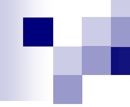
Pain = allergy – surely true?

Dr Warren Hyer
Consultant Paediatrician
Consultant Paediatric Gastroenterologist



Educational objectives

- Screamers
- "silent reflux" – is this an internet diagnosis
- PPI's for abdominal pain
- Functional abdominal pain in children
- New explanations for abdo pain

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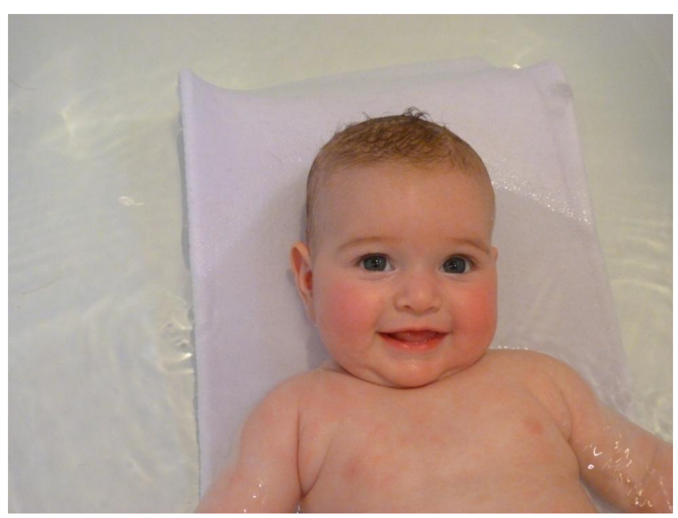
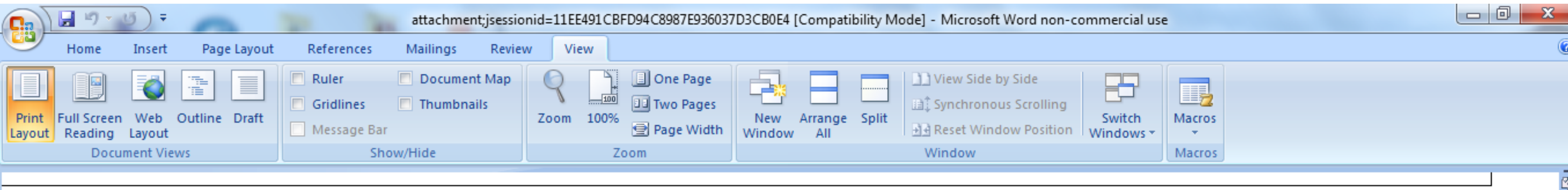
Chose your first consult.

- The baby
- The child/adolescent





Thank you for seeing this neonate who is screaming excessively.

She was born by planned LSCS because of delayed labour (Term + 12). In the immediate post natal period her mother tels me she needed mucous aspiration several times. Since discharge she has been very snuffly but has not responded to saline drops. She is on bottle milk and her parents have tried different milk, including lactose free milk, with no effect. On examination I can detect no abnormailities.

Her parents arer clearly a little fraugh and I would appreciate your opinion on whetehr you feel there is anything which can be done to help.

She has an oldder sibling, a 19month old sister you have seen and diagnosed lactose intolerane.

Thank you for yoru help.

Page: 1 of 1 | Words: 169 | English (United States) | 200%

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- What would you do for this child?
  - Commence anti reflux therapy
  - Start colief for lactose intolerance
  - Change formula to a bitter hydrolysate feed and possibly make the feed difficulties worse
  - Suggest start solids at the very earliest moment and keep going to then

IgE mediated immediate reaction

- Food allergy like urticaria or anaphylaxis
- Oral allergy syndrome

Non IgE mediated – delayed manifestation

- eczema
- Allergic colitis
- Infantile colic
- GORD
- Allergic dysmotility
- Enteropathy

Cows milk formulae

- Allergic
- Cheap
- tastes nice

Partially hydrolysed

- Soy not an option
- Questionable effectiveness
- NAN HA

Whey hydrolysate

- Palatable but allergic
- e.g. Pepti
- Nestle alfare

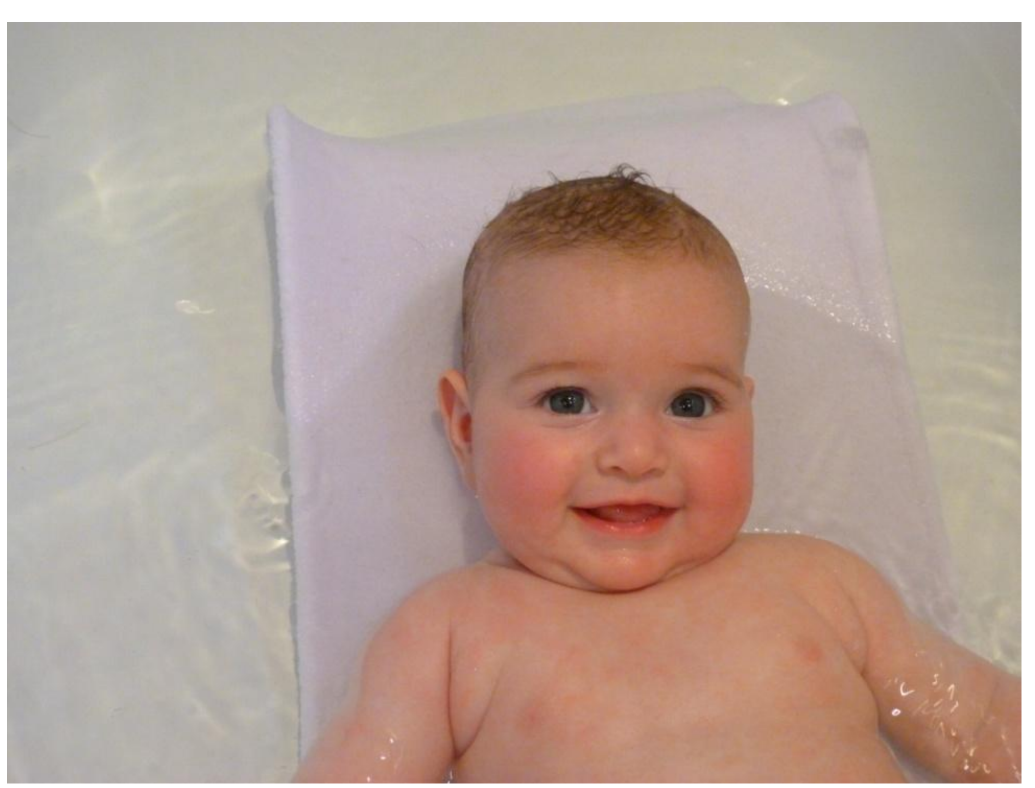
Caesin hydrolysate

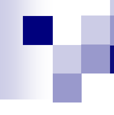
- First line for food allergy
- e.g. nutramigen
- Similac alimentum

Elemental

- Unpalatable
- Expensive
- First line if breast feeding
  - e.g.neocate
  - Nutramigen Puramino
  - Nestle
  - Alfaamino

Surely not all children who cry have reflux or colic?





