

GORD in infants and children

when to investigate and when to treat?

GPs commonly review infants and young children with suspected gastro-oesophageal reflux (GOR). Many of these patients are empirically treated with acid-suppressive medications. To avoid over-treatment, it is important to distinguish between uncomplicated GOR and gastro-oesophageal reflux disease (GORD), particularly in infants.

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Gastro-oesophageal reflux (GOR) is characterised by the involuntary and passive flow of gastric contents into the oesophagus. Although generally benign, it may occasionally be associated with significant morbidity. To avoid over-treatment, it is important to distinguish between uncomplicated GOR and gastro-oesophageal reflux disease (GORD), particularly in infants. Minor GOR in otherwise well infants is considered physiological. There are important differences between the clinical presentations of reflux disease in children and adults. Infants and young children with GORD often present with extra-oesophageal symptoms, including aversive feeding behaviours, failure to

thrive or respiratory manifestations. The 'classic' symptoms of GORD, such as regurgitation, epigastric pain and heartburn, are more common in older children and adolescents. This article provides an overview of the clinical presentation, investigation and treatment of GORD in infants and children.

Causes

Transient lower oesophageal sphincter relaxation is the main mechanism leading to reflux episodes in adults, children and even preterm infants. Most individuals with GORD have normal lower oesophageal sphincter pressures. During reflux episodes,

IN SUMMARY

- Infants and children commonly present to GPs with gastro-oesophageal reflux (GOR). It is important to distinguish between uncomplicated GOR and gastro-oesophageal reflux disease (GORD).
- Minor GOR in otherwise well infants is considered physiological. Children with GORD often present with extra-oesophageal symptoms, including aversive feeding behaviours, failure to thrive or respiratory manifestations, as well as the 'classic' symptoms such as regurgitation, epigastric pain and heartburn.
- GORD in infants may be caused by cow's milk protein intolerance. Other conditions such as eosinophilic oesophagitis should be considered in the differential diagnoses of GORD.
- The treatment of GORD should be based on the clinical manifestations and possible complications. It is important to establish whether the degree of GOR in each patient requires medical treatment or not.
- The prognosis of GORD in infancy is excellent, and symptoms usually remit by 12 to 18 months of age.

gastric contents move passively along a pressure gradient from the stomach into the oesophagus. Gastric acid is cleared from the oesophagus by a two-step process. The acid bolus is first removed from the oesophagus by a peristaltic wave. In a second step, swallowed saliva neutralises the remaining mucosal acid coating.

Clinical presentation

Physiological GOR in infants presents with effortless regurgitation of breast milk or formula. These infants are otherwise well and thriving. Regurgitation of feeds at least once per day occurs in about half of infants under 3 months of age, and clinical improvement occurs from about 7 months of age. Mild to moderate GOR symptoms usually resolve without intervention by 12 to 18 months of age.

The clinical manifestations of GORD can be divided into acid-peptic mucosal damage, nutritional problems and respiratory complications (Table 1). In infants and young children, extra-oesophageal manifestations are common, whereas acid-peptic complications predominate in older children and adolescents.

Oesophagitis is caused by prolonged acid exposure, often in association with delayed oesophageal acid clearance. Oesophagitis may cause low-grade upper gastrointestinal bleeding and iron deficiency anaemia. However, acute haematemesis is uncommon. Children and adults with oesophagitis commonly complain of upper abdominal pain, heartburn (pyrosis) or painful swallowing (odynophagia). In patients with nonerosive reflux disease, symptoms are similar (but there is no histological evidence of epithelial erosion). Peptic strictures in the distal oesophagus may develop as a result of persistent mucosal inflammation and ulceration. Clinically, patients with peptic strictures may present with difficulty swallowing or oesophageal food bolus obstruction. Barrett's metaplasia may develop in the distal oesophagus after decades of untreated reflux oesophagitis and is a precursor to adenocarcinoma of the gastro-oesophageal junction.

