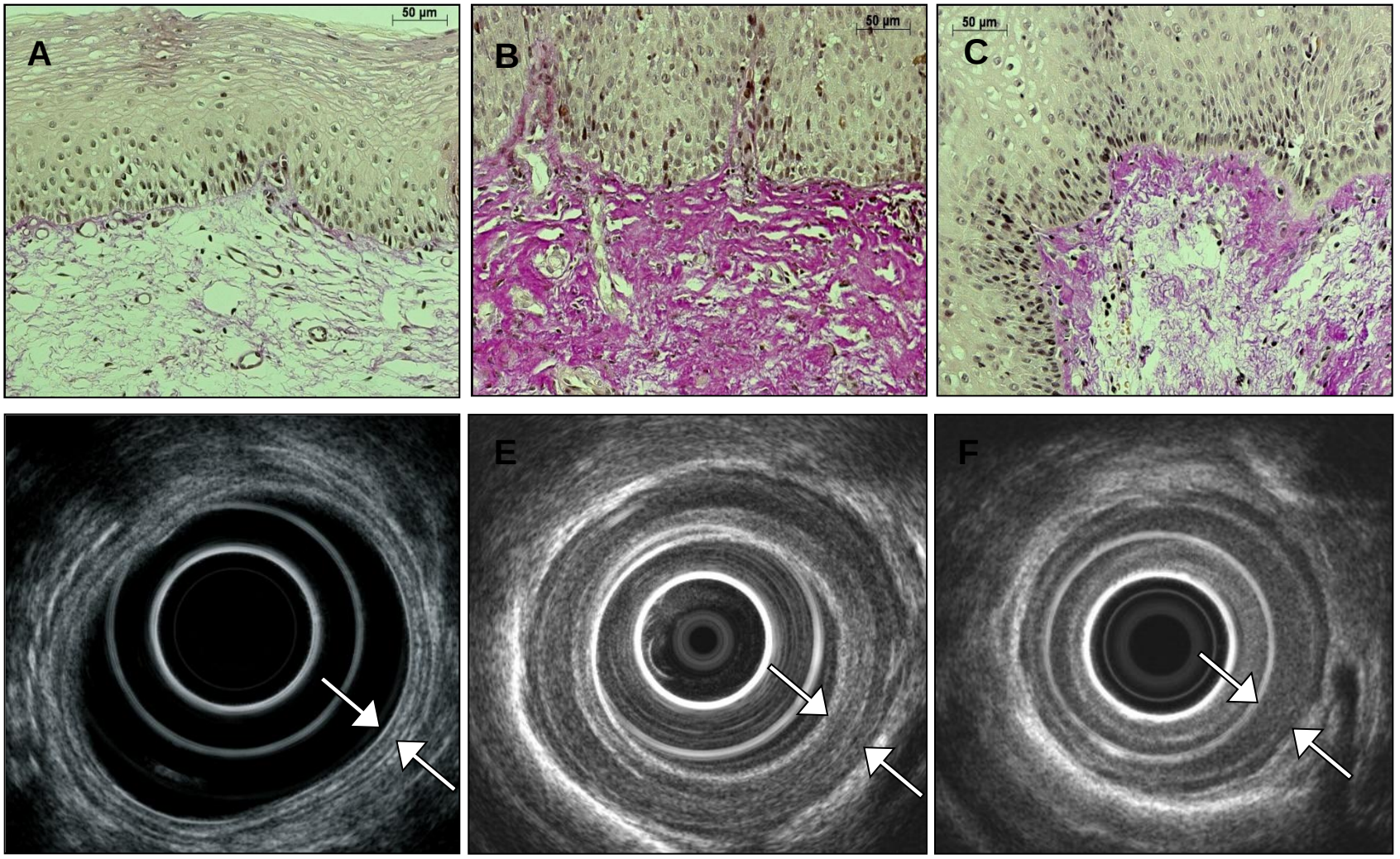
Control
(esophagus healthy)

EoE Patient
Pre-treatment

EoE Patient
Post-treatment

EvG

EUS



Straumann et al. *Clin Gastro Hepatol 2011*

Swallowed topical steroids: what form is best?

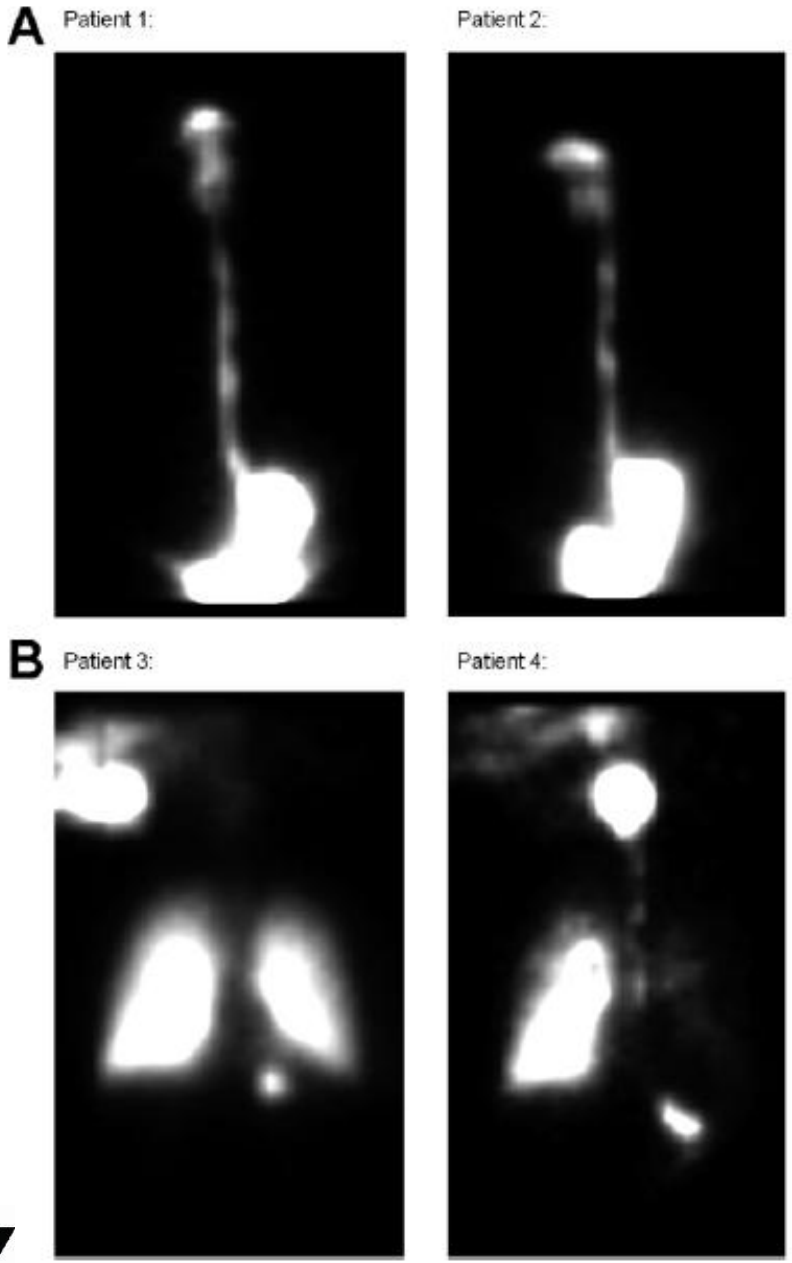
Viscous Topical Is More Effective Than Nebulized Steroid Therapy for Patients With Eosinophilic Esophagitis

