

34 Congresso Nazionale di **ANTIBIOTICOTERAPIA** in età pediatrica

La stipsi cronica

A. Staiano, Napoli

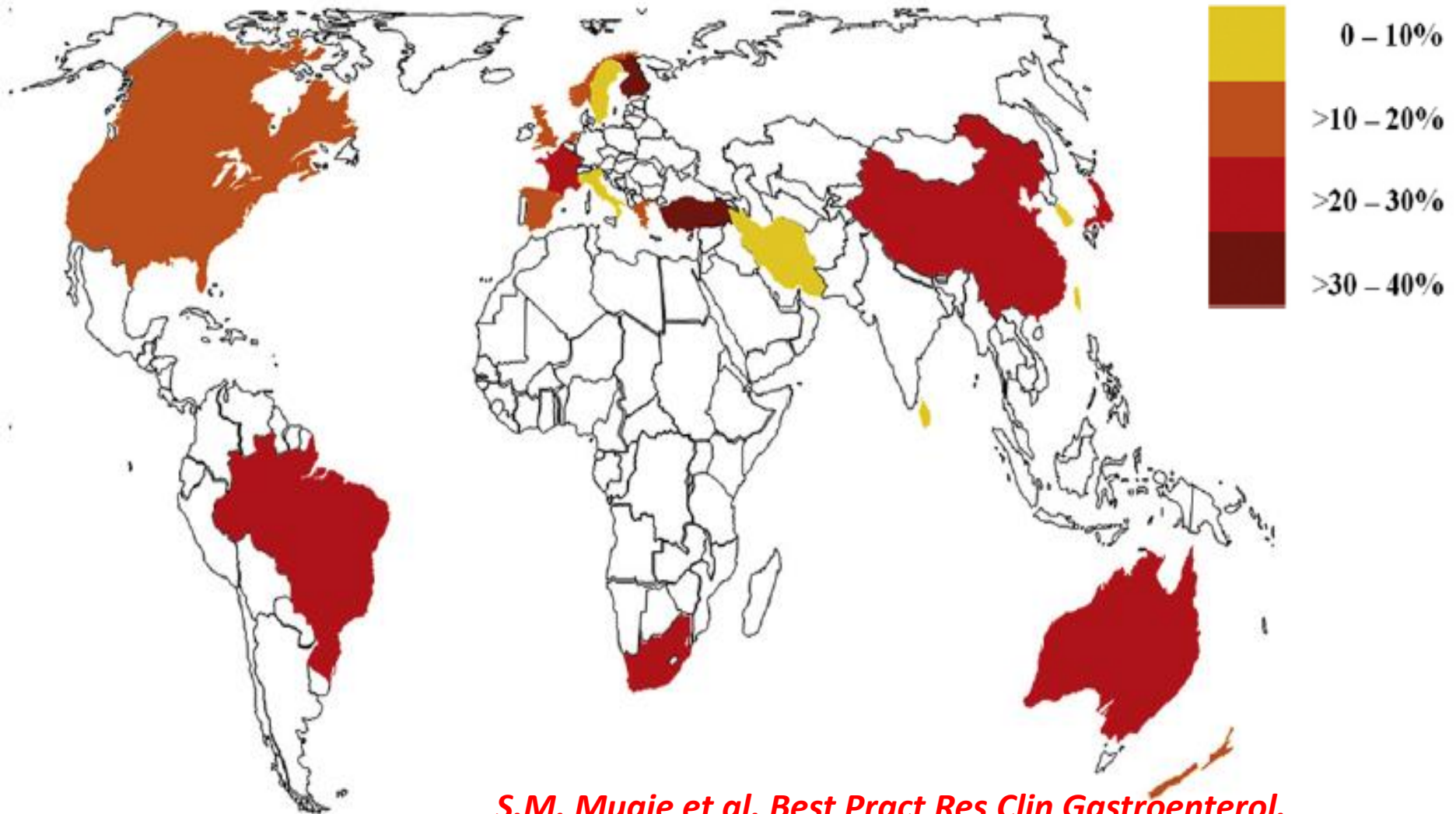
La stipsi cronica

Annamaria Staiano
Dipartimento di Scienze
Mediche Traslazionali
Università di Napoli
“Federico II” Italia
staiano@unina.it



Epidemiology of constipation in children and adults: A systematic review

Geographic distribution of constipation in children and adults, presented in median prevalence rates.



S.M. Mugie et al. Best Pract Res Clin Gastroenterol.

Chronic Constipation



LOWER QUALITY OF LIFE

Lower health-related quality of life (HRQoL) regarding disease-specific emotional and social functioning.

HIGHER MEDICAL CARE UTILIZATION

Children with constipation used more health services than children without constipation, resulting in significantly higher costs (\$ 3.430/yr vs \$ 1.099/yr)

Chogle A. Can J Gastroenterol. 2013

Bongers et al. J Pediatr 2009;154:749-53 Dec;27(12):e35-8

Choung; R. S. et al. JPGN.

