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# Gastro-oesophageal reflux in children

## What's the worry?

### Background

Gastro-oesophageal reflux is common and benign in children, especially during infancy. Distinguishing between gastro-oesophageal reflux, gastro-oesophageal reflux disease and other illnesses presenting as chronic vomiting can be difficult. The general practitioner has a key role to play in identifying if a child requires referral for further investigation.

### Objective

This article outlines the main differential diagnoses to be considered in children presenting with chronic vomiting and/or regurgitation. We also discuss key management decisions regarding gastro-oesophageal reflux disease in children and when to refer to a specialist for further investigation.

### Discussion

Chronic vomiting and regurgitation frequently occurs in infancy and is most commonly due to simple, benign gastro-oesophageal reflux, which is usually self limiting without requirement for further investigation. In contrast, gastro-oesophageal reflux disease requires considered management and may be a presenting symptom of food allergy requiring more intensive therapy than simple acid suppression. Regular review by the general practitioner to ascertain warning signs will ensure that other serious illnesses are not overlooked and that appropriate investigation and specialist referral are made.

### Keywords

gastroesophageal reflux; infant; child; cow's milk protein allergy; eosinophilic oesophagitis



### Case study

James, aged 3 months, was brought to his general practitioner due to concerns about recurrent vomiting after feeds, which were nonbilious with no suggestion of haematemesis. James was born at term via spontaneous unassisted vaginal birth without complications. Growth parameters at birth were all on the 50th percentile. Complementary feeds with cow's milk based formula were commenced from approximately 2 weeks of age due to maternal concern about poor feeding. Postfeed vomiting commenced around 4 weeks of age, although intake remained good. James was otherwise well between feeds, although bowel actions were frequent with 6–8 bowel actions per day with mild perianal excoriation noticed regularly. Eczema, which required the application of a mild topical steroid, commenced around this time. At his 3 month health check, the maternal and child health nurse noted that James' weight gain had slowed to the 10th percentile while his length and head circumference remained on the 25th percentile.

In view of the ongoing vomiting and slowed weight gain, James' GP prescribed ranitidine for the presumptive diagnosis of gastro-oesophageal reflux disease (GORD). Despite good medication compliance, James' weight continued to decrease to just above the third percentile, with length on the 10th percentile, by 6 months of age. He was referred to a paediatric gastroenterologist for further assessment due to failure to thrive.

Following paediatric gastroenterologist assessment, James was investigated with barium meal, which ruled out gastric outlet obstruction and malrotation. Oesophageal pH study was not requested. Gastroscopy was performed and the results were macroscopically unremarkable. Histological findings from endoscopic biopsies showed a mixture of neutrophils and mild eosinophilia in the lower oesophagus and duodenum. Oesophageal eosinophilia was less than 15 per high power field with no basal cell proliferation, ruling out eosinophilic oesophagitis. The other biopsies were unremarkable with normal small intestinal disaccharidases, ruling out lactose intolerance.

These findings were consistent with GORD. Due to the timing of symptom development, the possibility of cow's



milk protein allergy was considered. James' cow's milk based formula was changed to an extensive hydrolysed formula, which coincided with his mother's wish to cease breastfeeding. Over the subsequent 2 weeks his vomiting gradually improved with steady weight gain and resolution of frequent bowel actions, with 1–2 pasty bowel actions per day. Re-challenge with cow's milk formula at home resulted in symptom recurrence confirming the diagnosis of cow's milk protein induced GORD. Cow's milk protein elimination advice was implemented and by the age of 10 months James' weight and length had returned to the 25th percentile. At 18 months of age James was re-challenged with cow's milk, with no recurrence of symptoms. This demonstrated evidence of allergy resolution.

## What is gastro-oesophageal reflux?

Gastro-oesophageal reflux (GOR) is the passage of gastric contents into the oesophagus (with or without regurgitation and vomiting) lasting <3 minutes in the postprandial period with few or no symptoms.<sup>1</sup> It is the result of an abnormally functioning lower oesophageal sphincter, which in infants is usually due to developmental immaturity of the lower oesophageal sphincter. Infantile GOR peaks at 4 months of age<sup>2</sup> and is usually resolved by the age 12 months.<sup>3</sup> Gastro-oesophageal reflux is benign and does not impact on a child's health.