EVAN S. DELLON,*,‡ ARIF SHEIKH,§ OLGA SPECK,‖ KIMBERLY WOODWARD,‖ ANN B. WHITLOW,§ JESSICA M. HORES,* MARIJA IVANOVIC,§ ALLEN CHAU,§ JOHN T. WOOSLEY,‖ RYAN D. MADANICK,*,‡ ROY C. ORLANDO,*,‡ and NICHOLAS J. SHAHEEN*,‡

*Center for Esophageal Diseases and Swallowing and ‡Center for Gastrointestinal Biology and Disease, Division of Gastroenterology and Hepatology, Department of Medicine, §Division of Nuclear Medicine, Department of Radiology, and ‖Department of Pathology and Laboratory Medicine, University of North Carolina School of Medicine, Chapel Hill, North Carolina

	Spray (NEB)	Syrup (OVB)	P-value
Number of patients	11	11	
Peak eos count before treatment	101±85	83±89	0.62
Peak eos count after treatment	89±94	11±23	0.02
Mean eos count after treatment	21±37	3±7	0.02

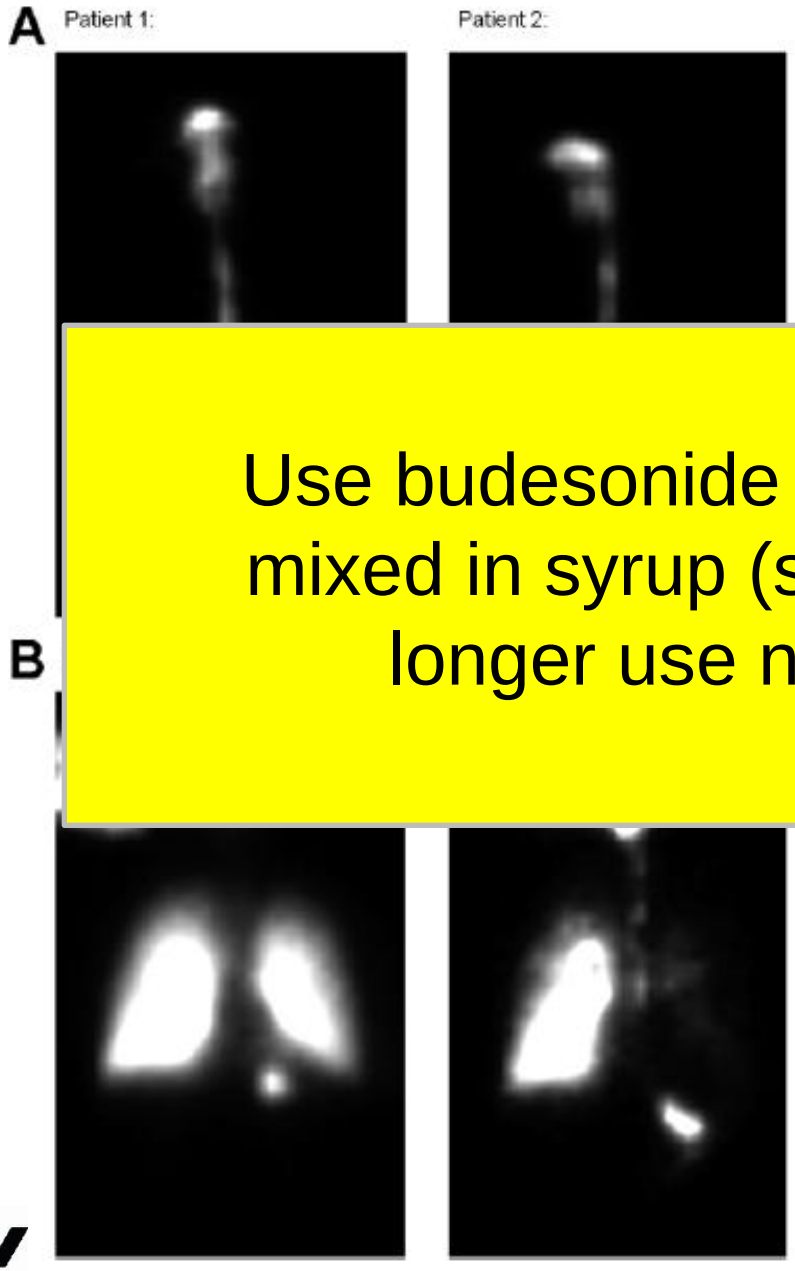
Gastroenterology 2012;321-4



Oral viscous budesonide (syrup)