2016;52(1):17-21

Cause di stipsi cronica in età pediatrica

- **Stipsi cronica funzionale (90-95%)**
- **Malformazioni anorettali**
- **Alterazioni delle strutture intestinali neuromuscolari**
 - Aganglionosi e/o alterazioni dei plessi intramurali
 - Alterazioni delle cellule muscolari lisce
- **Disordini endocrini e metabolici**
 - Ipotiroidismo
 - Ipercalcemia
- **Malattie neurologiche e neuromuscolari**
 - Disordini del SNC
 - Lesioni del midollo spinale
 - Distrofie muscolari
- **Effetti collaterali dei farmaci**
 - Antiacidi
 - Anticolinergici
 - Anticonvulsivanti
 - Bismuto



A Practical Guide for the Diagnosis of Primary Enteric Nervous System Disorders

**M.G. Schäppi, †A. Staiano, ‡P.J. Milla, ‡V.V. Smith, §J.A. Dias, ||R. Heuschkel, ¶S. Husby,
#M.L. Mearin, **A. Papadopoulou, ††F.M. Ruemmele,
§§Yvan Vandenplas, and ||||S. Koletzko*

Journal Pediatr Gastroenterol Nutr 2013; 57:677-86

Evaluation and Treatment of Functional Constipation in Infants and Children: Evidence-Based Recommendations From ESPGHAN and NASPGHAN

*M.M. Tabbers, C. DiLorenzo, M.Y. Berger, C. Faure, M.W. Langendam, S. Nurko,
A. Staiano, Y. Vandenplas, and M.A. Benninga*

Journal Pediatr Gastroenterol Nutr 2014;58: 258-274

Silvia

4 ANNI

Viene condotta in un ambulatorio pediatrico per:

- massa fecale in addome
 - incontinenza fecale
 - feci voluminose
 - atteggiamenti ritentivi
-
- ✓ Nata pretermine a 34 settimane
 - ✓ Peso alla nascita 2500 g.
 - ✓ Emissione di meconio dopo 48 ore di vita
 - ✓ Stipsi dal passaggio dal latte materno al latte in formula (10 mese di vita circa).

Silvia

4 ANNI

Nel sospetto di una stipsi cronica di natura funzionale...

- rammollitori fecali



- clisteri evacuativi



Silvia

4 ANNI



due mesi dopo...

Nuovo controllo
severa associata

esistenza di stipsi

➤ CLISMA OPACO

*Megaretto,
progressione
cieco.*

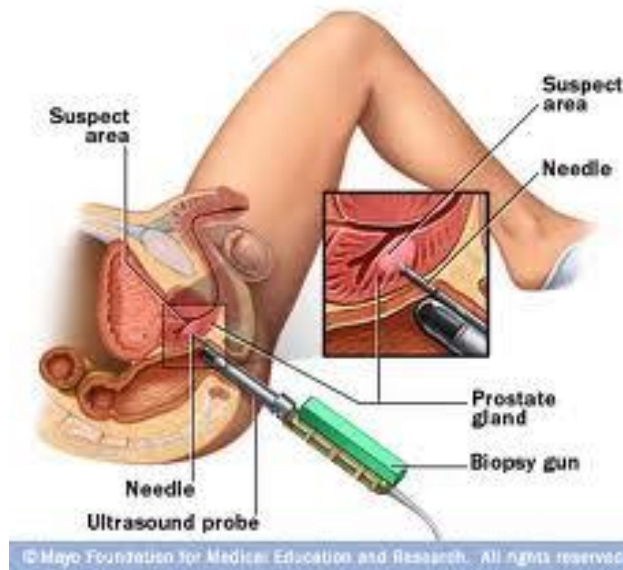


*un ostacolo alla
rografin) fino al*

Silvia

4 ANNI

- Biopsia rettale per suzione (1 cm al di sopra della linea dentata): all'analisi istologica si evidenzia l'assenza di elementi cellulari gangliari.



Nel sospetto di Morbo di Hirschsprung...

Silvia

4 ANNI

VIENE INVIATA ALLA NOSTRA ATTENZIONE ...