## What is gastro-oesophageal reflux disease?

Gastro-oesophageal reflux disease (GORD) is considered when gastro-oesophageal reflux causes troublesome symptoms and/or complications,<sup>1</sup> such as failure to thrive, haematemesis, refusal to eat, sleeping problems, chronic respiratory disorders, oesophagitis, stricture, anaemia, apnoea or apparent life threatening episodes. Complications of GORD are uncommon, however, it is important that it is identified early and managed appropriately. Referral to a specialist may be required for formal investigations such as combined intraluminal impedance and pH monitoring, barium study and/or endoscopy and biopsy. Intraluminal impedance combined with pH study is where a catheter-like nasogastric tube is inserted transnasally and the tip of catheter is allocated just above the lower oesophageal sphincter to allow for detection of GOR independent of pH (ie. detecting both acid and nonacid reflux).

## Cow's milk protein allergy

Cow's milk protein allergy (CMPA) is an immunologically mediated adverse reaction to cow's milk protein. It can present as a range of symptoms occurring from minutes to hours after ingestion to several days after cow's milk formula has commenced in the diet. It is estimated that up to 40% of infants with symptoms of GORD referred to specialist services have CMPA.<sup>4</sup>

Cow's milk protein allergy-induced GORD is one way that CMPA can present. It presents as a delayed reaction and can be difficult to diagnose due to nonspecific symptoms such as persistent vomiting.

The key element to note on history taking is that symptoms are most likely to develop within 4 weeks of exposure to cow's milk formula,<sup>5</sup> although if exposure is low grade and intermittent the presentation can be more subacute. Importantly, CMPA is not limited to formula-fed infants and can occur in exclusively breastfed infants, as intact cow's milk proteins can be secreted in breast milk.<sup>6</sup>

Delayed reaction CMPA is a non-IgE mediated food allergy, therefore skin prick testing (SPT) and food specific serum IgE antibody levels (cap-FEIA testing) are not required unless a mixed IgE/non-IgE syndrome is suspected, as in eosinophilic oesophagitis (EO). Elimination and re-challenge protocols are the only way to make a definitive diagnosis of non-IgE mediated CMPA with full resolution of symptoms via strict elimination followed by recurrence on reintroduction of cow's milk protein. Patients who do not have elevated IgE antibodies (ie. negative SPT or serum cow's milk protein IgE antibodies) are not at risk of anaphylaxis and therefore home based challenges can be safely recommended.

By contrast, an immediate reaction (ie. vomiting, perioral or periorbital oedema, urticaria or anaphylaxis) to cow's milk occurring within minutes (<1 hour) of ingestion is suggestive of IgE mediated food allergy. Skin prick testing or measurement of food specific serum IgE antibody levels should be performed to exclude or confirm whether the child is at risk of anaphylaxis.

## Distinguishing eosinophilic oesophagitis from GORD

Eosinophilic oesophagitis is a recently recognised panoesophagitis in children, with diagnosis based on histological evidence of at least 15 eosinophils per high power field on oesophageal biopsies obtained at gastroscopy.<sup>7</sup> It is closely associated with food allergy (including IgE and non-IgE mediated) and other atopic conditions such as eczema, allergic rhinitis, asthma or family history of atopy.

Eosinophilic oesophagitis can present at any age with nonspecific gastrointestinal symptoms, including regurgitation, vomiting, food refusal or dysphagia. A classic infancy EO presentation includes irritability, feeding refusal and failure to thrive, which often overlaps with GORD presentation. On the other hand, food bolus impaction is the most common EO presentation in school aged children and adolescents.<sup>7</sup> Complications of EO, such as food impaction requiring endoscopic disimpaction and oesophageal stricture, are uncommon but can be life threatening.<sup>7</sup> Management of suspected EO requires referral to a gastroenterologist for diagnosis by endoscopy. Treatment usually consists of a trial of food allergen elimination (ie. empirically or based on allergy testing – with referral to an allergist) or swallowed inhaled corticosteroids. An 8 week trial of proton pump inhibitors (PPIs) to exclude GORD as a differential diagnosis is recommended in North American guidelines.<sup>8</sup>

## Differential diagnosis in a child with chronic vomiting

Age of presentation and duration of symptoms are important indicators



in formulating the differential diagnosis of chronic vomiting. Careful history and physical examination are required to exclude other gastrointestinal, as well as other organ system causes.

