



# A walk through gut dysfunction in Down syndrome

Dr Mark Tighe: Consultant Paediatrician with Interest in  
Gastro+Oncology (Poole Hospital)  
Associate Editor ADC, and NICE fellow.

# Introduction

- Common and functional GI issues
  - GOR(D)
  - Food intolerances
  - Constipation
  - Links with hypotonia, co-morbidities (e.g. Congenital heart disease/hypothyroidism) and communication level
- Known associations and practical issues
  - Coeliac Disease
  - Atresias
  - Hirschsprung's

# Co-existing issues

- Hypotonia
- Congenital heart disease (where present)
- Facial/ENT differences = abnormal swallow
- Vulnerability to URTIs
  - 30% increased risk of death from sepsis (Garrison, 2005)
  - Impaired immune competence:
    - Reduced T and B lymphocyte subpopulations
    - Reduced neutrophil chemotaxis
    - Thymic abnormalities.
    - Alterations of Ig subclasses.

# Multidisciplinary discussion....



# GOR(D) Definition in children with DS

- Gastro-oesophageal reflux (GOR) = Effortless regurgitation into oesophagus.
- If GOR results in sequelae or failure to thrive = **Gastro-oesophageal reflux disease.**
- GI complications=

Oesophagitis	Haematemesis,
(Oesophageal strictures	Barrett's oesophagitis).
- Extra-intestinal=

Chronic otitis media	Failure to thrive
ALTE/Apnoea	Sinusitis
Chronic respiratory disease	Secondary anaemia

# Natural history

- Infant GOR is very common;
  - In 50% of infants less than 3 months old.
  - Improves with age (functional)
    - Oesophagus lengthens
    - More upright
    - Increased tone of lower oesophageal sphincter.
    - More solid diet.
- only 5-10% of children have symptoms after 2y.
- DS: worse with cardiac issues and hypotonia.
  - What happens at night? Any link with stress?

# NICE: Symptoms identifying GORD?

- Feed refusal
  - Choking/ gagging
  - Crying when feeding
  - Feeding problems
  - Head aversion, facial grimaces or body withdrawal when feeding
- 4 of 5 studies: not useful
  - 1 study, not useful
  - 1 study not useful, 1 study found not crying was useful to identify those without GORD
  - 1 study, not useful
  - 1 study, not useful