Peso: 10° pct

Altezza: 25° -50° pct

Rapporto P/A: 10-25° pct

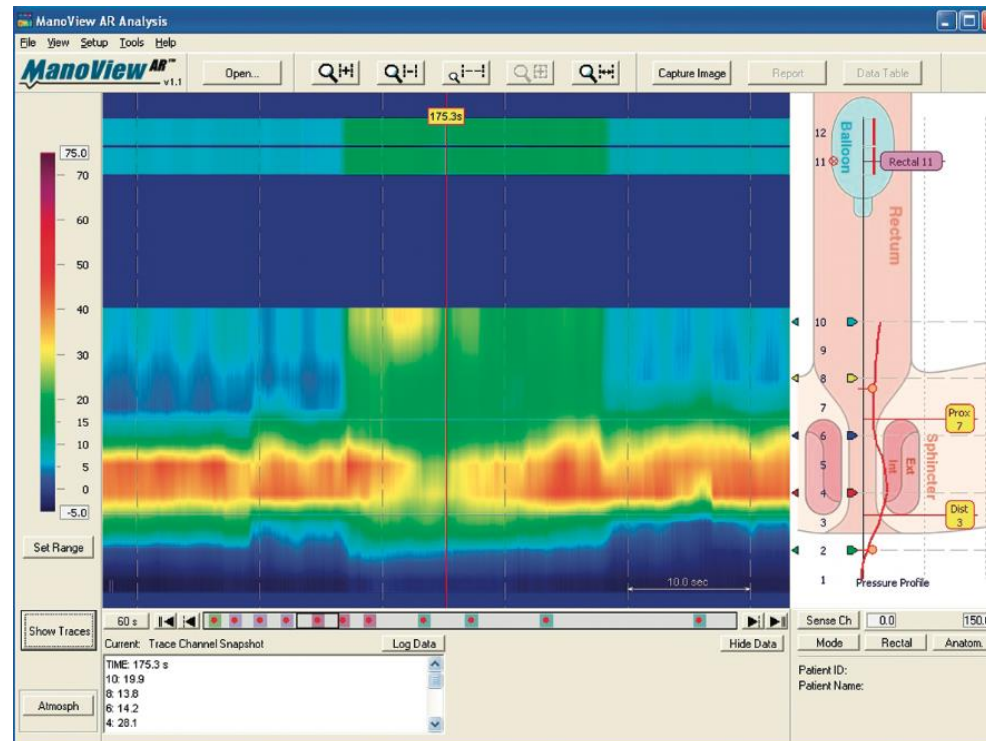


- Esame obiettivo: ampolla rettale piena di feci
- Esami ematochimici (profilo tiroideo, calcemia): nella norma
- Sierologia per celiachia: negativa
- Prick test e Rast: negativi

Silvia

4 ANNI

- ✓ **MANOMETRIA ANORETTALE:** presenza del riflesso inibitorio anale

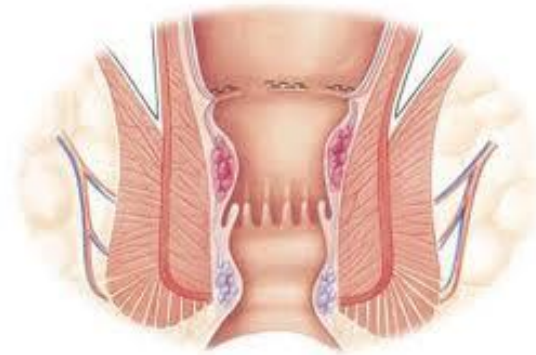


Silvia

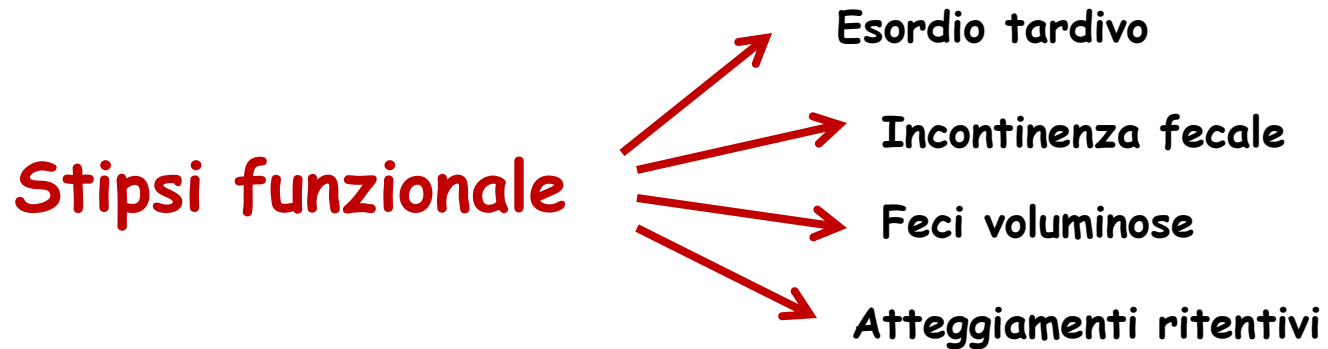
4 ANNI

✓ BIOPSIA RETTALE PER SUZIONE

Evidenza istologica di elementi cellulari gangliari; normale tono parasimpatico, come rilevato attraverso la colorazione per acetilcolinesterasi e calretinina nella tonaca propria e nella muscolaris mucosae (su campioni biotici prelevati 4 e 6 cm prossimalmente la linea dentata).



DIAGNOSI



- Rammollitori fecali (1 gr/kg/die)
- Follow-up a 1 anno: regolarizzazione dell' alvo

DIAGNOSI DI STIPSI CRONICA FUNZIONALE

- ANAMNESI
 - Età di insorgenza
 - Incontinenza fecale
 - Feci di grosse dimensioni
- ESAME OBIETTIVO
 - Massa addominale (77%)
 - Ispezione anale
 - Escludere disrafismo occulto
 - Esplorazione rettale



Diagnosis of functional constipation is based on history and physical examination.

