

## PERSONAL PRACTICE

# Diagnosis and treatment of gastro-oesophageal reflux

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Gastro-oesophageal reflux (GOR) is defined as the involuntary passage of gastric contents into the oesophagus, and is a common cause of morbidity in childhood. GOR is an occasional physiological event in normal adults and children,<sup>1,2</sup> but becomes pathological when its intensity or frequency increases or when complications arise (for example, oesophagitis, failure to thrive). GOR may be primary (due to anatomical or physiological abnormalities) or secondary to other diseases such as urinary tract infection, metabolic disorders, food allergy, etc (see table 1). The increasing availability of lower oesophageal pH monitoring, paediatric endoscopic skills, and newer more effective pharmacological agents has led to a greater awareness of the range of symptoms attributable to gastro-oesophageal reflux disease (GORD), and the need for a structured approach to diagnosis and management.

## Presenting symptoms

Although vomiting is the most common symptom of primary GORD, it is now recognised that children and infants may present with a wide variety of other symptoms (see table 2). These may be related to oesophagitis, for example, haematemesis, anaemia, chest pain, or general irritability or from respiratory complications such as recurrent aspiration pneumonia, apnoea, or stridor. GOR may also be a factor in the aetiology of apparent life threatening events. Certain seizure-like events or dystonic posturing (Sandifer-Sutcliffe syndrome) may result from GORD.<sup>3</sup>

## Clinical assessment

The history must establish the nature and fre-

quency of the vomiting if present, and a detailed dietary assessment is essential. Systematic inquiry should also establish the presence of associated failure to thrive, and respiratory or neurological symptoms. On examination, an assessment should be made of nutritional status, respiratory signs, and neurodevelopmental milestones, searching also for signs of the causes of secondary GOR.

## Investigations

In those patients with uncomplicated primary GOR, few initial investigations are needed, although we routinely check a urine culture to exclude urinary tract infection. We check a full blood count, and faecal occult blood tests if occult gastrointestinal blood loss is suspected clinically. An estimation of acid-base balance may also be helpful. Other tests to exclude complications for GOR (for example, chest radiography to exclude aspiration pneumonia) or causes of secondary GOR may be indicated (for example, antigliadin antibodies).

(1) LOWER OESOPHAGEAL pH MONITORING  
Extended oesophageal pH monitoring over 18-24 hours is now well established as the 'gold standard' for documenting acid GOR,

Table 2 Symptoms of GORD

(A) Oesophageal symptoms
(1) Specific symptoms
• Regurgitation
• Vomiting
• Nausea
• Failure to thrive
(2) Symptoms due to oesophagitis
• Haematemesis and melaena
• Dysphagia
• Epigastric or retrosternal pain
• Heartburn
• Symptoms related to anaemia
• General irritability
• Feeding problems
• Oesophageal obstruction due to stricture
(B) Respiratory symptoms
• Aspiration pneumonia, especially recurrent
• Apnoea, especially in the preterm infant
• Apparent life threatening events and sudden infant death syndrome
• Cyanotic episodes
• Cough
• Stridor
• Bronchospasm or wheezing, especially intractable asthma
• Worsening of existing respiratory disease, for example cystic fibrosis
(C) Neurobehavioural symptoms
• Sandifer-Sutcliffe syndrome
• Seizure-like events in infants

Table 1 Causes of secondary reflux

• <i>Infective</i>
Gastroenteritis, urinary tract infection
• <i>Intestinal obstruction</i>
Volvulus, intestinal atresia, pyloric stenosis
• <i>Intracranial pathology</i>
Hydrocephalus, neoplasia, subdural haematoma
• <i>Food intolerance; coeliac disease</i>
Cows' milk, soy or egg intolerance
• <i>Metabolic</i>
Diabetic ketoacidosis, uraemia, inborn errors of metabolism
• <i>Psychological</i>
Anxiety or as feature of cyclical vomiting
• <i>Drugs/toxins</i>
Cytotoxic agents, theophylline, iron or digoxin

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providing more physiological and accurate information about reflux as a dynamic phenomenon than barium studies.<sup>4-7</sup>

#### (A) Study techniques

We use a study period of 24 hours (minimum 18 hours), and record significant events during the study period such as symptoms, feeds, and changes in position. H<sub>2</sub> antagonists (cimetidine, ranitidine) should be discontinued 3-4 days before the procedure, prokinetic agents (cisapride, domperidone, metoclopramide) 48 hours before, and antacids 24 hours before. Care should be taken with the positioning of the electrode. The Strobel formula (length from nostril to lower oesophageal sphincter in cm = 5 + 0.252 [height]) gives an approximate guide for positioning, especially in infants under the age of 1 year, but we confirm this with chest radiography or fluoroscopy before starting the recording. Secure fixing of the probe wires to the face with adhesive tape is important to prevent accidental movement of the electrode position. A working group on GORD of the European Society of Paediatric Gastroenterology and Nutrition (ESPGAN) has published a protocol for lower oesophageal pH monitoring,<sup>8</sup> which provides a useful guide for those carrying out the procedure.