Table 1 lists warning features requiring investigations in infants with regurgitation or vomiting. Table 2 lists differential diagnoses, some of which will require specialist referral for assessment.

## Management of GOR

As GOR is a transient condition, the aims of management are parental education, guidance and support. Demonstrating appropriate growth in infants using growth charts may be a way of reassuring parents. The Royal Children's Hospital clinical practice guidelines recommend consideration of the prone position for infants with GOR after feeding. However, this should only be done in an infant who is awake and with parents present, and never in sleeping or nonobserved infants due to an increased risk of sudden infant death syndrome. Thickened feeds (eg. using antiregurgitation formula) can also be considered<sup>9</sup> to minimise the frequency of vomiting (see *Resources*).

Lifestyle changes can be recommended for older children and adolescents with GOR or GORD (Table 3).

## Management of CMPA induced GORD

In infants with suspected CMPA delayed reaction causing GORD, elimination of dairy products and a trial of formula change is warranted, which may include infant soy formula for 2 weeks in infants older than 6 months. If improvement is not noted following a trial of soy formula then specialist referral may be warranted to assess whether progression to extensively hydrolysed formula (eg. Pepti-Junior or Alfaré) is required. There is no place for the use of partially hydrolysed (known as HA formula) or other mammalian milks (such as goat's milk) in the treatment of CMPA.<sup>10</sup>

**Table 1. Warning features requiring investigation in infant with regurgitation or vomiting<sup>1</sup>**

- Bilious vomiting
- Gastrointestinal bleeding (haematemesis or haematochezia)
- Consistently forceful vomiting
- Onset of vomiting after 6 months of life
- Failure to thrive
- Diarrhoea
- Constipation
- Fever
- Lethargy
- Hepatosplenomegaly
- Bulging fontanelle
- Macro/microcephaly
- Seizures
- Abdominal tenderness or distension
- Documented or suspected genetic/metabolic syndrome

Infants with evidence of immediate reactions to CMPA suggestive of IgE mediated food allergy should be urgently referred to a paediatric allergist for formal investigations and management. In the interim, cow's milk protein should be strictly eliminated and replaced with soy formula in infants older than 6 months and extensively hydrolysed formula in infants less than 6 months. A written allergy action plan (see *Resources*) needs to be given to parents. Prescribing an adrenaline autoinjector, if appropriate, is recommended.<sup>6</sup>

**Table 2. Differential diagnosis of vomiting in childhood (modified)<sup>1</sup>**

- Other gastrointestinal disorders
  - gastroenteritis
  - food allergy
  - eosinophilic oesophagitis
  - peptic ulcer
  - inflammatory bowel disease
  - pancreatitis
  - appendicitis
  - achalasia
- Gastrointestinal obstruction
  - pyloric stenosis
  - malrotation with intermittent volvulus
  - Hirschsprung disease
  - foreign body
  - incarcerated hernia
- Neurology
  - hydrocephalus
  - subdural haematoma
  - intracranial haemorrhage
  - intracranial mass
- Infectious
  - sepsis
  - meningitis
  - urinary tract infection
  - pneumonia
  - otitis media
- Renal
  - obstructive uropathy
  - renal insufficiency
- Toxic
  - lead
  - iron
  - medicines (eg. digoxin, theophylline)
- Cardiac
  - congenital heart failure
  - vascular ring
- Other
  - Munchausen syndrome by proxy
  - child neglect or abuse
  - self induced vomiting
  - cyclic vomiting syndrome
  - rumination syndrome
  - metabolic syndrome



There may be some initial investigations that GPs can order before referral. However, investigations are usually ordered based on the clinical assessment of the patient as differential diagnosis can vary significantly with different age groups. Noninvasive test for lactose intolerance (malabsorption) using lactose hydrogen breath test can be ordered, however, accessibility can be difficult. Stool reducing substances are unreliable and nonspecific for lactose intolerance and therefore are no longer recommended.

Food specific serum IgE antibody (cap-FEIA testing) always requires clinical history for the appropriate interpretation. If the GP is comfortable with their interpretation (ie. clinical history of non-IgE mediated and negative SPT or serum cow's milk protein IgE antibodies), home based challenge can occur. Otherwise, referral to a specialist is recommended.

Table 4 shows when referral to a specialist is recommended in children with CMPA.