Evaluation and Treatment of Functional Constipation in Infants and Children: Evidence-Based Recommendations From ESPGHAN and NASPGHAN

What are the alarm signs and symptoms that suggest the presence of an underlying disease causing the constipation?

- Constipation starting very early in life (<1 month)**
- Passage of meconium > 24 hours**
- Family history of Hirschsprung's disease
- Ribbon stools**
- Blood in the stools in the absence of anal fissures
- Failure to thrive
- Fever
- Bilious vomiting
- Abnormal thyroid gland
- Severe abdominal distension**
- Perianal fistula
- Abnormal position of anus
- Absent anal or cremasteric reflex
- Decreased lower extremity strength/tone/reflex
- Tuft of hair on spine**
- Sacral dimple
- Gluteal cleft deviation**
- Extreme fear during anal inspection
- Anal scars

It is recommend to use alarm signs and symptoms and diagnostic clues to identify an underlying disease responsible for the constipation.

Evaluation and Treatment of Functional Constipation in
Infants and Children: Evidence-Based Recommendations
From ESPGHAN and NASPGHAN

Which of the following diagnostic tests should be performed in children with constipation in order to diagnose an underlying disease?

1. *Laboratory investigations to diagnose (cow's milk) allergy, celiac disease, hypothyroidism and hypercalcemia?*
2. *Anorectal manometry or rectal suction biopsy to diagnose Hirschsprung's disease (HD)?*
3. *Use of barium enema to diagnose organic causes like Hirschsprung's disease (HD)?*

Journal Pediatr Gastroenterol Nutr 2014;58: 258-274

Evaluation and Treatment of Functional Constipation in Infants and Children: Evidence-Based Recommendations From ESPGHAN and NASPGHAN

- ✓ *Routine allergy testing to diagnose cow's milk allergy are not recommend in children with functional constipation.*
- ✓ *Based on expert opinion, routine laboratory testing for hypothyroidism, celiac disease and hypercalcemia are not recommend in children with constipation in the absence of alarm symptoms.*
- ❖ **Evidence is conflicting for allergy testing to diagnose cow's milk allergy in children with functional constipation.**

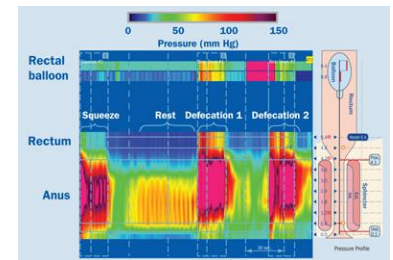
Journal Pediatr Gastroenterol Nutr 2014;58: 258-274

Evaluation and treatment of functional constipation in infants and children: evidence-based recommendations from ESPGHAN and NASPGHAN.

A Practical Guide for the Diagnosis of Primary Enteric Nervous System Disorders

Other diagnostic tools: which is their role?

- ✓ Anorectal manometry may be a confirmatory investigation, or a tool to exclude HD in older children with constipation since infancy.
- ✓ Barium enema should not be the first diagnostic investigation, but may be indicated in confirmed cases to provide information on the length of the aganglionic bowel.



Journal Pediatr Gastroenterol Nutr 2014;58: 258-274

Journal Pediatr Gastroenterol Nutr 2013; 57:677-86

A Practical Guide for the Diagnosis of Primary Enteric Nervous System Disorders

TABLE 1. Sensitivity and specificity of different diagnostic procedures for the diagnosis of HD

Index test	Parameter	
	Mean sensitivity,% (95% CI)	Mean specificity,% (95% CI)
Barium enema	70 (64–76)	83 (74–90)
Anorectal manometry	91 (85–95)	94 (89–97)
Rectal suction biopsy (stained for AchE activity)	93 (88–95)	98 (95–99)