In infancy, GORD may cause significant feeding difficulties. Failure to thrive may ensue because of decreased feeding and loss of nutrients due to frequent regurgitation. Although irritable behaviour and persistent crying are commonly seen in these infants, the distress may not be directly related to GORD but caused by underlying

GORD in infants and children

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Gastro-oesophageal reflux is a common and generally benign condition in infants and young children. These patients will generally improve without treatment and they usually do not require diagnostic investigation. However, infants and children with severe gastro-oesophageal reflux disease, presenting with haematemesis, failure to thrive, aversive feeding behaviours, respiratory manifestations or hypoxic episodes, should be referred for specialist assessment.

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conditions, such as cow's milk protein allergy. This type of allergy may also occur in breastfed infants because maternal dietary cow's milk protein may be secreted as intact antigen into human milk.

GORD in young children may present with respiratory complications, including aspiration, laryngitis, apparent life-threatening events or apnoeic episodes. The respiratory complications of GORD require a high degree of clinical awareness. It is important to understand that in patients with neurological impairment, aspiration episodes

Table 1. GORD in childhood: clinical manifestations**Acid-peptic mucosal damage**

Haematemesis
 Frequent regurgitation
 Poor feeding/feeding refusal
 Painful swallowing (odynophagia)
 Heartburn (pyrosis)
 Upper abdominal pain
 Difficulty swallowing
 Oesophageal food bolus obstruction

Nutritional problems

Failure to thrive
 Micronutrient deficiencies (e.g. iron)

Respiratory complications

Pulmonary aspiration
 Laryngitis
 Apparent life-threatening events
 Apnoeic episodes

may be relatively asymptomatic. GORD-associated chronic lung disease should be considered in all patients with impaired protective airway reflexes or dysphagia.

History

A detailed clinical history is important in the diagnosis of GORD. In infancy, most GORD episodes manifest as regurgitant reflux, and significant nonregurgitant ('silent') GORD is uncommon. The severity of regurgitant reflux, including frequency, estimated volume and associated symptoms, should be documented. Infants with reflux oesophagitis may present with aversive feeding behaviours or refusal. Older children can often describe their symptoms as retrosternal pain or heat sensation when swallowing, and may complain of intermittent regurgitation of gastric contents. Peptic strictures may present with oesophageal food bolus obstruction. A detailed dietary history, including review of growth parameters, should be obtained in all patients.

Physical examination

The physical examination of paediatric patients with GORD is not usually rewarding as most are relatively healthy. Pneumonia, persistent wheeze, stridor or a hoarse voice may point to respiratory complications of GORD. Weight and height should be measured in all paediatric patients.

Investigation

In general, GORD is a clinical diagnosis that does not require confirmation by investigations, unless specific complications are suspected. Three main investigations, described below, are used in infants and children with severe or atypical GOR symptoms. These are upper gastrointestinal barium study, oesophageal 24-hour pH monitoring and gastroscopy. The use of these investigations depends on the severity of GOR symptoms and response to basic therapeutic interventions. Chest x-ray, nuclear medicine scans or bronchoalveolar lavage may be indicated in patients with suspected respiratory manifestations.

Barium studies

Barium studies are mainly used to exclude anatomical abnormalities, such as hiatus hernia, peptic strictures, webs, extrinsic compression of the oesophagus or intestinal malrotation (which may present with persistent vomiting in infants and young children). Barium contrast liquid is administered by mouth or nasogastric tube. Radiological demonstration of reflux episodes under fluoroscopy does not reliably indicate the clinical severity of GORD or risk of complications.

Oesophageal 24-hour pH monitoring

Single or multilevel oesophageal 24-hour pH monitoring allows the quantification of GOR. The oesophageal environment above the lower oesophageal sphincter is normally alkaline. During reflux of gastric acid, the oesophageal pH drops rapidly to below 4, and pepsinogen is activated. Oesophageal pH monitoring measures the number and duration of

reflux episodes. Apart from being a diagnostic tool for GORD, pH monitoring is also helpful in monitoring the efficacy of medical antireflux treatment or fundoplication. Oesophageal pH monitoring is of limited value in assessing respiratory complications of GORD.