Nebulized budesonide (spray)

Dellon ES, et al. Gastroenterology 2012;321-4



Oral viscous budesonide

Use budesonide or fluticasone mixed in syrup (sucralose), no longer use nebulizers

budesonide (spray)

Dellon ES, et al. Gastroenterology 2012;321-4

Prevalence of food allergies

Allergen	Prevalence	Remarks	Refer.
All	6-8% at one year 3-4% at age 14-16	Higher prevalence for IgE compared to symptoms	1,2
Cow milk	2-3% until age 2 yrs	Most often outgrown, high IgE correlated to lower chance for outgrow	3
Hen‘s egg	1-2% until age 2 yrs	Mostly outgrown with childhood	4
Peanut / tree nut	0.5-1.4% of children 0.5-1% of general pop.	Mostly lifelong disorder	5
wheat	0.4-1% of children	Mostly outgrown in childhood	6

1 Osborne NJ, et al. JACI 2011;127:668

2 Sicherer SH, et al. JACI 2006;117:470

3 Venter C, et al. JACI 2006;117:1118

4 Nickel R, et al. JACI 1997;99:613

5 Sicherer SH, et al. JACI 1999;103:559

6 Keet CA, et al. Ann All Asthm Immunol 2009;102:410

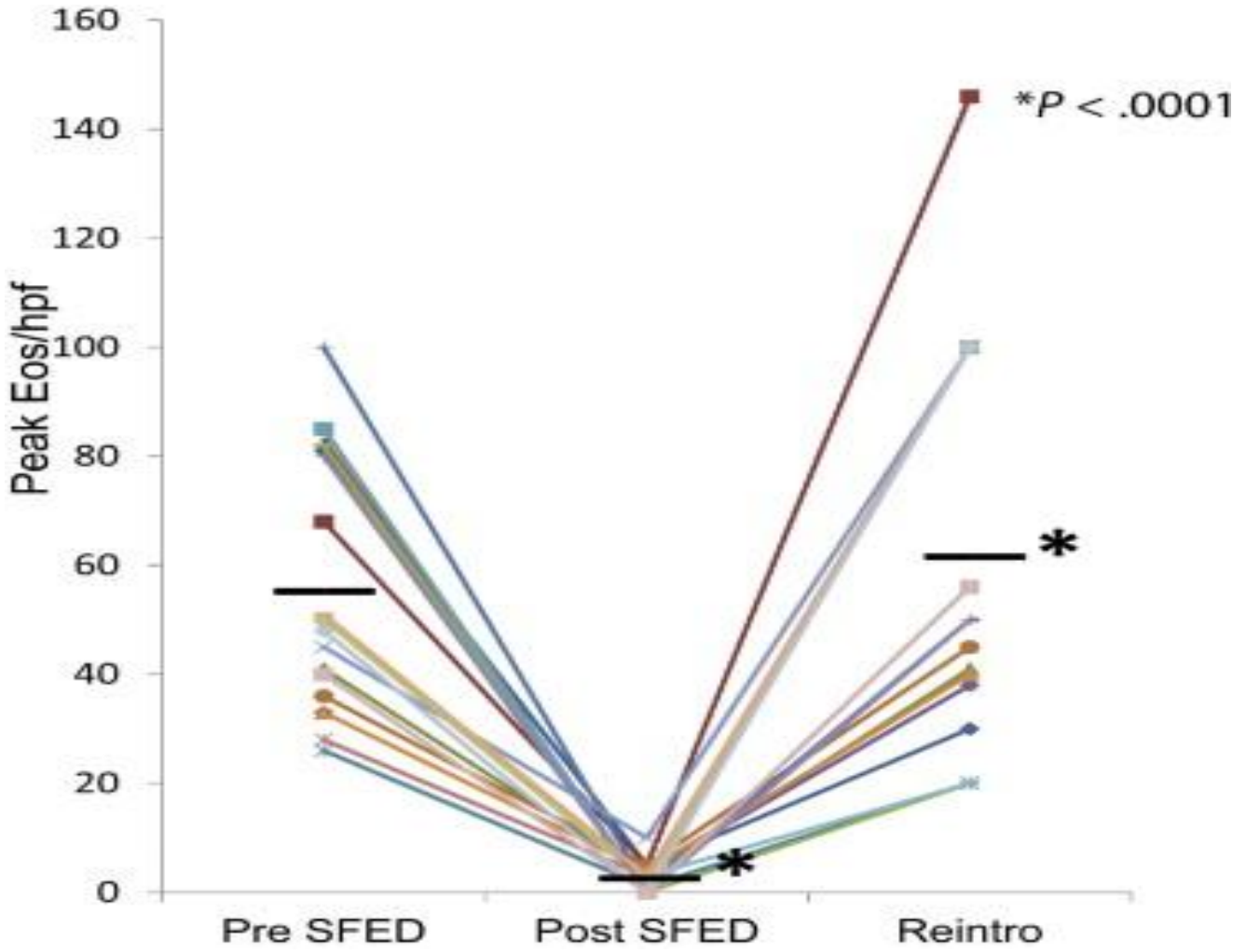
Most common food allergens

90% of IgE mediated allergies in young adults are caused by

- Cow‘s milk
- egg
- soy
- peanut / tree nuts
- wheat
- seafood

Sicherer SH, et al. JACI 2006;117:470

Elimination Diet Effectively Treats Eosinophilic Esophagitis in Adults; Food Reintroduction Identifies Causative Factors