The unsettled baby: how complexity science helps

Pamela Sylvia Douglas,[1] Peter Stewart Hill,[2]
Wendy Brodribb[1]

diverse cultures. But unsettled behaviour may emerge if disruption of feedback loops exceeds the capacity of the mother–baby CAS to compensate, or adapt. For example, unidentified breastfeeding difficulty, including problems with attachment, positioning and suck–swallow–breath co-ordination, may interfere with self-organising neurohormonal and autocrine breastfeeding feedback loops, causing cry-fuss behaviours, failure to thrive, or both.[36 39] The

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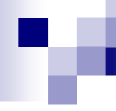
months of life.[16 42 48 62] Because of human evolutionary biology, babies sleep safest in same room as parents,[51 69 70] and are more settled in the first few months of life if they are breastfed on demand and in close physical contact with the care giver.[53] Attunement contrasts with



Pediatric Gastroesophageal Reflux Clinical Practice Guidelines: Joint Recommendations of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN) and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN)

4.1. History and Physical Examination In infants and toddlers, there is no symptom or symptom complex that is diagnostic of GERD or predicts response to therapy. In older children and adolescents, as in adult patients, history and physical examination may be sufficient to diagnose GERD if the symptoms are typical.

No discriminating aspect to history

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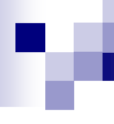
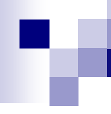


6.1.3. Infants With Unexplained Crying and/or Distressed Behavior Reflux is not a common cause of unexplained crying, irritability, or distressed behavior in otherwise healthy infants. Other causes include cow's milk protein allergy, neurologic disorders, constipation, and infection (especially of the urinary tract). Following exclusion of other causes, an empiric trial of extensively hydrolyzed protein formula or amino acid–based formula is reasonable in selected cases, although evidence from the literature in support of such a trial is limited. There is no evidence to support the empiric use of acid suppression for the treatment of irritable infants.

Screaming ≠ reflux

(206,207). Studies support the use of extensively hydrolyzed or amino acid formula in formula-fed infants with bothersome regurgitation and vomiting for trials lasting up to 4 weeks (206–208). Cow's milk protein and other proteins pass into human breast milk in small quantities. Breast-fed infants with regurgitation and vomiting may therefore benefit from a trial of withdrawal of cow's milk and eggs from the maternal diet (209,210). The symptoms of infant reflux are almost never so severe that breast-feeding should be discontinued. There are no

There is a role for change in formula
Trial of withdrawal of cows milk from mothers diet



(336). A meta-analysis of 7 RCTs of metoclopramide in developmentally healthy children 1 month to 2 years of age with symptoms of GER found that metoclopramide reduced daily symptoms and the RI but was associated with significant side effects (215). Metoclopramide com-

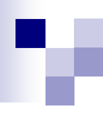
recent systematic review of studies on domperidone (341) identified only 4 RCTs in children, none providing "robust evidence" for efficacy of domperidone in pediatric GERD. Domperidone occasionally causes extrapyramidal central nervous system side effects (342).

Evidence does not support use of domperidone

group (46). A large double-blind study of 162 infants randomized to 4 weeks of placebo or lansoprazole showed an identical 54% response rate in each group, using an endpoint of >50% reduction of measures of feeding-related symptoms (crying, irritability, arching) and other parameters of the I-GERQ questionnaire (9). Furthermore, this study showed a small but significant increase in the numbers of infants that experienced lower respiratory symptoms during the treatment trial.

Lack of evidence for PPI in infantile agitation

Orenstein SR, Hassall E, Furmaga-Jablonska W, et al. Multicenter, double-blind, randomized, placebo-controlled trial assessing efficacy & safety of proton pump inhibitor lansoprazole in infants with symptoms of gastroesophageal reflux disease. *J Pediatr* 2009; 154:514–20.



PEDIATRICS®

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Efficacy of Proton-Pump Inhibitors in Children With Gastroesophageal Reflux Disease: A Systematic Review

Rachel J. van der Pol, Marije J. Smits, Michiel P. van Wijk, Taher I. Omari, Merit M. Tabbers and Marc A. Benninga

Pediatrics 2011;127;925-935; originally published online Apr 4, 2011;

CONCLUSIONS: PPIs are not effective in reducing GERD symptoms in infants. Placebo-controlled trials in older children are lacking. Although PPIs seem to be well tolerated during short-term use, evidence supporting the safety of PPIs is lacking. *Pediatrics* 2011;127:925–935

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COMMENTARY

Over-Prescription of Acid-Suppressing Medications in Infants: How It Came About, Why It's Wrong, and What to Do About It

Eric Hassall, MBChB, FRCPC, FACG[1]

Chelsea and Westminster Hospital NHS
NHS Foundation Trust

Cows milk formulae

- Allergic
- Cheap
- tastes nice

Partially hydrolysed

- Soy not an option
- Questionable effectiveness
- NAN HA

Whey hydrolysate

- Palatable but allergic
- e.g. Pepti
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- Unpalatable
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  - Nestle
  - Alfaamino

Gastro-oesophageal reflux disease: recognition, diagnosis and management in children and young people

NICE guideline
Published: 14 January 2015
nice.org.uk/guidance/ng1

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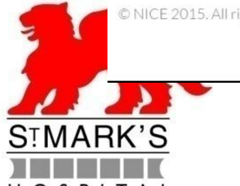
- Avoid PPI's in young children with distress
- Avoid prokinetics – they don't work and can harm
- So can PPI's



BMJ 2011;343:d7772 doi: 10.1136/bmj.d7772 (Published 15 December 2011)