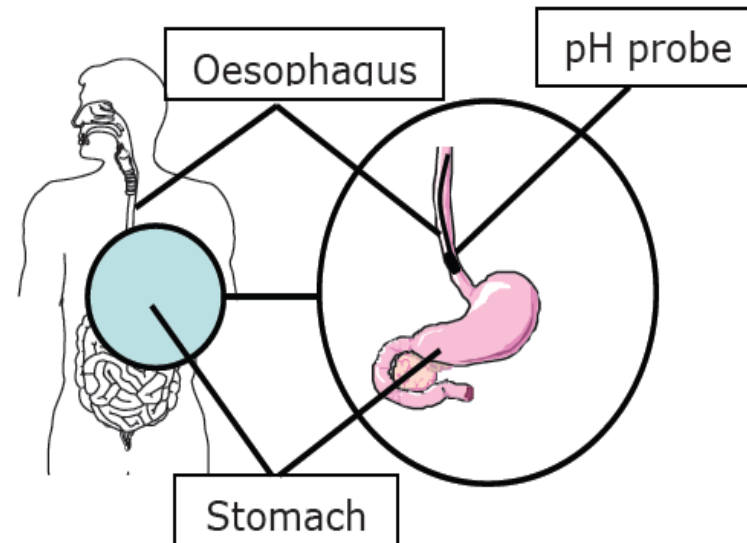
# NICE (NG1) Red Flag GI Symptoms

GI symptoms and signs	Possible diagnostic implications	Suggested actions
1. Frequent, forceful (projectile) vomiting.	May suggest hypertrophic pyloric stenosis (infants up to 2 months old).	Paediatric surgery referral.
2. Bile stained (green or yellow-green) vomit.	May suggest intestinal obstruction.	Paediatric surgery referral.
3. Haematemesis (blood in vomit) with the exception of swallowed blood.	May suggest potentially serious bleed from oesophagus, stomach or upper gut.	Specialist referral.
4. Onset of regurgitation and/or vomiting after 6 months old or persisting after 1 year old.	Late onset suggests cause other than reflux, e.g. UTI. Persistence suggests alternative diagnosis.	Urine microbiology Ix. Specialist referral.
5. Blood in stool.	May suggest variety of conditions, e.g. bacterial gastroenteritis, infant CMPA/surgical condition.	Stool microbiology Ix. Specialist referral.
6. Abdominal distension, tenderness or palpable mass.	May suggest intestinal obstruction or another acute surgical condition.	Paediatric surgery referral.



# Diagnosis

- Symptoms: avoids expensive +/- harmful Ix.
- Investigations if in doubt
  - 24hr pH/impedance probe (episodes of concern)
  - Endoscopy/biopsy
  - Barium swallow(malrotation)
  - Gastric emptying scan
  - IgE/RAST Milk?
  - USS?



## Treatment: Babies:

- In formula-fed infants with regurgitation AND distress:
  - Review feeding history, **then**
  - reduce the feed volumes if excessive **then**
  - offer a trial of smaller, more frequent feeds **then**
  - offer a trial of thickened formula
- If not improving stop thickened formula and offer alginates for a trial of 1–2 weeks.
  - If successful: continue, but stop at intervals to reassess.
- Don't offer PPIs or H<sub>2</sub>RAs for overt regurgitation in isolation in infants and children.
- Don't offer metoclopramide, domperidone or erythromycin to treat GORD without seeking specialist advice and considering potential adverse events.

## Costs of thickeners vs alginates

	Cost per month (£)
<b>Feed thickener/thickened feed</b>	
Aptamil Anti Reflux Powder <sup>ab</sup>	59.44
Cow & Gate Anti Reflux Powder <sup>ab</sup>	49.37
Enfamil Anti Reflux <sup>a</sup>	36.65
SMA Staydown Powder <sup>a</sup>	32.29
Instant Carobel Powder <sup>a</sup>	16.80
<b>Alginate</b>	
Gaviscon Infant <sup>a</sup>	22.14

# Recommendations in Children

- Consider 4-weeks of PPI/H<sub>2</sub>RA for those with regurgitation AND: unexplained feeding difficulties
  - distressed behaviour
  - faltering growth.
- Consider 4-weeks of PPI/H<sub>2</sub>RA for those with heartburn, retrosternal or epigastric pain.
- Assess response: consider endoscopy if the symptoms:
  - do not resolve **or**
  - recur after stopping the treatment.
- When choosing PPIs/H<sub>2</sub>RAs, consider:
  - the availability and cost of age-appropriate preparations
  - Preference of parent (or carer), and child (as appropriate)

**Table 1 Top 3 most commonly prescribed medication for infants highlighted by the GDG**

	Cost per month (£)
Oral alginate formulations (cost given for Gaviscon Infant <sup>a</sup> )	22.14
Ranitidine 75mg/5ml (liquid) <sup>a</sup>	2.82
Omeprazole oral formulations (cost given for Omeprazole 10mg dispersible gastro-resistant tablets (LOSEC MUPS) <sup>b</sup> )	8.30
<sup>a</sup> eMC Dictionary of Medicines (November 2014).	
<sup>b</sup> Electronic drug tariff November 2014.	

# NICE guidelines on Enteral Feeding

- Consider for poor weight gain in infants/children with regurgitation & faltering growth if:
  - other explanations for poor weight gain have been explored **and/or**
  - recommended feeding and medical management of overt regurgitation fail.
- Before starting enteral tube feeding for infants and children with faltering growth associated with overt regurgitation, agree in advance:
  - a specific, individualised nutrition plan
  - a strategy to reduce AND
  - an exit strategy, when appropriate, to stop it as soon as possible.

## Surgery: fundoplication

- Consider fundoplication in those with severe, intractable GORD if:
  - appropriate medical treatment has been unsuccessful **or**
  - feeding regimens to manage GORD prove impractical, for example, in the case of long-term, continuous, thickened enteral tube feeding
- Offer an upper GI endoscopy +/- combined oesophageal pH and impedance monitoring and contrast study beforehand.