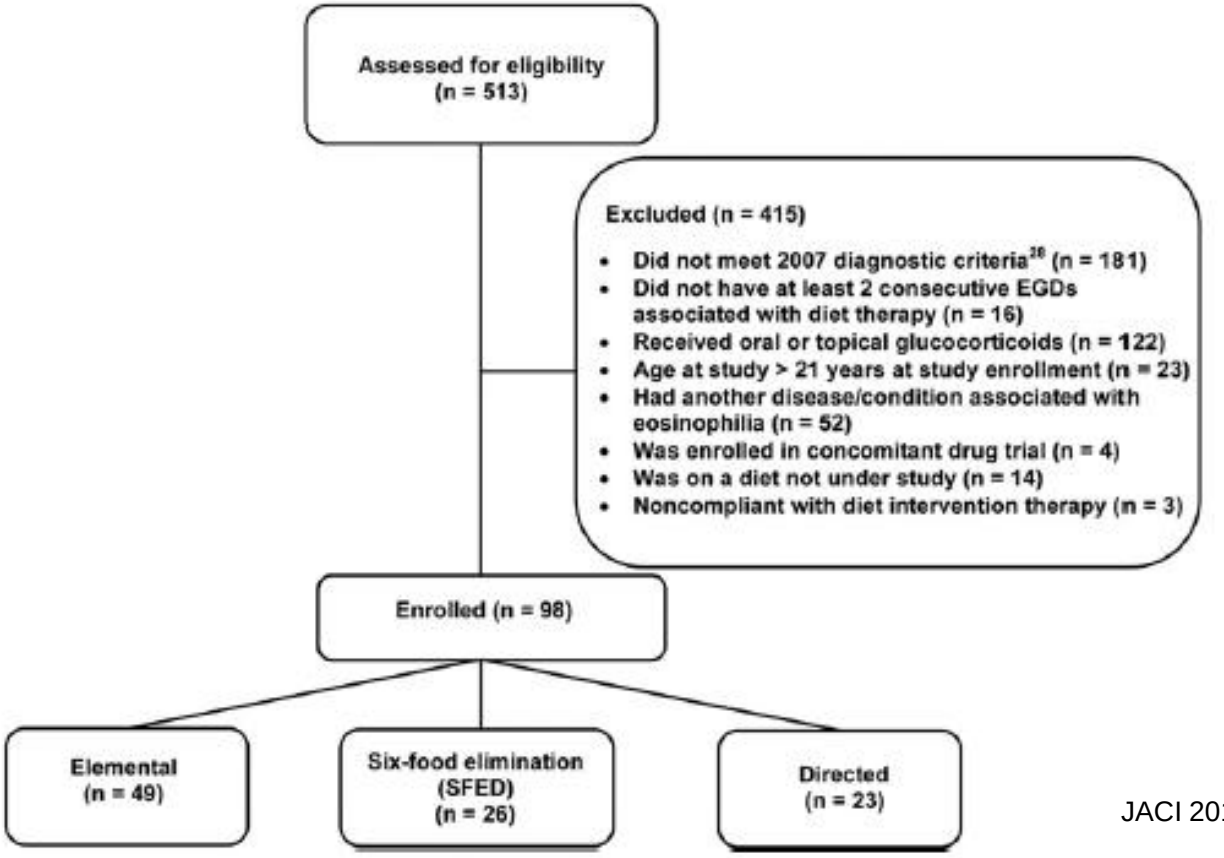


Gonsalves N, et al. Gastroenterology Volume 142, Issue 7 2012 1451 - 1459.e1

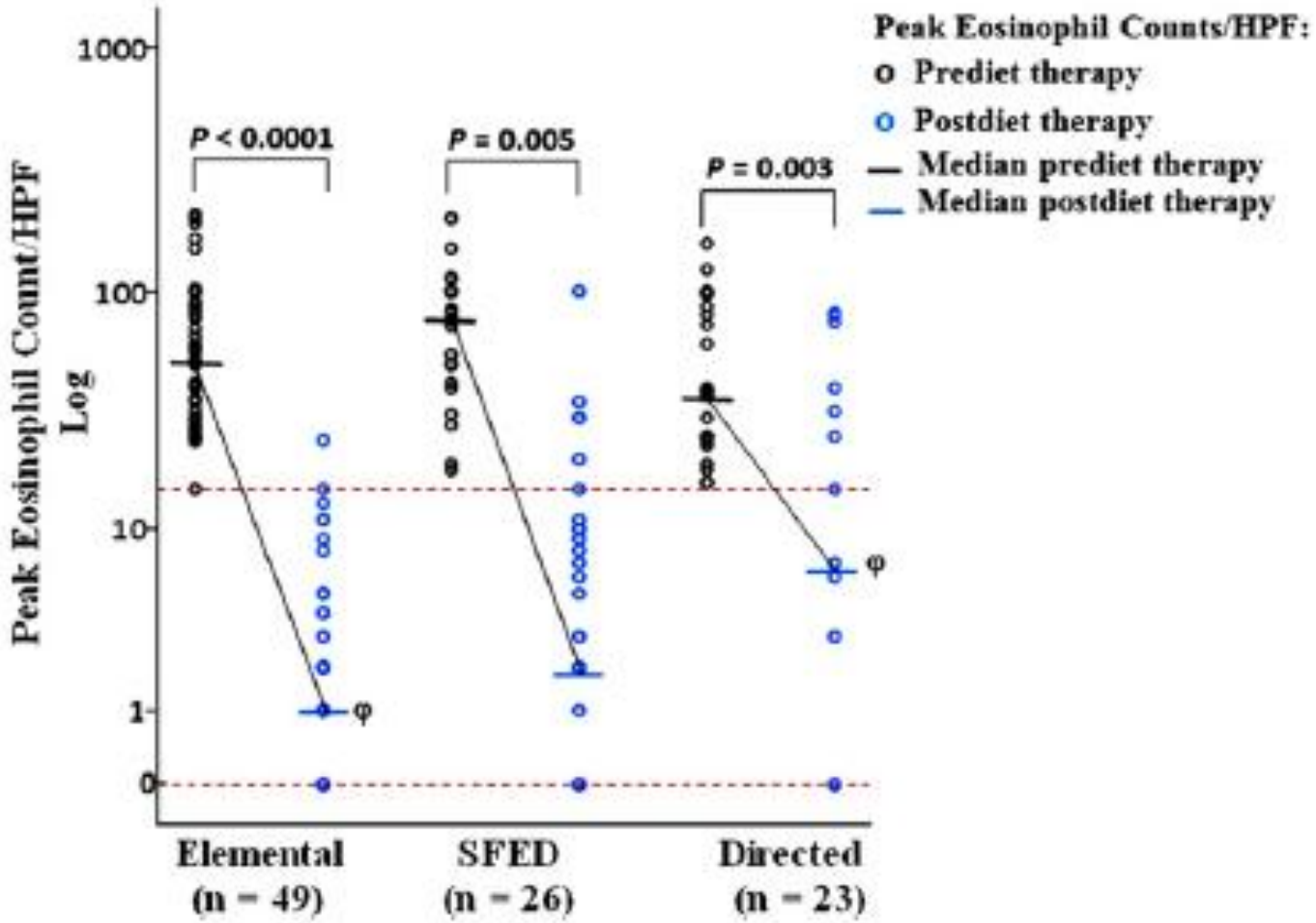
Which is the best diet?