CLINICAL REVIEW

Managing infants who cry excessively in the first few months of life

Chelsea and Westminster Hospital NHS
NHS Foundation Trust

Gastro-oesophageal reflux disease

According to expert consensus, gastro-oesophageal reflux disease is not a cause of excessive crying in the first months of life.[6 w4] Proton pump inhibitors increase the baby's risk of infection and possibly of food allergies.[15 16 w6] These drugs are

BMJ 2011;343:d7772 doi: 10.1136/bmj.d7772 (Published 15 December 2011)

CLINICAL REVIEW

Managing infants who cry excessively in the first few months of life

- Differential diagnosis cited in this paper:
  - Maternal reasons - expectations
  - Feeding problems
  - Functional lactose overload
  - Allergy
  - Infection

GER

CMA

DYSPHAGIA
HAEMATEMESIS
MELENA
RUMINATION
NAUSEA/BELCHING
ARCHING
BRADYCARDIA
HICCUPS
SANDIFER'S SYNDROME
ASPIRATION
LARINGITIS/STRIDOR
RESPIRATORY INFECTIONS
HOARSENESS

CRYING
IRRITABILITY
COLIC
PARENTAL ANXIETY
FEEDING REFUSAL
FAILURE TO THRIVE
VOMITING
REGURGITATION
SIDEROPENIC ANAEMIA
WHEEZING
APNEA/ALTE/SIDS
SLEEP DISTURBANCES
CONSTIPATION

DIARRHEA
BLOODY STOOLS
RHINITIS
NASAL CONGESTION
ANAPHYLAXIS
ECZEMA/DERMATITIS
ANGIOEDEMA
LIP SWELLING
URTICARIA/ITCHING

- Food allergy like urticaria or anaphylaxis
- Oral allergy syndrome

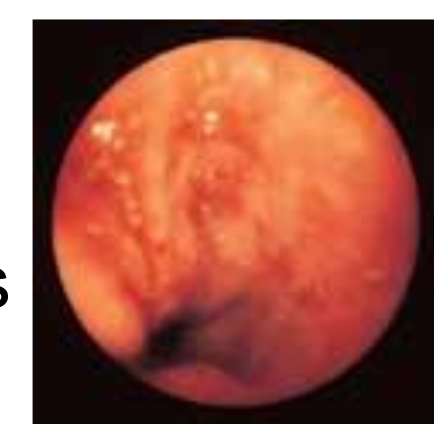
Non IgE mediated – delayed manifestation

- eczema
- Allergic colitis
- Infantile colic
- GORD
- Allergic dysmotility
- Enteropathy

Learning points in GOR and infantile colic

Avoid treating reflux when there is little evidence to support the use of anti reflux therapy in infantile colic

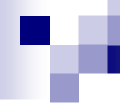
Realise that infantile colic is not the same as reflux



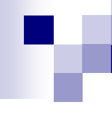
Next please………

- Shane has been complaining of abdominal pain for months. He’s been in pain now for 3 weeks and hasn’t been to school.
- His trips to A+E resulted in a diagnosis of constipation

- Take a urine sample
- Under take blood tests
- Perform an ultrasound
- Examine his anus

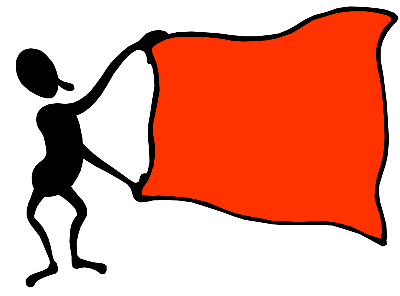


- 13% of normal children have abdo pain
- 4% of all GP paediatric visits
- 8% of all children consult the GP for pain
- Lots of children have unnecessary investigations
- IBD presents late in childhood – mainly through lack of awareness



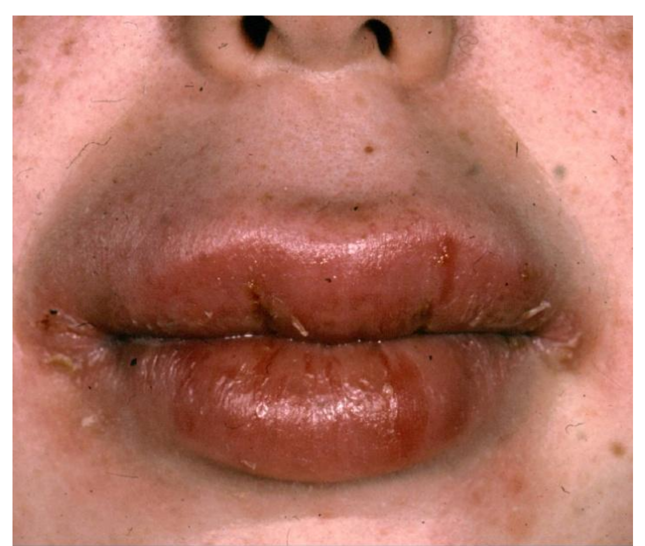
Red flags in history of RAP

- Pain localised from umbilicus +/- radiation
- Changes in bowel habit
- Vomiting
- Awakens child at night????
- Dysuria
- Rectal bleeding
- Constitutional symptoms
- Age < 4, >15
- Relevant family history



Red flags on physical examination of RAP

- Documented weight loss
- Faltering height
- Pubertal delay
- Anal fissure & perianal fissure
- Organomegaly
- Extra intestinal manifestations e.g. joints, eyes.