# Dietary Intolerances and DS

- Common. Issues include:
- Restrictive intake/Lack of variation (autism)
  - 1 study: 19 patients with DS and matched controls
  - Shorter breastfeeding, higher carbohydrate intake
- Dairy-related (CMPA or intrinsic?)
- Coeliac vs non-coeliac gluten sensitivity
  - Screening or symptoms?
  - 1/3 adult IBS responds to GFD.
  - Test prior to treating



# Coeliac Disease and DS

- Children often asymptomatic and picked up on annual screening.
  - Carlsson (1998): 43 well children with Down syndrome: 0 had celiac disease at entry; 37% (16/43) were found to have TTG levels above normal, and 16% (7/43) to be EMA-positive.
  - Zachor (2000): 75 asymptomatic patients assessed: 1 in 14 positivity rate
  - Carnicer (2008): 18/284 children in Barcelona had coeliac disease: 8 classical Sx, 7 had atypical Sx, 3 silent.

Classic coeliac disease	Atypical/extraintestinal
Abdominal pain	Asymptomatic/from screening
Diarrhoea, constipation	Anaemia, fatigue
Distension, bloating	Vitamin deficiencies
Anorexia	Muscle wasting
Faltering growth	Short stature/delayed puberty
Irritability, lethargy.	Dermatitis Herpetiformis/ Aphthous ulcers

# Endoscopy (new)

## 2012 BSPGHAN guidance (**symptomatic** patients):

- Not required if TTG > 10x upper limit of normal/EMA +ve and HLA DQ2/8 +ve.
- Endoscopy should rarely be considered in patients with negative serologic test results who are at high risk/high index of suspicion.
- When testing: should be on gluten-containing diet > 6g/day.
- Saves cost of endoscopy, and morbidity.
- Allows children to start gluten-free diet earlier
- **Asymptomatic children with raised TTG IgA/EMA+ve need scope**

# So why Gluten-free diet?

- Better energy and reduced GI symptoms
- Better growth, normal puberty.

## Long-term consequences

- Osteopenia/osteoporosis.
- Increased cardiovascular morbidity
- Anaemia
- Malignancies (GI tract [e.g. intestinal T-cell lymphoma 200x]).
  - Screening strategy: costs >\$500000 per life-year gained.  
Screening children with Down syndrome for coeliac disease costs ~\$5 million per case of lymphoma: Swigonski (2006)
- Infertility.

# Treatment of coeliac disease

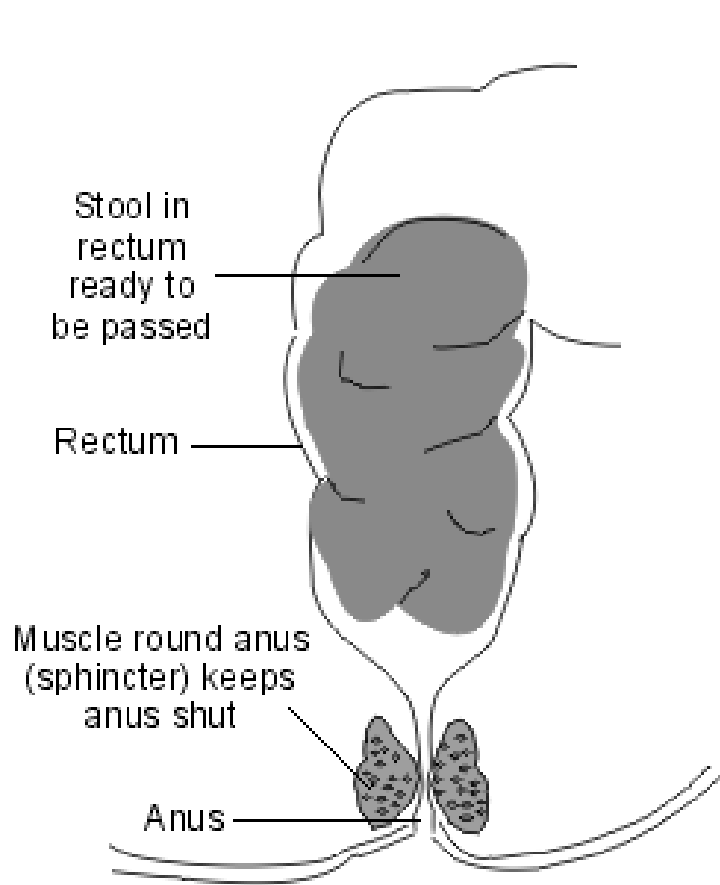
- Avoid food products containing <20ppm gluten (prescription....for now).
- Follow-up improves compliance.
  - 85% compliance with annual follow-up
  - 45% compliance with diagnosis then discharge
- Support by a trained dietitian is key.
- Coeliac UK provides information and support.