Comparative dietary therapy effectiveness in remission of pediatric eosinophilic esophagitis

Carol J. Henderson, PhD, RD,[a] J. Pablo Abonia, MD,[a] Eileen C. King, PhD,[b] Philip E. Putnam, MD, FAAP,[c] Margaret H. Collins, MD,[d] James P. Franciosi, MD, MS, MSCE,[c] and Marc E. Rothenberg, MD, PhD[a] *Cincinnati, Ohio*



JACI 2012;129:1570-8



JACI 2012;129:1570-8

Which is the best diet?

- histologic remission rates:
  - ED 96%
  - SFED 81%
  - TED 65%
- Neg predictive values of skin tests: 40-67%

  (milk 40%, egg 56%, soy 64%, wheat 67%)

JACI 2012;129:1570-8

Conclusions on steroids and diets

Swallowed steroids can partially reverse subepithelial fibrosis in adult and pediatric EoE patients *
(max. 12 months observation time)
Elimination diets work, skin tests are not perfect for identification of causative foods

Straumann A et al. Clin Gastro Hepatol 2011
Aceves SS, et al. JACI 2007
Chehade M, et al. Allergy 2012

Esophageal Dilation

Study		Number of Patients	Perforation	Chest Pain	Hospitalization for Chest Pain
Vassilopoulos	2002	5	0	2	2
Kaplan	2003	8	1	NR	NR
Croese	2003	17	0	2	0
Straumann	2003	5	0	NR	NR
Potter	2004	13	0	2	2
Eisenbach	2006	1	1	NR	NR
Cohen	2007	36	3	NR	NR
	7	85	5/85 6%	6/85 7%	4/85 5%
Schoepfer	2010	207	0	15	0
Dellon	2011	36	0	3	0
Jung	2011	161	3	NR	NR
		489	8/489 1.6%	6/489 1.2%	4/489 0.8%

Effectiveness

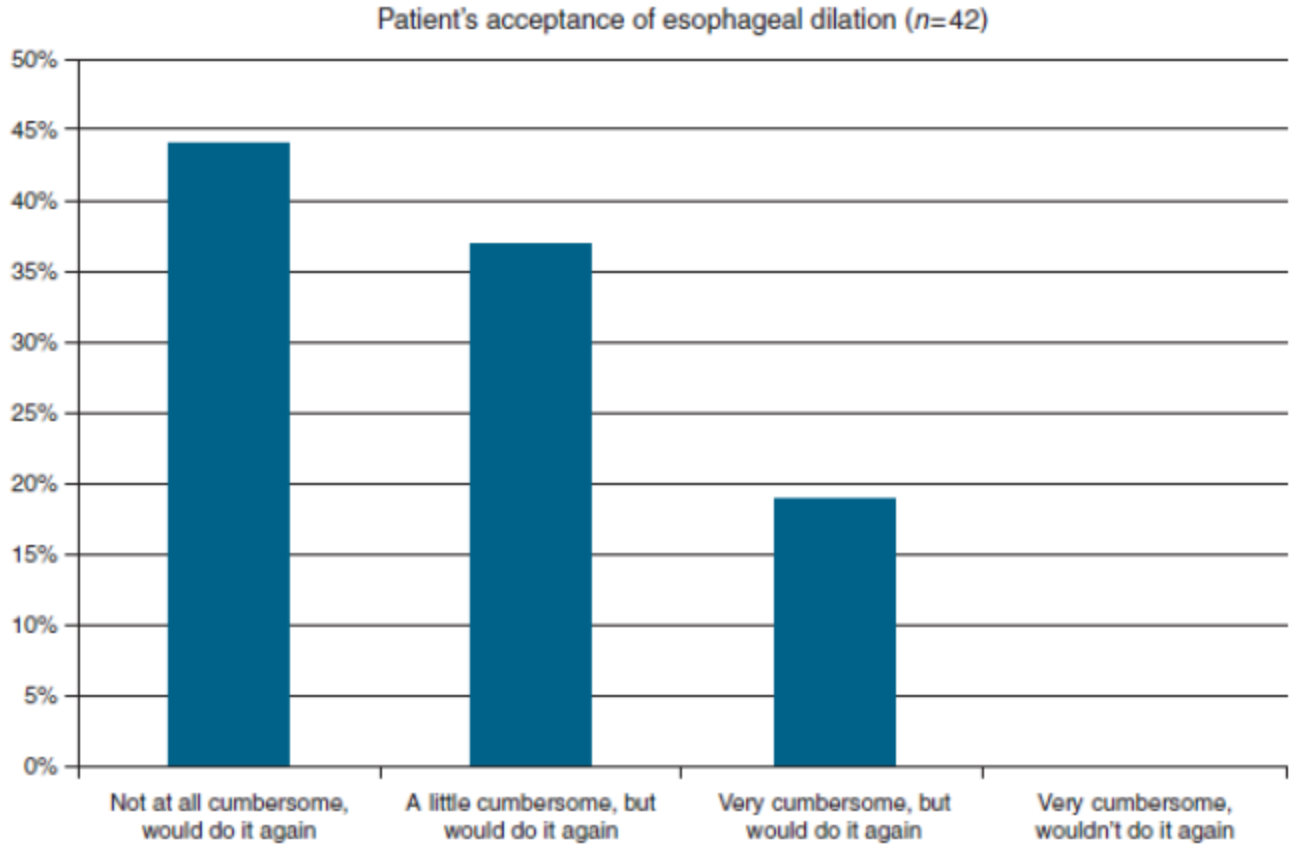
Item	Cohort 1: dilation only	Cohort 2: dilation + antieosinophilic medication	*P* value
Dilation method			
Savary bougies	46/63 (73%)	115/144 (80%)	NS
Balloon	17/63 (27%)	29/144 (20%)	
Esophageal diameter (mm) before dilation	11±3 (4–15)[a]	10±3 (5–15)[a]	NS
Esophageal diameter (mm) after dilation	16±2 (11–20)[a]	17±2 (13–20)[a]	NS
Increase of esophageal diameter (mm) per dilation session	3, 3.2±1.3 (1–8)	3, 2.9±1.1 (1–6)	NS
Number of dilation sessions performed until clinically successful	2, 2.4±2.6 (1–13)	2, 2.1±1.8 (1–8)	NS
Major complications (perforation, bleeding)	0	0	NA
Time until endoscopic follow-up (months)[b]	18, 28±24 (1–96)	21, 23±15 (1–62)	NS
Duration of symptomatic improvement (months)[c]	15, 23±22 (1–92)	17, 20±14 (1–65)	NS