Bioelectrical impedance monitoring is a novel, pH-independent technique that detects all fluid and air movements along the oesophagus. Although mainly a research tool at present, it is likely that this technique will supersede oesophageal pH monitoring over the next decade.

Gastrointestinal endoscopy

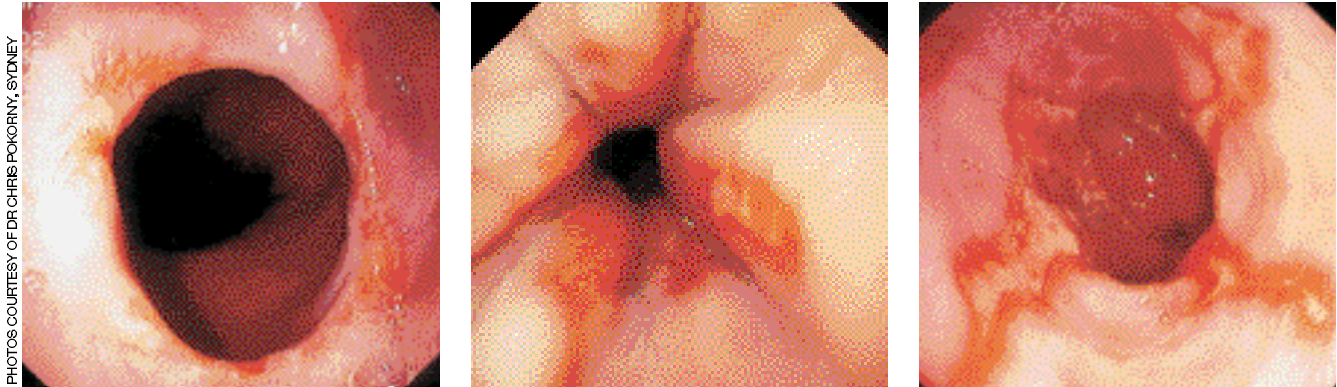
Upper gastrointestinal endoscopy is the most useful procedure in the investigation of upper abdominal pain, dysphagia, vomiting or haematemesis. A gastroscopy can be safely performed in infants and children under general anaesthesia. Gastroscopy allows visualisation of the mucosa in the oesophagus, stomach and duodenum (Figures 1a to c).

Oesophageal biopsies can be examined for signs of oesophagitis. Mucosal eosinophil counts of below 10 to 15 per high power field in lower oesophageal biopsies may be seen in patients with reflux oesophagitis; whereas higher eosinophil counts in specimens from the upper and lower oesophagus are suggestive of eosinophilic oesophagitis.

Differential diagnoses

As a first diagnostic step it should be ascertained whether GOR episodes are likely to be physiological or associated with adverse manifestations – that is, reflux disease. Clinicians should also try to differentiate between vomiting and GOR. Vomiting involves active expulsion of gastric and duodenal contents through retrograde peristalsis. This is mediated via the emetic reflex and is usually preceded by vagal symptoms, including nausea and pallor. By contrast, GOR is a passive event that is not preceded by nausea. In infants it may be difficult to distinguish between vomiting

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Figures 1a to c. Mild (a. left), moderate (b. centre) and severe (c. right) ulcerative oesophagitis on endoscopy.

and GOR. Vomiting is associated with a broad range of paediatric conditions, including gastroenteritis, urinary tract infection, sepsis, food allergy, metabolic diseases or raised intracranial pressure.

Eosinophilic oesophagitis

Over the past decade, eosinophilic oesophagitis has emerged as a form of oesophagitis. It is closely associated with food allergy and atopic disorders, such as asthma or eczema. It can occur in any age group but typically affects children and young adults.