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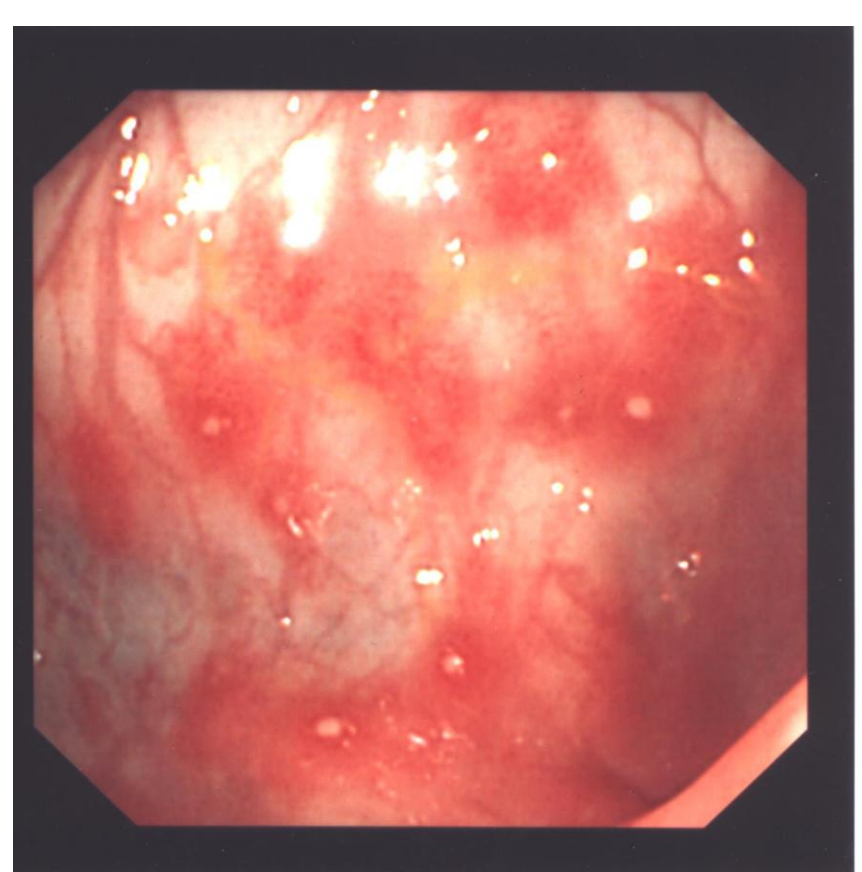

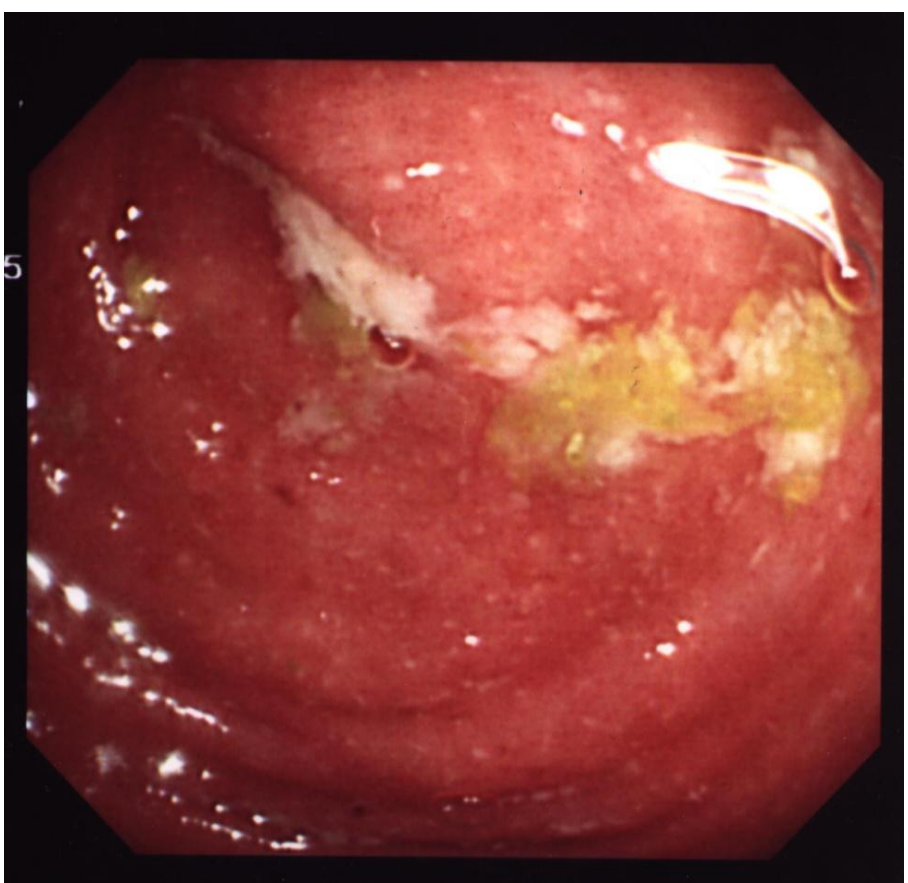

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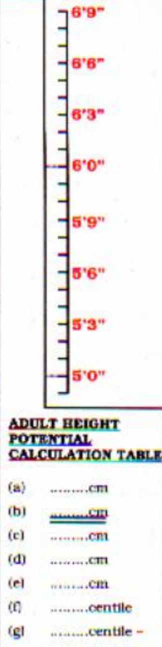
Decimal Years



ADULT HEIGHT POTENTIAL CALCULATION TABLE

(a) ....cm
(b) ....cm
(c) ....cm
(d) ....cm
(e) ....cm
(f) ....centile
(g) ....centile – ....centile

WEIGHT kg

PUBERTAL STAGES

Breast development

Stage 1 – Pre-adolescent: elevation of papilla only.
Stage 2 – Breast bud stage: elevation of breast and papilla as small mound. Enlargement of areola diameter.
Stage 3 – Further enlargement and elevation of breast and areola, with no separation of their contours.
Stage 4 – Projection of areola and papilla to form a secondary mound above the level of the breast.
Stage 5 – Mature stage: projection of papilla only, due to recession of the areola to the general contour of the breast.

Pubic Hair

Stage 1 – Pre-adolescent: The vellus over the pubes is not further developed than that over the abdominal wall, i.e. no pubic hair.
Stage 2 – Sparse growth of long, slightly pigmented downy hair, straight or slightly curled, chiefly along labia.
Stage 3 – Considerably darker, coarser and more curled. The hair spreads sparsely over the junction of the pubes.
Stage 4 – Hair now adult in type but the area covered is still considerably smaller than in the adult. No spread to the medial surface of the thighs.
Stage 5 – Adult in quantity and type.

Growth at Adolescence 2nd ed.; J.M. Tanner
Blackwell Sci. Publ. 1962.