# Stooling issues and DS

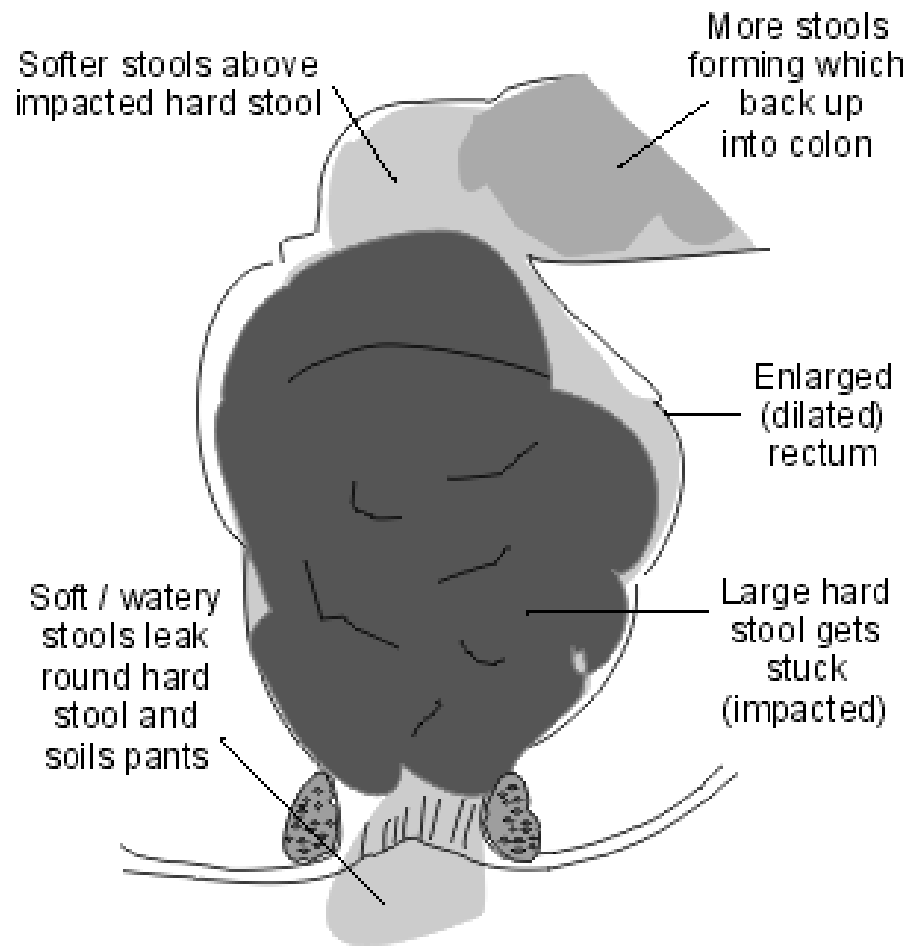
- Constipation Prevalence 20-36%
  - Increased with hypotonia , communication and behaviour issues, supplementary feeds.
  - Need to exclude organic disease
  - Overflow/withholding common misconceptions
  - May benefit more from stimulants.
- Diarrhoea: often due to overflow.
  - If associated with initial pyrexia ?gut dysbiosis
  - Lactose intolerance/malabsorption

# Triggers

- Varies between children
  - Elucidate in the history: age of onset.
  - Parental expectations
  - Address them in the treatment strategy.
- Also consider: pain (e.g. a fissure)
  - Fever/dehydration
  - Dietary intake (in terms of fibre content)
  - Psychological issues and expression of distress
  - Toilet training/aversion
  - Other medicines, other conditions
  - Family history of constipation.