Response	Percentage of patients (n=42)
Improvement of dysphagia after dilation	
No more dysphagia at all	48
Slight dysphagia	45
Still considerable dysphagia	7
No improvement at all	0
Duration of improved dysphagia	
24 Months or longer	41
Up to 18 months	5
Up to 12 months	21
Up to 6 months	14
Up to 3 months	12
Up to 1 month	7

67% have improved dysphagia ≥ 12 months

Schoepfer AM, et al. Am J Gastroenterol 2010;105:1062-70

Patient acceptance



No one would refuse undergoing dilation again !

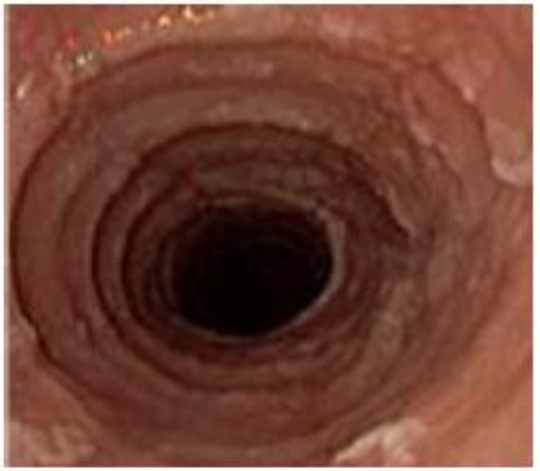
Schoepfer AM, et al. Am J Gastroenterol 2010;105:1062-70

Dilation: a balanced appraisal

Advantages	Shortcomings
Long response	No influence on underlying inflammation
Safe	Chest pain temporarily
Good patient acceptance	Potential endoscopic complications

Jung KW, et al. Gastrointest Endosc 2011;73:15-21
Dellon ES, et al. Gastrointest Endosc 2011;71:706-12
Schoepfer AM, et al. Am J Gastroenterol 2010;105:1062-70

Dilation for everyone?



Inflammatory — **Stricturing**

Anti-inflammatory medication

Elimination diets — **Dilation**

Pigneur B, et al. Inflamm Bowel Dis 2010;16:953-61
Straumann A, et al. Clin Gastroenterol Hepatol 2008;6:598-600

Questions

- Est-ce que c‘est une EoE?
- impaction alimentaire: dangereux ou pas?
- Quelle thérapie à choisir?
- comment suivre?

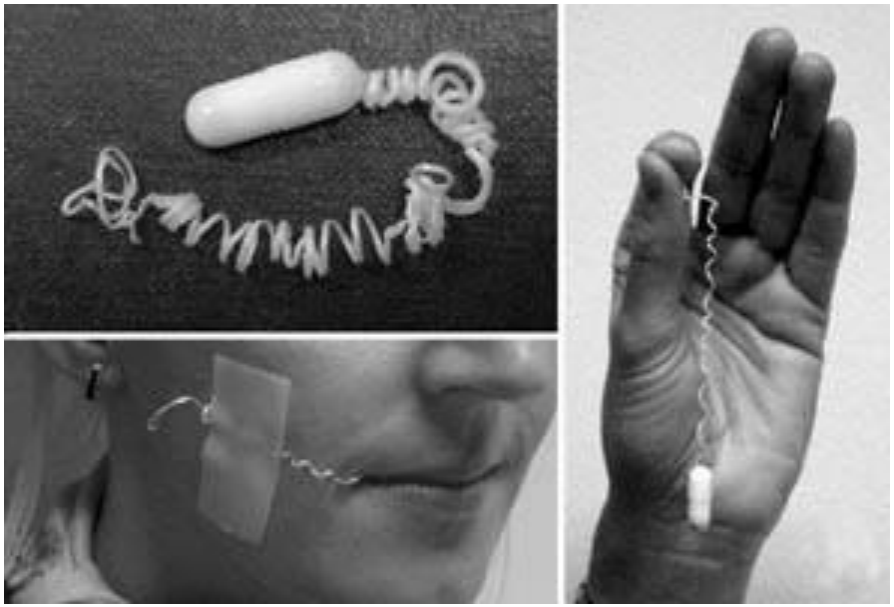
The oesophageal string test: a novel, minimally invasive method measures mucosal inflammation in eosinophilic oesophagitis