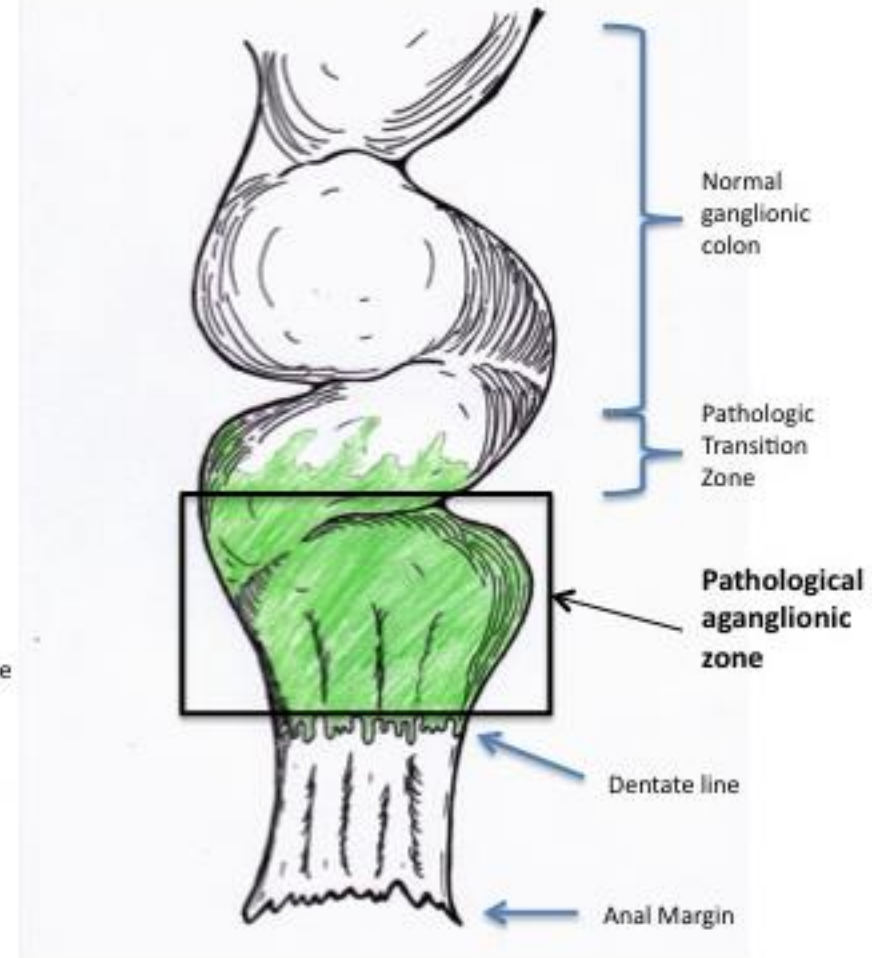
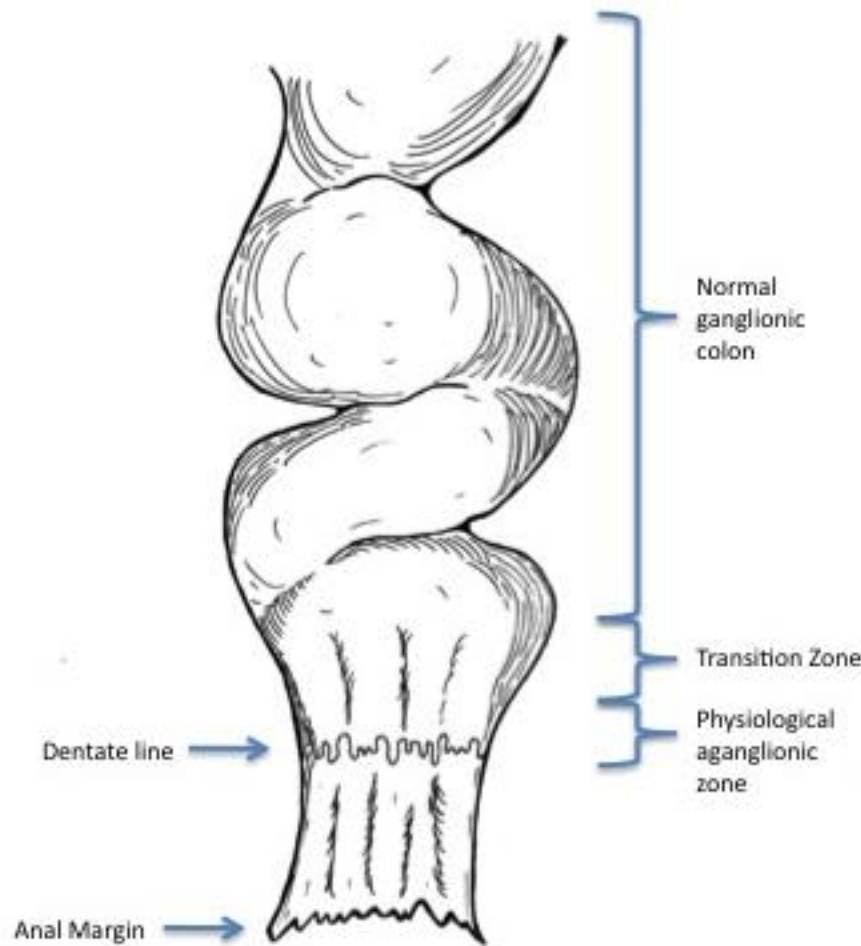
Modified after (35). AchE = acetylcholinesterase; CI = confidence interval; HD = Hirschsprung disease.

*Hirschsprung's disease:
Rectal biopsy*



- ❖ The best means of obtaining adequate submucosa in rectal biopsies in infants is by rectal suction biopsy
- ❖ An accurate diagnosis is only possible if 2 – 3 suction biopsies are taken 2-3 cm above the dentate line and if they include part of the submucosa
- ❖ Biopsies taken closer to the dentate line may be misleading because of the normal zone of submucosal hypoganglionosis or even aganglionosis

A Practical Guide for the Diagnosis of Primary Enteric Nervous System Disorders



A.