## Pharmacological therapy for GORD

Antacids (magnesium hydroxide/aluminium hydroxide) as a buffering gastric agent may provide rapid symptom relief for some children with GORD symptoms. Caution should be exercised with the use of antacids in infants with GORD, especially with long term use, as aluminium toxicity can result in renal disease. As alternative pharmacological therapies are available, chronic antacid therapy is generally not recommended for children with GORD.<sup>1</sup>

**Table 3. Lifestyle change recommendations for older children with GOR or GORD (if appropriate<sup>1</sup>)**

- Dietary modification – avoiding caffeine, chocolate or spicy food if they provoke symptoms
- Weight loss in overweight children
- Sleeping position changes for adolescents (left lateral decubitus sleeping position with elevation of head of the bed)
- Avoidance of alcohol and smoking

**Table 4. Recommendations for further referral to specialist in children suspected to have cow's milk protein allergy<sup>6</sup>**

- Urgent referral
  - anaphylaxis
  - food protein induced enterocolitis syndrome
  - severe failure to thrive
  - hypoproteinaemia/protein losing enteropathy
- Referral if trial of cow's milk elimination fails
  - haematemesis
  - chronic diarrhoea
  - persistent vomiting
  - persistent rectal bleeding
  - iron deficiency anaemia
  - severe eczema

Histamine-2 receptor antagonists (H2RAs) (eg. ranitidine) reduce acid secretion from gastric parietal cells and have a rapid onset of action. They can be considered in older children and adolescents for relieving GORD symptoms and for healing oesophagitis, although PPIs are preferred.<sup>1</sup> Histamine-2 receptor antagonists have the potential for tolerance with chronic usage.

Proton pump inhibitors are gastric acid reduction agents with superior efficacy to H2RAs and are effective in treating symptoms of GORD and healing of oesophagitis. A recent systemic review was unable to demonstrate that PPIs are effective in reducing GORD symptoms in infants.<sup>11</sup> In older children or adolescents with GORD symptoms, an empiric PPI trial is justified for up to 4 weeks to improve symptoms.<sup>1</sup> There are currently five PPIs available in Australia (omeprazole, esomeprazole, lansoprazole, pantoprazole and rabeprazole) and although none is preferred for use in the paediatric setting, the form of delivery tends to determine the preferred agents in selection for paediatric patients. For example, omeprazole can be made in liquid form and lansoprazole comes in dispersible tablets, which are more convenient for younger patients. Proton pump inhibitors are well tolerated in short term usage but long term safety evidence in children is still lacking.

Other prokinetic agents such as metoclopramide, domperidone and erythromycin have insufficient evidence for routine use in GORD.

## Is there a role for surgical procedures in children with GORD?

Surgical antireflux procedures such as laposcopic fundoplication are only considered in children with confirmed chronic GORD who have failed optimal medical therapy, are dependent on medical therapy over a long period, are significantly noncompliant with medical therapy or who have life threatening complications of GORD.<sup>1</sup> In these circumstances, referral to a specialist paediatric surgeon to receive appropriate education and understanding of the potential complications of surgery is required before a decision can be undertaken.

## Key points

- Gastro-oesophageal reflux is commonly seen in infants and usually only requires reassurance, education and support for parents.
- A thorough history and physical examination are required to exclude other causes of chronic/persistent vomiting in a child. Assessment should also include further investigation if there are warning signs of serious illness.
- Children with suspected cow's milk protein allergy induced GORD can trial dairy product elimination and change of formula before referral for specialist assessment.
- Eosinophilic oesophagitis should be considered in children with persistent GORD symptoms or when not responding to treatment. Early identification and treatment of eosinophilic oesophagitis can prevent serious complications that may occur later.
- Nonpharmacological and pharmacological therapies can be considered in treating children with GORD symptoms.



## Resources

### For parents

- The Royal Children's Hospital Melbourne – Reflux. Available at [www.rch.org.au/kidsinfo/handout/index.php?doc\\_id=9921](http://www.rch.org.au/kidsinfo/handout/index.php?doc_id=9921)

### For GPs

- The Royal Children's Hospital Melbourne. Clinical practice guidelines: reflux (GOR). Available at [www.rch.org.au/clinicalguide/cpg.cfm?doc\\_id=9746](http://www.rch.org.au/clinicalguide/cpg.cfm?doc_id=9746)
- Australasian Society of Clinical Immunologist and Allergists: [www.allergy.org.au](http://www.allergy.org.au).

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Conflict of interest: none declared.

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