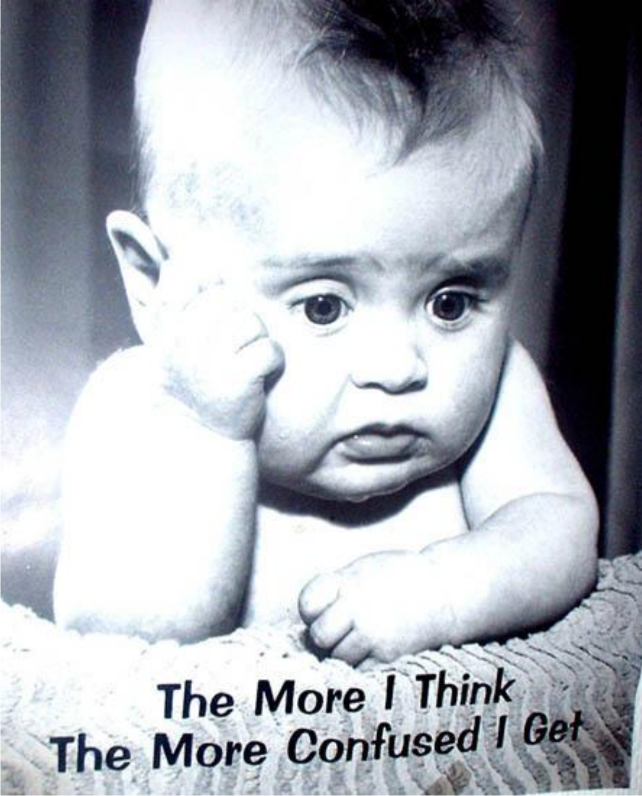
Menarche

© CHILD GROWTH FOUNDATION 1996/1

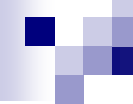
Decimal Years

9 10 11 12 13 14 15 16 17 18 19 20

Shall I do a…..



- Urine test
- Stool test for H pylori
- Test for coeliac disease
- Organise an ultrasound of the abdomen
- Refer to paediatrics after months of pain



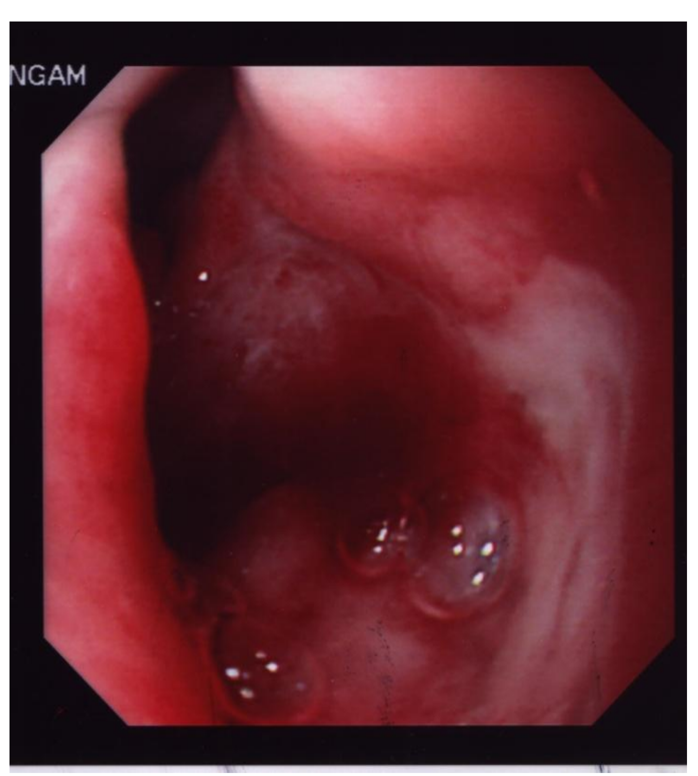
Helicobacter tests in paediatrics

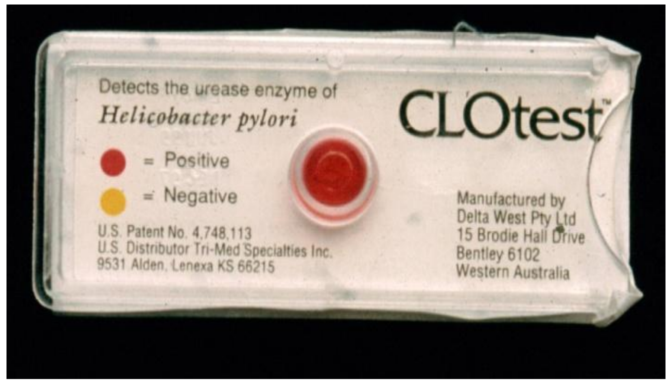
- No role for them esp. for assessing abdominal pain.
- Only in combination with endoscopy
- Only the UBT has adequate accuracy
- Stool antigen – not predictive enough

Epidemiology series

Uses and abuses of screening tests

David A Grimes, Kenneth F Schulz





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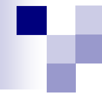
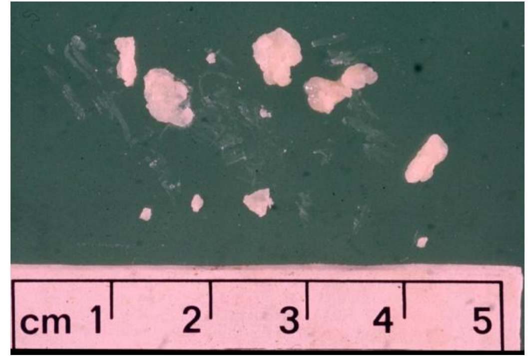