**Normal**



**Chronic Constipation**



- Examination

- Plot growth on appropriate growth chart
- Abdominal palpation to assess for impaction,
- Assessment of the spine and lower limb reflexes.
- Examining the perineum visually for fissures or streptococcal infection is also useful.
- Rectal examination should not be performed in those over 1 year of age except in a specialist setting.



# Investigations

- Low yield (<5% pickup of disease)
- Bloods: FBC, U+E, inflammatory markers.
  - Coeliac serology (TTG/EMA + total IgA)
  - TFTs if not growing well
  - IgE+ food allergy panel (egg, wheat, milk, soya)
- Imaging: AXR (to convince parents?)
  - Shapes study



# NICE recommended treatment

- Investigate children with red flags
- For faecal impaction
  - NICE: Polyethylene glycol 3350 + electrolytes (e.g. Movicol Paediatric Plain)
    - Escalating dose regimen (= first-line treatment).
    - Adjust the dose of Movicol according to response.
    - Risk of increased overflow (consider school).
    - Review soon
    - Reduce the dose of Movicol when disimpaction is achieved
      - Maintenance dose might be half disimpaction dose.
- **BUT....**

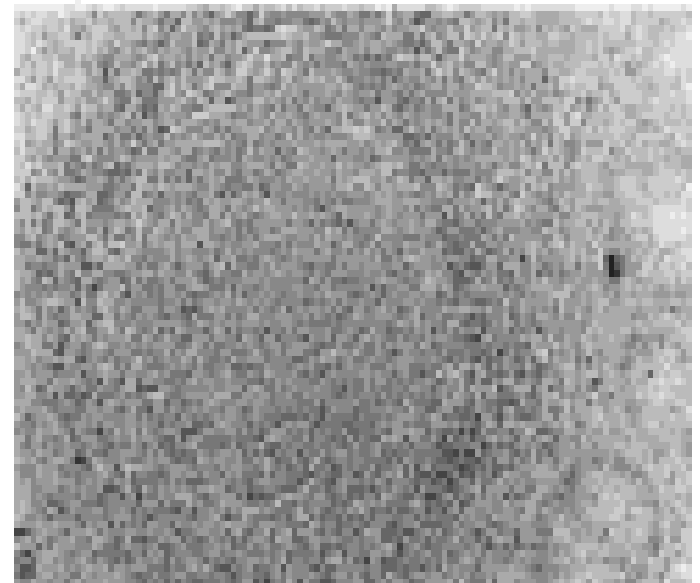
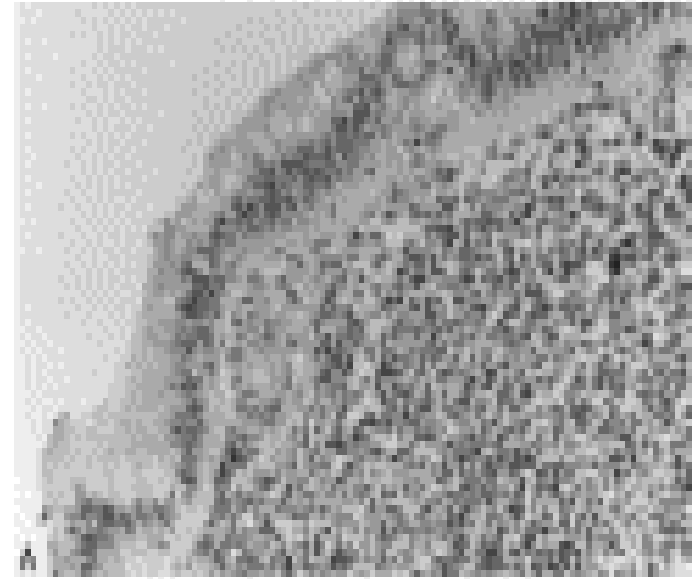
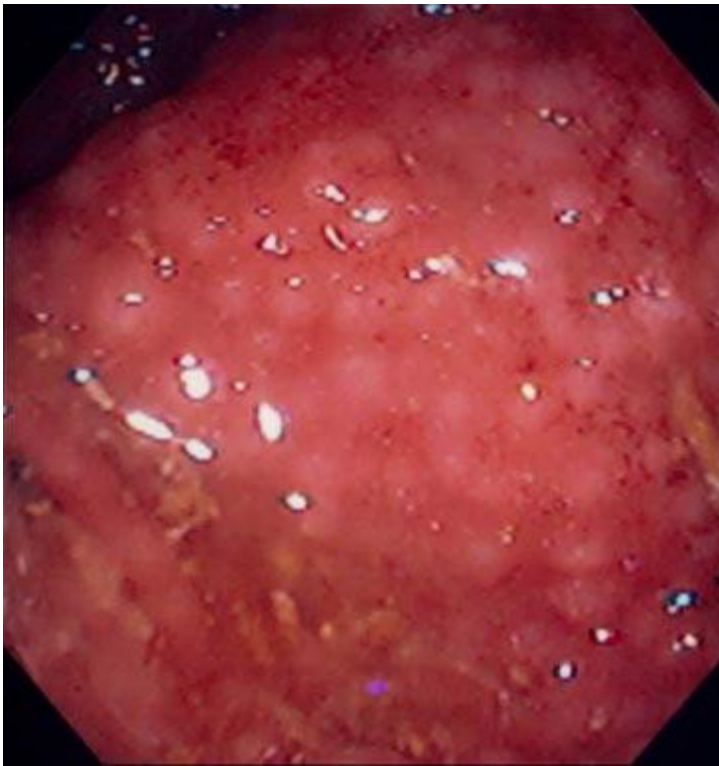
- Add stimulant (senna/picosulphate) if Movicol alone does not work (can cause overflow++).
- Substitute a stimulant laxative if Movicol is not tolerated.
- Add another laxative such as lactulose (toddlers) or bisacodyl (older children) if stools are hard.
- Medication may be needed for weeks/months.
- Children who are toilet training should remain on laxatives until toilet training is well established.
- Gradually reduce the dose over a period of months in response to stool consistency and frequency; and increase if symptoms relapse.
- 20-30% children with DS may require laxatives for several years.