Patients with eosinophilic oesophagitis have symptoms that are indistinguishable from GORD; however, they fail to respond to medical antireflux treatment or fundoplication. In school-aged children and young adults, oesophageal food bolus impaction is a typical presentation of eosinophilic oesophagitis, whereas in infants and young children, aversive feeding behaviours and failure to thrive are common presentations.

The diagnosis of eosinophilic oesophagitis is made by oesophageal biopsy and demonstration of mucosal eosinophil counts of more than 15 to 20 per high power field in upper and lower oesophageal biopsies. Treatment relies on hypoallergenic elimination diets or swallowed corticosteroid aerosols.

Food protein-induced GORD

A small proportion of infants with food

allergies may present with features of GORD. The most common food allergen causing infantile GORD is cow’s milk protein. Infants with this allergy present with GORD within the first few weeks of life, often in association with feeding difficulties, diarrhoea, eczema or failure to thrive. Cow’s milk allergy may occur in exclusively breastfed infants due to the presence of intact cow’s milk protein of maternal dietary origin in breast milk. The food allergy is usually non-IgE-mediated, and skin prick testing or specific serum IgE-antibodies are negative.

The diagnosis of food protein-induced GORD is made by strict cow’s milk protein elimination, usually by use of a hypoallergenic formula (extensively hydrolysed or amino acid-based formulas), and then later rechallenge. In breastfed infants, a maternal elimination diet may be effective.

The prognosis of infants with food protein-induced GORD is usually excellent. In infants who have responded to an elimination diet, cow’s milk-containing formulas or foods can be cautiously reintroduced within one to two months of the clinical resolution of GOR symptoms, as tolerated.

Treatment

The treatment of GORD should be based on the clinical manifestations and possible complications (Table 2). It is important to establish if the degree of GOR in each

patient requires medical treatment.

In infancy, simple measures may help to reduce the frequency or volume of reflux episodes. These include head-up posturing of the infant. For this purpose, the head end of the cot should be elevated to a 30° angle. Prone posturing is no longer recommended due to the increased risk of sudden infant death syndrome. In addition to posturing, thickening of infant formula, using for example corn starch, may decrease overt regurgitation and improve weight gain. In infants with unexplained crying or persistent irritability without significant regurgitation, there is no evidence to support the use of acid-suppressive medications.

Pharmacotherapy

In older children and adults, treatment of GORD relies mainly on pharmacotherapy. Acid-suppressive treatment in infants and young children usually involves a proton pump inhibitor – e.g. omeprazole. Other proton pump inhibitors that have also been used in children with GORD esomeprazole, lansoprazole and pantoprazole. In patients with mild GORD, a H₂-receptor antagonist (e.g. ranitidine or famotidine) may be suitable, although levels of acid suppression are much lower than those in patients who take a proton pump inhibitor. Antacids have a limited role in children due to possible aluminium toxicity. It is important to highlight to parents that

Table 2. Management of gastro-oesophageal reflux disease (GORD) in infants and children

Age group	Clinical presentation	Considerations	Management
Infants (0 to 12 months)	Infrequent regurgitation, but otherwise well and normal weight gain	Likely to be physiological GOR	Reassure parents Monitor growth Head-up supine posturing No specific treatment required
	Frequent regurgitation and/or haematemesis	Reflux oesophagitis Consider gastritis	Refer patient to a gastroenterologist for gastroscopy Treat reflux oesophagitis with omeprazole 1 mg/kg (max dose 10 mg) once daily
	Frequent regurgitation and poor weight gain	May be caused by loss of nutrients through recurrent regurgitation, insufficient oral intake or both	Organise dietetic review of oral intake Advise fortification of formula/nutritional supplementation Advise thickening of formula feeds (e.g. corn starch)
	Unsettled behaviour, and feeding difficulties or refusal	GOR unlikely cause of persistent crying, therefore, consider cow's milk protein intolerance or eosinophilic oesophagitis	Trial maternal hypoallergenic elimination diet or hypoallergenic formula (extensively hydrolysed formula) Involve dietitian and monitor nutritional progress
Children and adolescents (12 months and older)	Epigastric or retrosternal pain Regurgitation of gastric contents Halitosis Dental erosions	Likely reflux oesophagitis Consider eosinophilic oesophagitis if patient does not improve in response to standard medical antireflux treatment	Refer patient to a gastroenterologist for gastroscopy Prescribe omeprazole 1 mg/kg (max dose 20 mg) once daily
	Pulmonary aspiration or other respiratory manifestations of GORD	May present as persistent wheeze or chronic pneumonia Common in children with cerebral palsy or dysphagia Aspiration may occur during oral feeding (oropharyngeal inco-ordination) or after GOR episode Can be oligosymptomatic in children with significant neurological impairment	Refer patient to a respiratory medicine, gastroenterology and/or speech pathology specialist Patient may require video fluoroscopy, nuclear medicine studies, gastroscopy and/or bronchoalveolar lavage Consider enteral tube feeding (nasogastric tube or gastrostomy; postpyloric feeding in gastroparesis) or fundoplication