B.

A) Diagram of the normal rectum showing the physiological, hypo- or even aganglionic zone above the dentate line. Above this is a transition zone to normal, more proximal, ganglionic bowel. Biopsies taken too close to the dentate line may be hypo or aganglionic and hence reported falsely positive for Hirschsprung disease. B) In Hirschsprung's disease the aganglionic zone extends from the dentate line proximally for a variable distance, before a transition zone leads to normal innervation.

Evaluation and Treatment of Functional Constipation in Infants and Children: Evidence-Based Recommendations From ESPGHAN and NASPGHAN

M.M. Tabbers, C. DiLorenzo, M.Y. Berger, C. Faure, M.W. Langendam, S. Nurko, A. Staiano, Y. Vandenplas, and M.A. Benninga

NON-PHARMACOLOGICAL and PHARMACOLOGICAL TREATMENT

Journal Pediatr Gastroenterol Nutr 2014;58: 258–274

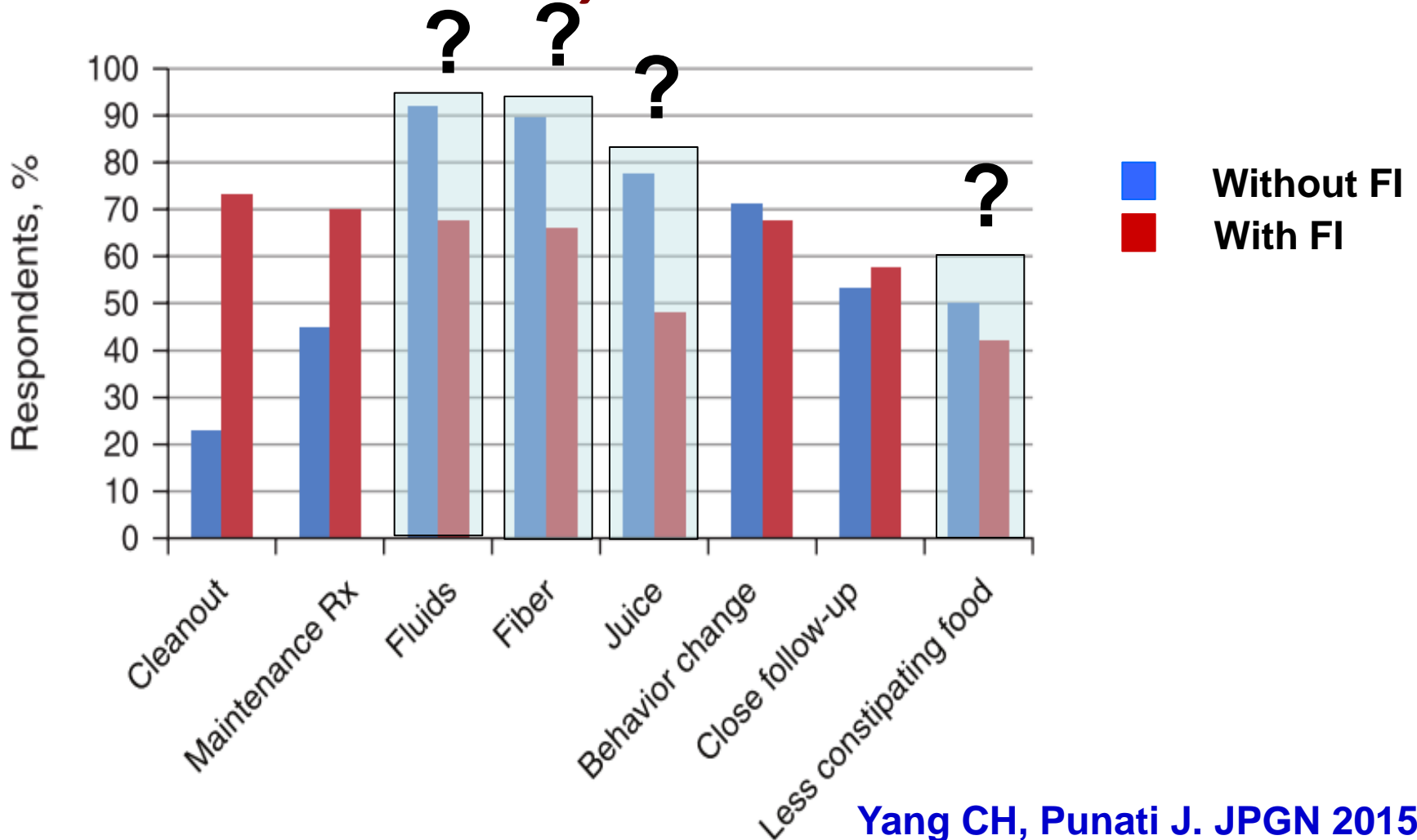
Evaluation and Treatment of Functional Constipation in Infants and Children: Evidence-Based Recommendations From ESPGHAN and NASPGHAN

What is the additional effect of nonpharmacological treatments in children with functional constipation?