# Also....

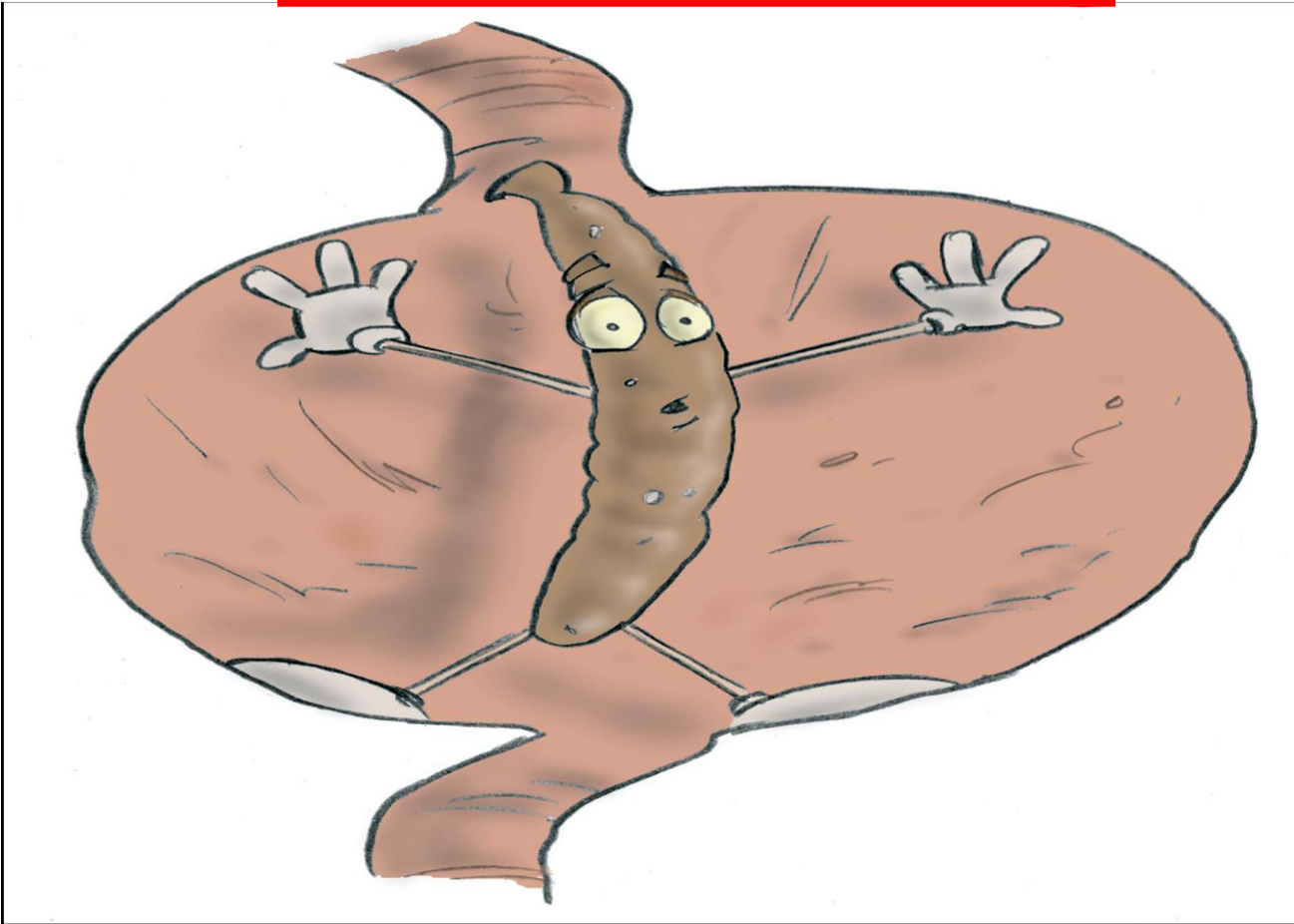
- Laxatives are only half the story.....
- Increase fibre content (to normal).
- Ensure adequate hydration
- Increase exercise levels (all evidence based).
  
- Positive behavioural interventions/rewards suited to the child's level.
- Explain that treatment may take years.
- Addressing the underlying trigger,
  - Understanding of parents
  - Fear of toilets in younger children
  - Access to school toilets in school age children.
- Early reassessment and reinforcement of initial messages is also key.
  
- Other resources: Social stories/school nurse/health visitor/continence nurse

# IgE/non-IgE mediated CMP Allergy

- Cow's milk protein exclusion:
  - Consider if family history, eczema, or suggestive history.
  - Or refractory to laxatives (10% have marked improvement).



# Bowel Training



“I’m not going down there –I haven’t been trained!!!”



# Atresias: Oesophageal Atresia

- Incidence in DS is 0.5–0.9%.
- Following surgical repair
  - Resp. problems: bronchitis, cough, pneumonia, wheezing.
  - 44% of patients hospitalised with respiratory illnesses in the years following repair; 2/3 have ongoing respiratory symptoms in the first 5 years.
  - GI problems:
    - >50% have ongoing GORD
    - TOF cough causing vomiting

# Hirschsprung's and DS

Increased incidence (2-15%): ?on chromosome 21

Long-term consequences: most diagnosed in neonatal period.

Delayed passage of meconium in DS easily missed  
(e.g. Admission to NICU)

Problems post-operatively: incontinence/constipation.

Recurrent enterocolitis

Hirschsprung's disease and congenital central hypoventilation syndrome (CCHS), Haddad (1978) are DIFFERENT to those with DS and Hirschsprung's disease,

- Differences in length+ distribution of the aganglionosis
- ?related to PHOX2B gene

Any questions?