the frequency of regurgitation will not significantly change while children are taking acid-suppressive therapy. Symptomatic improvement usually occurs within two to four weeks of therapy. Patients' responses to treatment should be reviewed within four to six weeks, and discontinuation of the medication attempted, as tolerated. In patients with significant persistent or relapsing symptoms, referral for further diagnostic evaluation should be considered.

The role of prokinetic agents (e.g. domperidone or metoclopramide) in the

treatment of paediatric GORD is limited. Prokinetic agents are sometimes used in combination with acid-suppressive medications, particularly if delayed gastric emptying is suspected. However, their use is generally not recommended in the first-line treatment of GORD in children.

Review of diet

In infants with persistent crying and symptoms of GOR, acid-suppressive therapy is often ineffective. In these infants, gastrointestinal cow's milk protein allergy should be suspected. These patients should trial

an extensively hydrolysed formula for two to four weeks. In infants with ongoing significant GOR symptoms who have failed to respond to extensively hydrolysed formula, an amino acid-based formula may be tried. Alternatively, a maternal hypoallergenic elimination diet can be attempted in breastfed infants with GORD. Use of these elimination diets should be supervised by a paediatric dietitian to safeguard the nutritional adequacy of the diet for the mother and infant.

Thickened formula has been shown to reduce regurgitation in infants with

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mild to moderate GOR. Similarly, casein-predominant antiregurgitation formulas have been marketed for infants with regurgitant GOR. Although these formulas appear to reduce the frequency of overt regurgitation, their efficacy in reducing acid reflux and preventing reflux oesophagitis has not been proven.

Fundoplication

In infants and children, fundoplication is the treatment of choice for refractory, erosive oesophagitis or significant reflux aspiration. Fundoplication creates a high pressure zone at the gastro-oesophageal junction and thus prevents GOR episodes. Fundoplication can be performed as an open procedure or via laparoscopy. In children with neurological impairment and significant GORD, fundoplication may be required, sometimes in conjunction with a gastrostomy. Complications of fundoplication include dysphagia, gas bloat syndrome, wrap herniation and dumping syndrome.

Conclusion and recommendation for specialist referral

GOR is a common and generally benign condition in infants and young children. Infants with mild or moderate GOR will generally improve without treatment and do not require diagnostic investigation. However, patients with severe GORD, presenting with haematemesis, failure to thrive, aversive feeding behaviours, respiratory manifestations or hypoxic episodes, should be referred for specialist assessment.

Infants with GORD who have failed to respond to a trial of acid-suppressive therapy may have a cow's milk protein intolerance or eosinophilic oesophagitis. Early recognition of underlying food allergies is important to prevent nutritional or behavioural complications in infants and young children.

Most infants will outgrow their GOR symptoms by 12 to 18 months of age. Those with persistent regurgitation beyond

18 months of age may require further specialist evaluation if their symptoms appear significant. **MT**

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COMPETING INTERESTS: None.

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