Glenn T Furuta,[1,2,3,4] Amir F Kagalwalla,[5,6] James J Lee,[7] Preeth Alumkal,[8] Brian T Maybruck,[8] Sophie Fillon,[1,2,3] Joanne C Masterson,[1,2,3] Sergei Ochkur,[7] Cheryl Protheroe,[7] Wendy Moore,[1,2,3,4] Zhaoxing Pan,[1,3] Katie Amsden,[5] Zachary Robinson,[1,2] Kelley Capocelli,[1,9] Vince Mukkada,[1,2,3] Dan Atkins,[1,4] David Fleischer,[1,4] Lindsay Hosford,[1,2,3] Mark A Kwatia,[8] Shauna Schroeder,[1,2,3] Caleb Kelly,[1,2] Mark Lovell,[1,9] Hector Melin-Aldana,[5,10] Steven J Ackerman[8]

Table 1 Summary of histological and gross features of mucosal eosinophilia

	EoE-active (untreated), n=14	EoE-remission (treated), n=8	GORD, n=4	Normal oesophagus, n=15	p Values untreated EoE versus treated, GORD, normal
Eosinophil peak count (±SEM)					
Proximal	30.1±6.0	0.4±0.3	0.3±0.2	0	p<0.001
Distal	45.4±8.9	0	0.8±0.4	0	p<0.001
Eosinophil average of five random fields (±SEM)					
Proximal	17.4±3.9	0.1±0.1	0.3±0.2	0	p<0.001
Distal	28.9±6.0	0	0.3±0.2	0	p<0.001
EPX Staining Index*					
Proximal	34.2±5.3	4.4±2.3	0	2.8±2.8	p<0.001
Distal	41.1±1.9	6.5±3.5	11.3±6.0	5.9±3.3	p<0.001
Endoscopic evidence of exudate (% of total patients)	6 (43%)	2 (25%)	1 (25%)	0	p<0.001
Microabscess† (% of total patients)	11 (79%)	0	0	0	p<0.001
Superficial layering‡ (% of total patients)	9 (64%)	0	0	0	p<0.001