- ✓ *It is recommended a normal fiber intake in children with constipation.*
- ✓ *It is recommended a normal fluid intake in children with constipation.*
- ✓ *It is recommended a normal physical activity in children with constipation.*
- ✓ *It is not recommended the routine use of prebiotics or probiotics in the treatment of childhood constipation.*

Practice Patterns of Pediatricians and Trainees for the Management of Functional Constipation Compared With 2006 NASPGHAN Guidelines

Most commonly used initial interventions



Constipation in children: fibre and probiotics

Key points

- Low fibre intake is associated with constipation. We found insufficient evidence from RCTs showing that extra fibre reduces constipation compared with placebo. We found insufficient evidence on the effects of increased fibre intake compared with lactulose.
- We found insufficient evidence from RCTs on the effects of probiotics versus placebo or versus osmotic laxatives at improving symptoms of constipation.
- Overall, many of the studies we found used different definitions and outcomes measures, and the quality of evidence was low. There is a need for further large high-quality RCTs in this condition.



Systematic review: the effect of prunes on gastrointestinal function

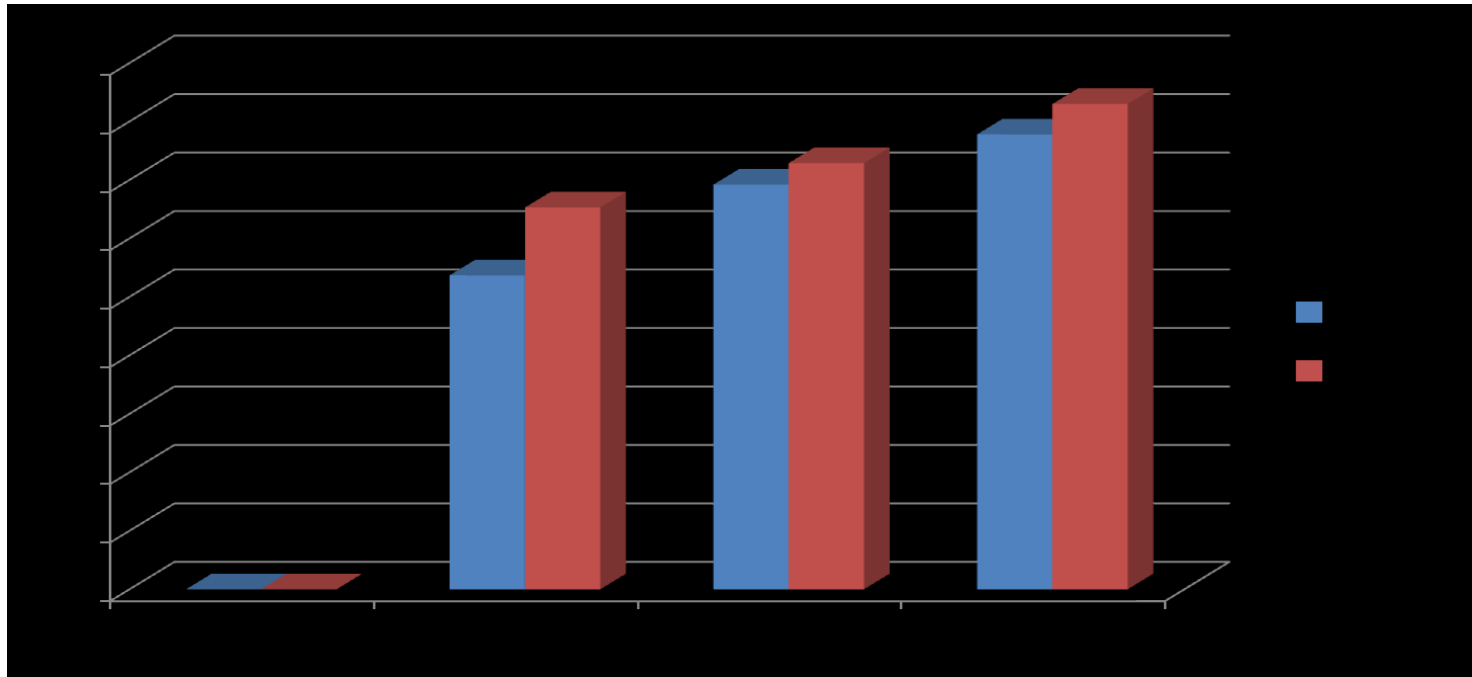
- ❖ Prunes (dried plums) are high in fibre and are perceived to promote healthy gastrointestinal (GI) function.
- ❖ In constipation, prunes appear superior to psyllium for improving stool frequency and consistency, however, the evidence for other outcomes and the effects in non-constipated subjects is weak.
- ❖ Although prunes may be a promising intervention for the management of constipation and increasing stool weight, this needs to be confirmed by further rigorous research.