Should I take a urine sample

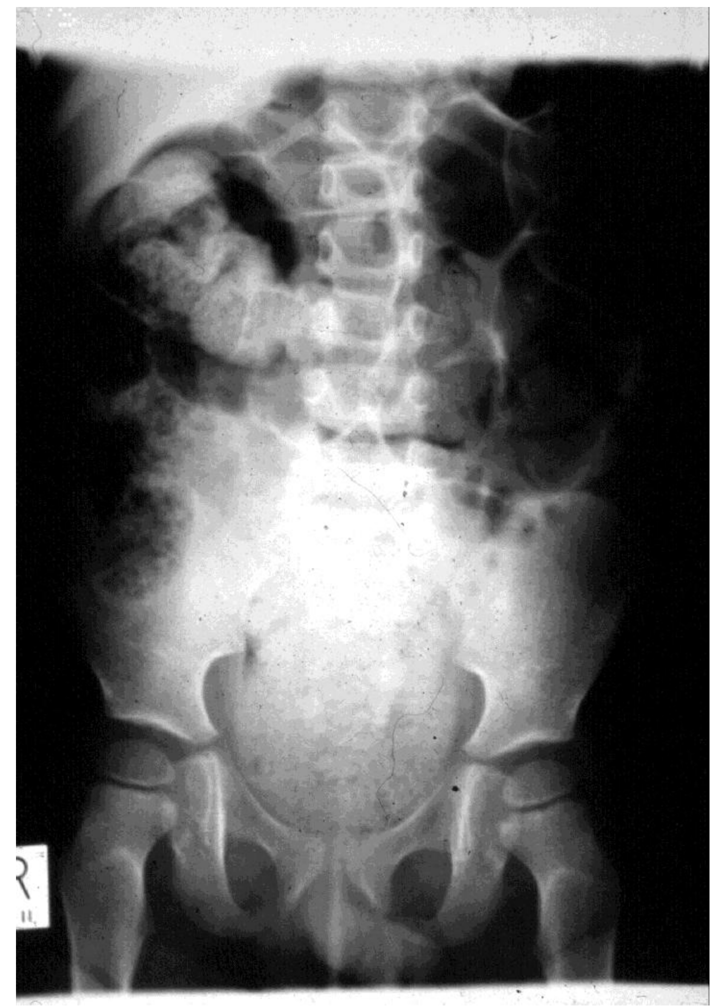
Does This Child Have a Urinary Tract Infection?

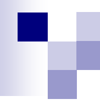
Nader Shaikh; Natalia E. Morone; John Lopez; et al.

JAMA. 2007;298(24):2895-2904 (doi:10.1001/jama.298.24.2895)



Does constipation cause pain?

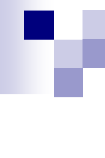




If no red flags, you probably have….

TABLE 1. *Currently Used Definitions to Describe Childhood Abdominal Pain*

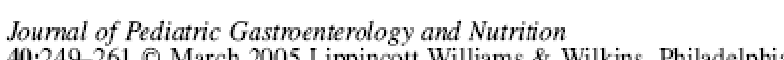
Recurrent abdominal pain as defined by Apley	3 or more episodes of abdominal pain, over a period of 3 or more mo, severe enough to affect activities.
RAP	A common abbreviation for recurrent abdominal pain that has been used in the literature to depict recurrent abdominal pain as defined by Apley. Many physicians incorrectly use this term to imply functional abdominal pain.
Chronic abdominal pain	Abdominal pain with a minimum duration of 3 mo. Some clinicians believe that pain that lasts more than 1–2 mo is chronic.
Rome II criteria for abdominal pain	Abdominal pain for at least 12 wk, which need not be consecutive, in the preceding 12 mo. These criteria apply to IBS, functional dyspepsia, and functional abdominal pain.
Functional abdominal pain	Abdominal pain that occurs in the absence of anatomic abnormality, inflammation, or tissue damage.
Nonorganic abdominal pain	A term that is often used interchangeably with functional abdominal pain.
Psychogenic abdominal pain	A term that is often used interchangeably with functional abdominal pain.



Epigastric –
non ulcer dyspepsia

RAP

IBS pain


Journal of Pediatric Gastroenterology and Nutrition
40:249–261 © March 2005 Lippincott Williams & Wilkins, Philadelphia

Technical Report

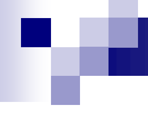
Chronic Abdominal Pain In Children: A Technical Report of the American Academy of Pediatrics and the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition

AAP Subcommittee and NASPGHAN Committee on Chronic Abdominal Pain

Chelsea and Westminster Hospital NHS
NHS Foundation Trust

If you you have functional abdo pain…

- What do we know:
  - No evidence to predict value of blood tests
  - No evidence to support use of ultrasound
  - Little evidence to support use of endscopy
  - Insufficient evidence to support pH monitoring
- Contribution of daily stressors
- These patients have more symptoms of anxiety and depression



What evidence is there to support treatments for functional pain?

- Evidence to support treatment with peppermint oil in children with IBS
- Inconclusive evidence to support use of H_2 antagonist in dyspepsia
- Inconclusive evidence that fibre decreases attacks
- Inconclusive evidence to support lactose free diet
- Limited data for use of pizotifen in abdominal migraines

Irritable bowel syndrome in adults: diagnosis and management of irritable bowel syndrome in primary care

Issued: February 2015

NICE clinical guideline 61

guidance.nice.org.uk/cg61

Chelsea and Westminster Hospital NHS
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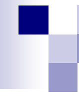


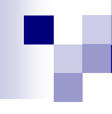
Bottom line

Epigastric –
non ulcer dyspepsia → Endoscopy plus PPI

Look for red flags

RAP →

IBS pain → Red flags and bloods



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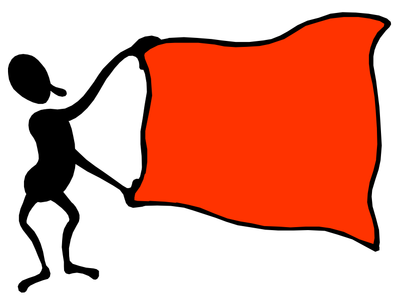

Red flags on physical examination of RAP

- Documented weight loss
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- Anal fissure & perianal fissure
- Organomegaly
- Extra intestinal manifestatio[illegible] joints, eyes.

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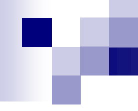
No red flags – consider functional pain

Reassess – it will become apparent

No medicines without a diagnosis



Current patient suggestions/ conditions or explanations for abdominal pain

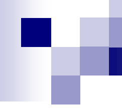
- Hypermobility +/- POTS
- Coeliac disease
- How bad I H pylori – are we striving to remove a commensal.
- Is it allergy?
- Is it migraine?
- Is this eosinophilic disease?