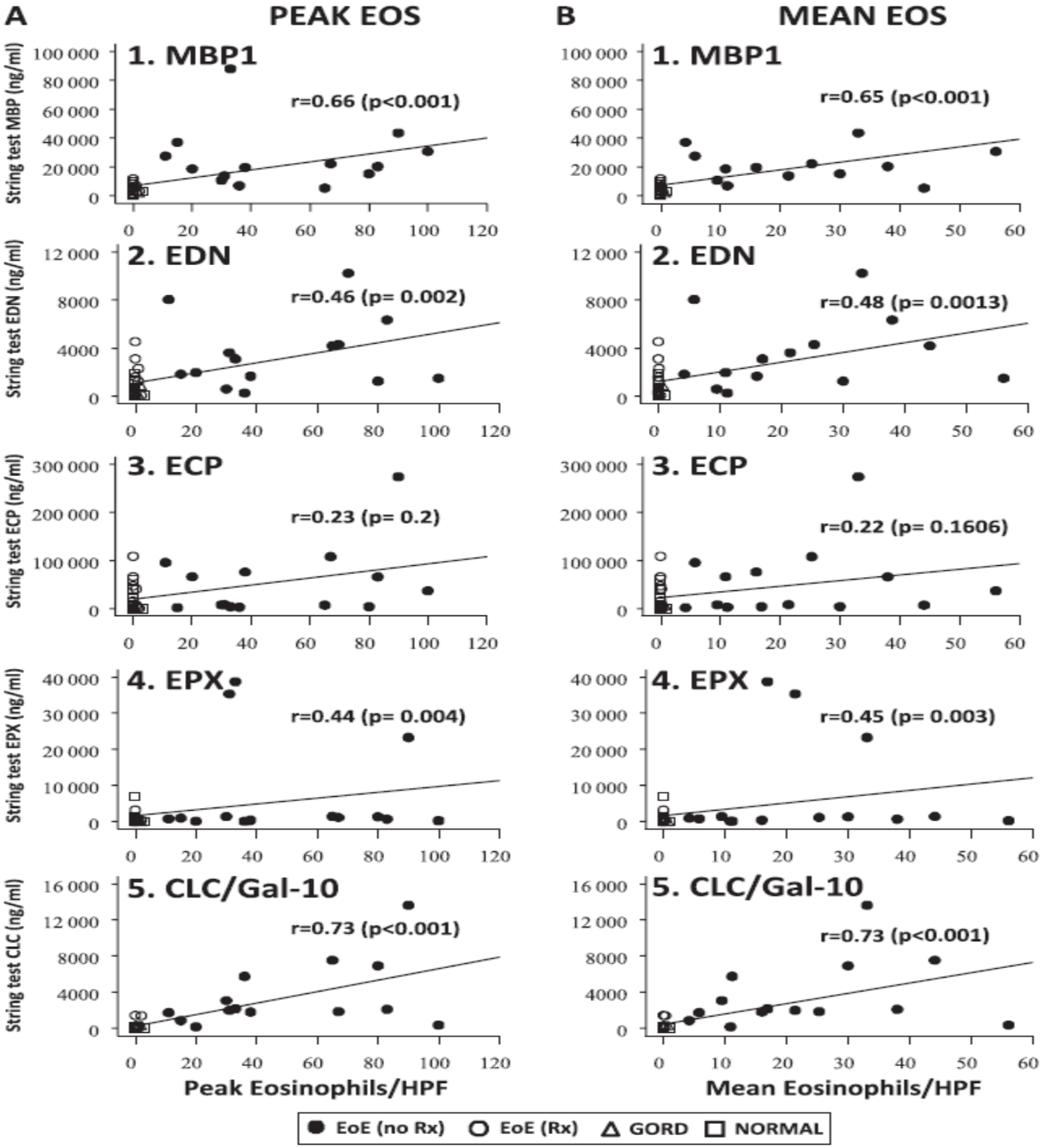
Gut 2012, epub

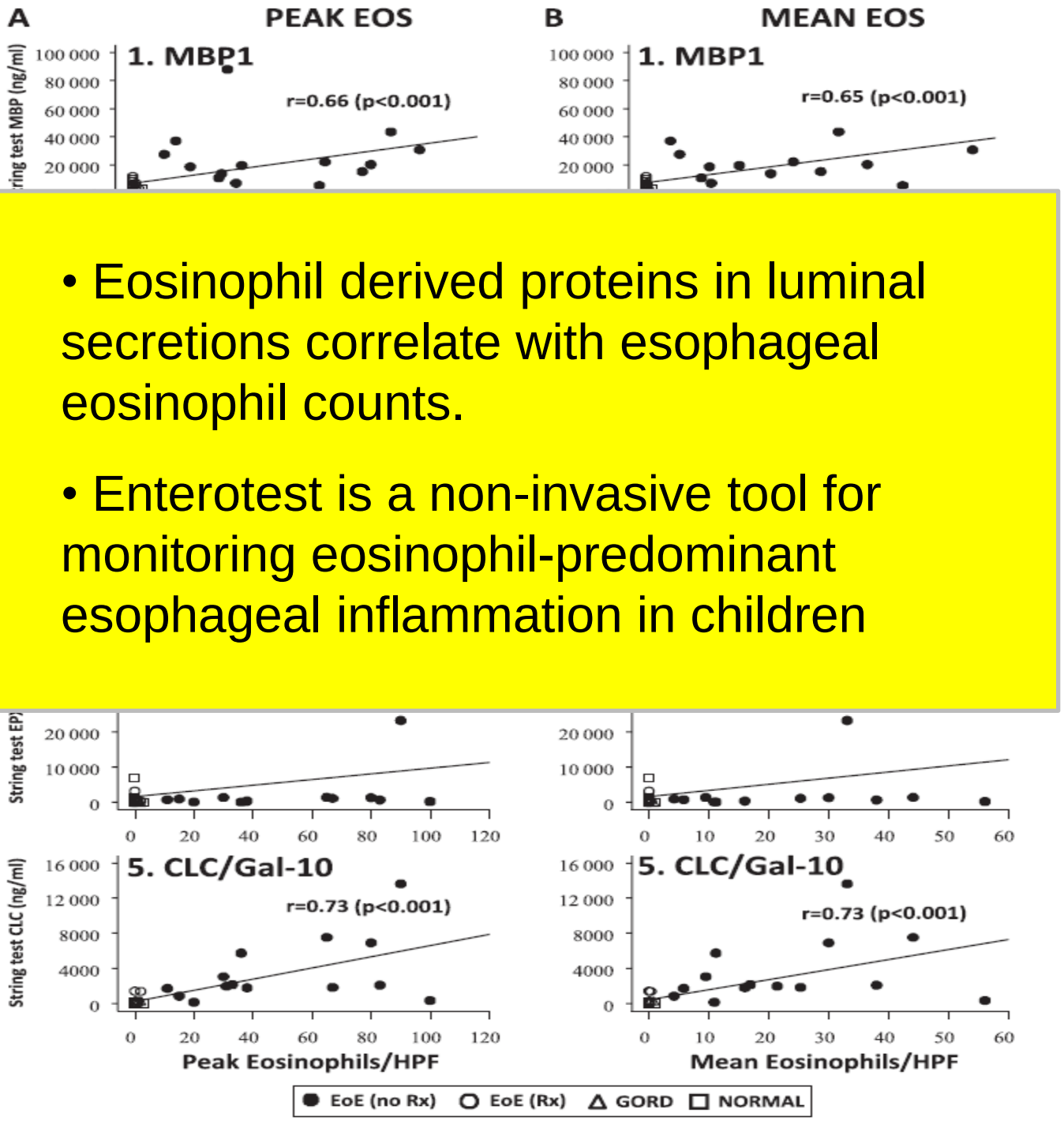


Enterotest®, evaluated for detection of Giardia lamblia in duodenum

Oesotest®, evaluated for detection of esophageal dysplasia (Actimed SA, Switzerland)

Furuta GT, et al. Gut 2012, epub


A
PEAK EOS
B
MEAN EOS
1. MBP1
String test MBP (ng/ml)
r=0.66 (p<0.001)
r=0.65 (p<0.001)
2. EDN
String test EDN (ng/ml)
r=0.46 (p= 0.002)
r=0.48 (p= 0.0013)
3. ECP
String test ECP (ng/ml)
r=0.23 (p= 0.2)
r=0.22 (p= 0.1606)
4. EPX
String test EPX (ng/ml)
r=0.44 (p= 0.004)
r=0.45 (p= 0.003)
5. CLC/Gal-10
String test CLC (ng/ml)
r=0.73 (p<0.001)
r=0.73 (p<0.001)
Peak Eosinophils/HPF
Mean Eosinophils/HPF
EoE (no Rx)
EoE (Rx)
GORD
NORMAL



- Eosinophil derived proteins in luminal secretions correlate with esophageal eosinophil counts.
- Enterotest is a non-invasive tool for monitoring eosinophil-predominant esophageal inflammation in children

Take home messages

- EoE prevalence 1/2,000, increasing incidence
- typical pattern: young male, dysphagia, allergies
- untreated inflammation leads to strictures and food bolus impactions => perforation risk
- reasons to treat EoE: QoL, prevention of esophageal remodeling and food bolus impactions
- treatment options: diets, drugs, dilation
- unmet needs: many