Kiwifruit-derived supplements increase stool frequency in healthy adults: a randomized, double-blind, placebo-controlled study★

- In this randomized, double-blind, placebo-controlled study, we examined the effects of Actazin and Gold, kiwifruit derived nutritional ingredients, on stool frequency, stool form, and gastrointestinal comfort in healthy and functionally constipated (Rome III criteria for C3 functional constipation) individuals
- In the healthy cohort the Actazin-H and Gold interventions significantly increased the mean daily bowel movements compared with the washout.
- In a subgroup analysis of responders in the healthy cohort, Actazin-L, Actazin-H, and Gold consumption significantly increased the number of daily bowel movements by greater than 1 bowel movement per week.
- *In the functionally constipated cohort (n = 9), there were no significant differences between interventions for bowel movements and the Bristol stool scale values or in the subsequent subgroup analysis of responders.*

Ansell J et al. Nutr Res. 2015 Apr 11.

A Randomized, Prospective, Comparison Study of a Mixture of Acacia Fiber, Psyllium Fiber and Fructose (AFPFF) versus Polyethylene Glycol 3350 with Electrolytes (PEG+E) for the Treatment of Chronic Functional Constipation in Childhood



- ✓ A significant improvement of constipation was seen in both groups.
- ✓ After 8 weeks, 77.8% of children treated with AFPFF and 83% of children treated with PEG+E had improved

Evaluation and Treatment of Functional Constipation in Infants and Children: Evidence-Based Recommendations From ESPGHAN and NASPGHAN

Which pharmacological treatment should be given for disimpaction?

- ❑ **PEG with or without electrolytes orally 1-1.5 gr/kg/day 3-6 days as first-line treatment for children presenting with fecal impaction.**
- ❑ **Sodium docusate enemas once a day during 3-6 days as treatment for children presenting with fecal impaction.**

Evaluation and Treatment of Functional Constipation in Infants and Children: Evidence-Based Recommendations From ESPGHAN and NASPGHAN

Which pharmacological treatment should be given for maintenance therapy?

- ❖ PEG with or without electrolytes orally as first-line maintenance treatment for children with functional constipation. It is suggest a starting dose of 0.4 gram/kg/day and this should be adjusted according to response.
- ❖ Lactulose 1-2 gr/kg/day as maintenance treatment in children with functional constipation when PEG is not available.

Journal Pediatr Gastroenterol Nutr 2014;58: 258–274

...e ritorniamo al nostro caso clinico...

Silvia

4 ANNI

Viene condotta in un ambulatorio pediatrico per:

- **massa fecale in addome**
 - **incontinenza fecale**
 - **feci voluminose**
 - **atteggiamenti ritentivi**
-
- ✓ **Nata pretermine a 34 settimane**
 - ✓ **Peso alla nascita 2500 g.**
 - ✓ **Emissione di meconio dopo 48 ore di vita**
 - ✓ **Stipsi dal passaggio dal latte materno al latte in formula (10 mese di vita circa).**

Silvia

4 ANNI



due mesi dopo...

Nuovo controllo ambulatoriale per la persistenza di stipsi severa associata ad incontinenza fecale.



➤ **clisma opaco**

Megaretto, megasigma, aoiicocoion; nessun ostacolo alla progressione del mezzo di contrasto (gastrografin) fino al cieco.

➤ **Biopsia rettale per suzione (1 cm al di sopra della linea dentata): all'analisi istologica si evidenzia l'assenza di elementi cellulari gangliari.**

TAKE HOME MESSAGES

Stipsi cronica

Stipsi cronica funzionale  95%

Funzionale

Organica

++++

INCONTINENZA FECALE

----+ (?)

++++

FECI DI GROSSE DIMENSIONI

99.9%STIPSI
FUNZIONALE

++++

POSTURE RITENTIVE

++++

AMPOLLA RETTALE PIENA

++++

INSORGENZA TARDIVA <6 mesi

----+

++--

INCONTINENZA + ENURESI

--++

La stipsi cronica: *Conclusioni*

- ✓ *La diagnosi di stipsi funzionale si basa sull'anamnesi e sull'esame obiettivo, utilizzando i sintomi ed i segni di allarme per escludere una patologia sottostante.*
- ✓ *PEG con o senza elettroliti è raccomandato come prima linea per la terapia di mantenimento della stipsi. Si raccomanda un dosaggio di partenza di 0.4 gr/kg/day da modificare in base alla risposta clinica.*
- ✓ *Più del 90% dei neonati a termine e <10% dei bambini con Morbo di Hirschsprung, presentano una emissione di meconio nelle prime 24 ore di vita*
- ✓ *Il clisma opaco va effettuato solo per confermare la diagnosi di Morbo di Hirschsprung, per valutare l'estensione del segmento agangliare.*
- ✓ *La biopsia rettale per suzione deve essere effettuata a 2-3 cm dalla linea dentata*