What about abdominal migraine

What is the pattern of abdominal migraine

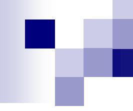
Functional abdominal pain

Abdominal migraine



Jack, age 5 describes abdominal pain with rice and wheat. He has eczema and mild asthma .Mother wants allergy testing

- Take blood for RAST testing
- Refer to hospital for skin testing
- Discourage any allergy testing
- Treat his constipation, assuming it's the cause of his pain

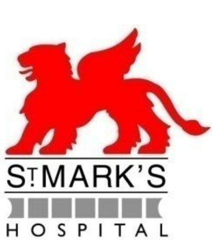


Inaccuracy of histories

"Unlike any other area in medicine, the history of adverse reaction to food is more often incorrect than it is correct"

Bock, 1998

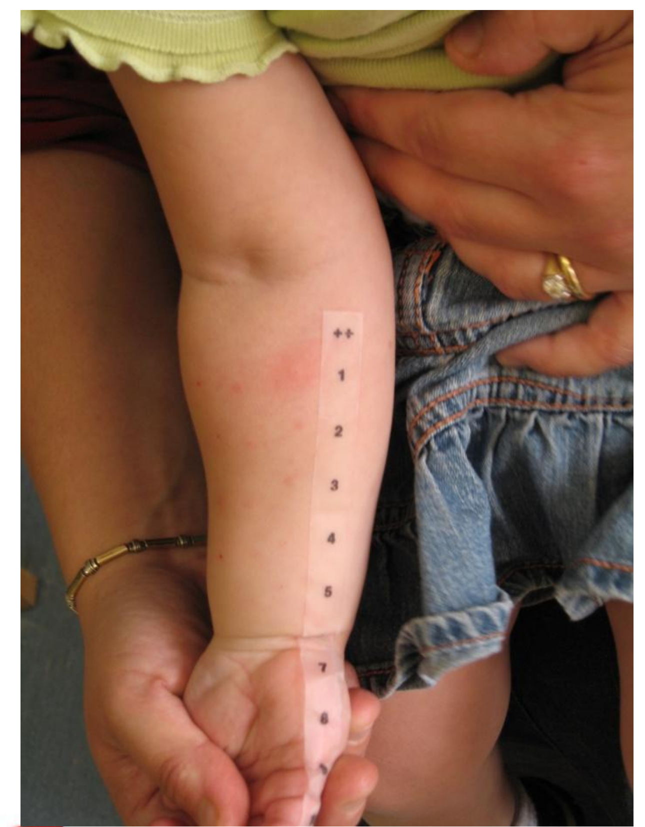
Professor Paediatrics, Colorada



Clinical and Experimental Allergy, 2000, Volume 30, pages 1495–1498

EDITORIAL

Food allergy–getting more out of your skin prick test



0.1
0.2
0.5
1
2
5
10
20
30
40
50
60
70
80
90
95
99

Post-test probability

1000
500
200
100
50
20
10
5
2
1
.50
.20
.10
.05
.02
.01
.005
.002
.001

Likelihood ratio

99
95
90
80
70
60
50
40 %
30
20
10
5
2
1
0.5
0.2
0.1

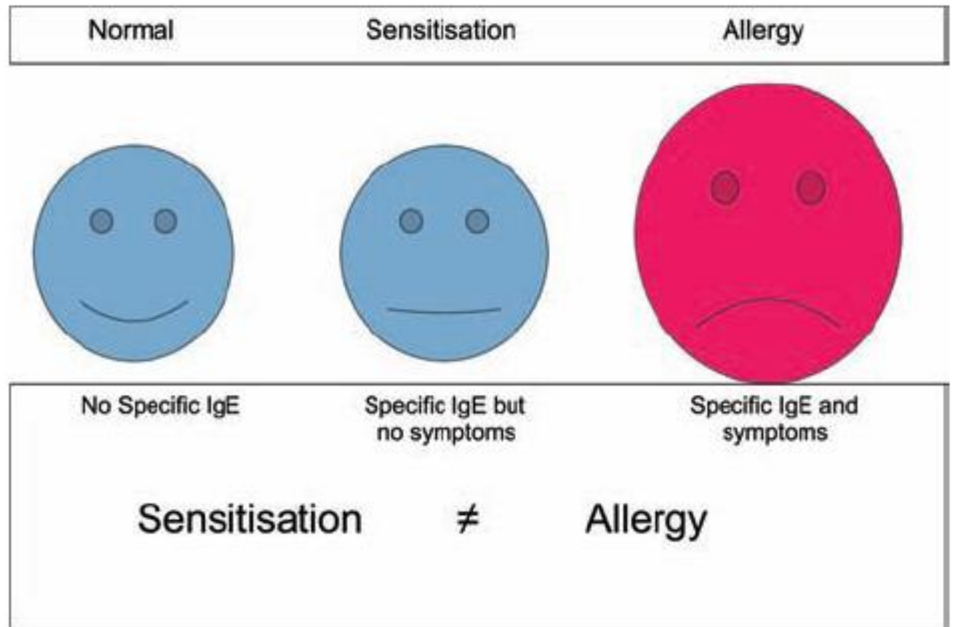
Pre-test probability

ST MARK'S HOSPITAL

NHS Foundation Trust

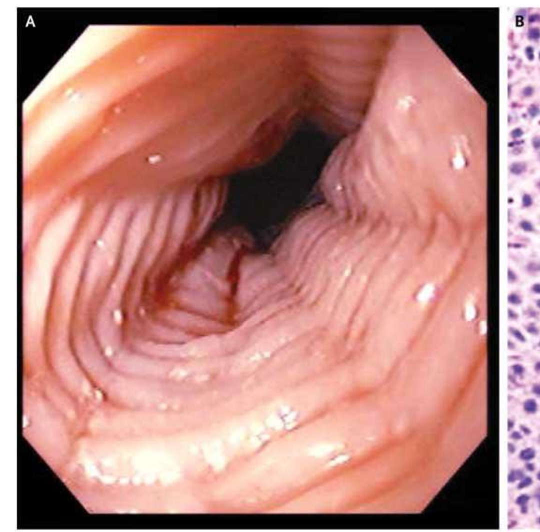
How to use serum-specific IgE measurements in diagnosing and monitoring food allergy

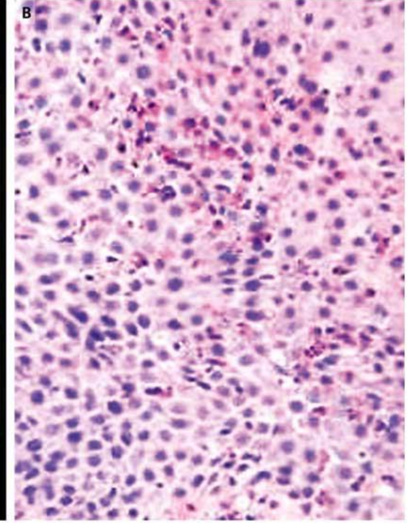
Gary Stiefel,[1] Graham Roberts[1–3]

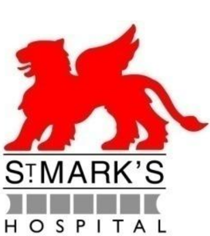


Food sticking doctor

- Therapeutic choices:
  - PPI
  - Dietary change
  - Swallow budesonide respules
  - Leave alone







- Food allergy like urticaria or anaphylaxis
- Oral allergy syndrome

Non IgE mediated – delayed manifestation

- eczema
- Allergic colitis
- Infantile colic
- GORD
- Allergic dysmotility
- Enteropathy

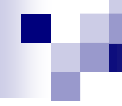
IgE mediated immediate reaction

- Food allergy like urticaria or anaphylaxis
- Oral allergy syndrome

EE

Non IgE mediated – delayed manifestation

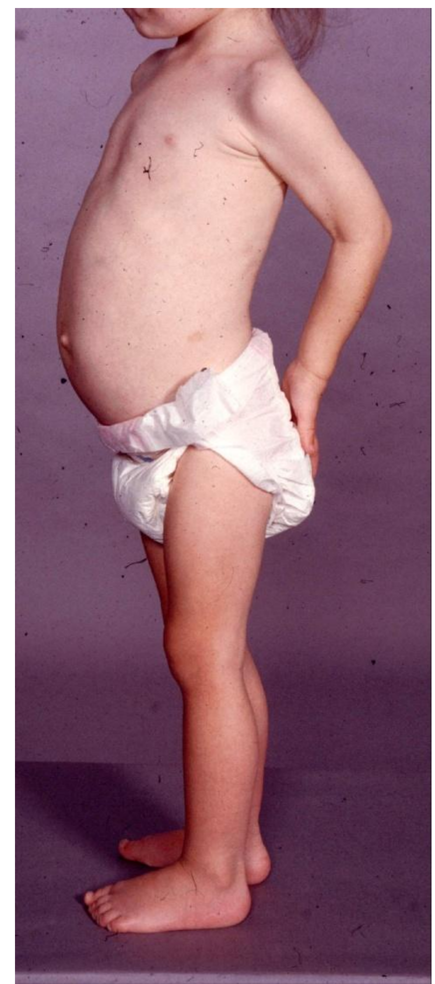
- eczema
- Allergic colitis
- Infantile colic
- GORD
- Allergic dysmotility
- Enteropathy

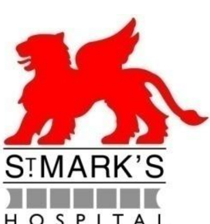


Eosinophilic GI disease

- Controversial treatment options
  - PPI
  - Asthma therapies
  - Dietary change
  - Elemental diet
  - How much is reflux
- How often to scope?
- Significance of eosinophils?
- Risk of strictures

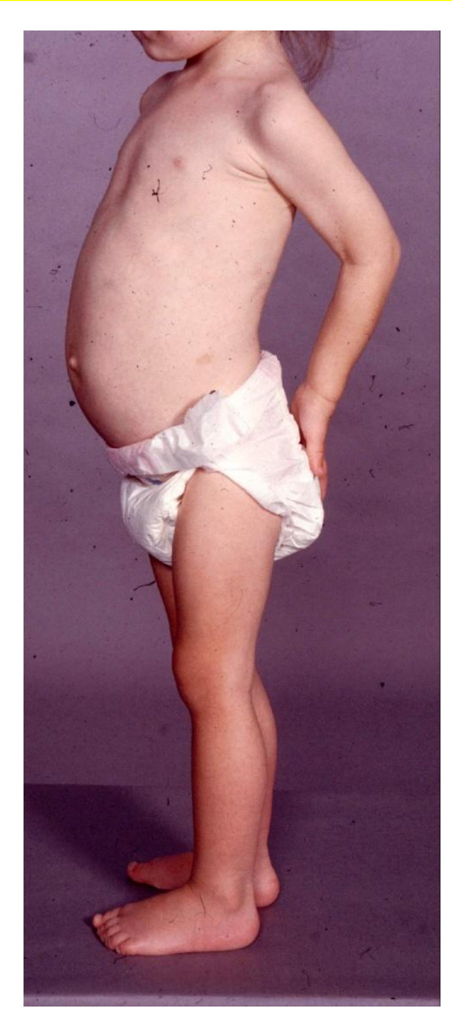
Does CD cause pain?

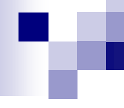




What should you do?

- Enteropathic build, +ve TTG
  - Refer for small bowel biopsy
  - Gluten free diet
  - Send to a paediatric gastroenterologist
  - Ask for AEN





New guidelines for coeliac disease

Clinical Guideline

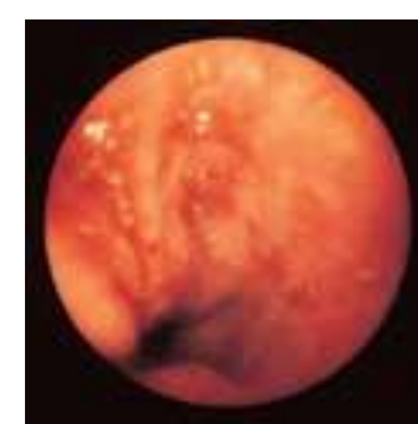
European Society for Pediatric Gastroenterology, Hepatology, and Nutrition Guidelines for the Diagnosis of Coeliac Disease

*S. Husby, †S. Koletzko, ‡I.R. Korponay-Szabó, §M.L. Mearin, ||A. Phillips, ¶R. Shamir, #R. Troncone, **K. Giersiepen, ††D. Branski, ‡‡C. Catassi, §§M. Lelgeman, ||||M. Mäki, ¶¶C. Ribes-Koninckx, ##A. Ventura, and ****K.P. Zimmer, for the ESPGHAN Working Group on Coeliac Disease Diagnosis, on behalf of the ESPGHAN Gastroenterology Committee

Chelsea and Westminster Hospital NHS
NHS Foundation Trust

Learning points in GOR and infantile colic

A rethink about reflux, screaming and PPI prescription



No red flags – consider functional pain

Reassess – it will become apparent

No medicines without a diagnosis