#### (B) Interpretation of data

Although several different scoring systems have been developed for the interpretation of pH studies, we use the normal values based on studies by Vandenplas and Sacre-Smits (table 3).<sup>9</sup> A 'reflux episode' occurs when the lower oesophageal pH falls below pH 4. The reflux index is the percentage time of the study during which the lower oesophageal pH is less than 4, and provides a useful summary of a period of monitoring. However, data on the duration of the longest reflux episode and the number of prolonged reflux episodes (five minutes or longer) may also be of value, as such episodes may be matched with clinical events such as cyanotic episodes or seizure-like events. When using pH 4 to indicate reflux, it must be remembered that non-acid reflux may occur and will not be detected. In general, those children with a reflux index of 5-10% (mild) or 10-20% (moderate) will often be controlled by medical treatment, but those with over 30% reflux (severe) often require surgical intervention such as a Nissen fundoplication. Although a computerised summary of these values is produced at the end of a study period, it is of vital importance that the results are interpreted with the printout of actual pH data from the entire study period by a person with understanding both of the methodology and of the clinical problem. We

Table 3 Scoring system for oesophageal pH monitoring

- Per cent of time pH <4 for total period (the reflux index)
- Number of reflux episodes lasting 5 minutes or longer
- Duration of the longest reflux episode
- Total number of reflux episodes

have found that it may be totally misleading and even dangerous to evaluate the study on the summary data alone, as events such as accidental probe disconnection or slipping of the probe position may pass undetected unless the whole trace is examined carefully.

#### (2) BARIUM RADIOGRAPHY

We request barium studies if an anatomical abnormality is suspected, such as hiatus hernia, oesophageal stricture, malrotation, or gastric outlet obstruction. Although used historically for diagnosis, barium studies should not be used to diagnose or quantify GOR, as gastro-oesophageal dynamics are only examined over a very short period of time; results may be totally unreliable and misleading as severe GOR may be missed, and physiological reflux detected.<sup>10</sup>

#### (3) SCINTIGRAPHY

If facilities are easily available, this may be particularly useful in the diagnosis of non-acid reflux and for studying gastric emptying time. However, we do not use it as a routine investigation unless surgical intervention is planned.

#### (4) ENDOSCOPY

Upper gastrointestinal endoscopy enables a definite diagnosis of oesophagitis to be made, both macroscopically and histologically. Oesophageal strictures, hiatus hernia, Barrett's oesophagus, and other conditions which cause epigastric pain or haematemesis may all be diagnosed endoscopically. Histological confirmation of oesophagitis is important in a patient suspected of reflux associated oesophagitis, both to show oesophagitis where endoscopy is equivocal or negative, and to confirm that the oesophagitis is due to reflux in the patient where endoscopy is positive.<sup>11</sup>

#### Management of uncomplicated GOR

Infants with uncomplicated GOR, usually those under 12 months of age with regurgitation, may be diagnosed on the basis of history and examination alone, and often respond to a regimen of fairly simple measures. We use antacids, positioning, and simple dietary advice, and add cisapride if these measures have already been tried.

#### (1) POSITIONING

The baby should be positioned for sleep with the head raised to 30 degrees from the horizontal,<sup>12</sup> best arranged by a folded blanket placed under the head end of the mattress. Although lower oesophageal pH monitoring studies have previously shown GOR to be reduced by positioning the infant in the raised *prone* position, we do not recommend this position as the prone sleeping position has been found in many studies to be an independent risk factor for sudden infant death syndrome, and the Department of Health guidelines currently recommend lying babies in the

supine position.<sup>13</sup> Our preferred position is for the babies with GOR to be nursed on the side with the head raised to 30 degrees and with the lower arm placed well in front of the body to avoid rolling to the prone position. Blankets or wedges should not be used to support the position because of the risk of rolling into the prone position.

#### (2) ANTACIDS

Antacids such as infant Gaviscon (Reckitt and Colman; sodium salt of alginic acid) may be added to milk (1–2 g/100 ml) and are effective<sup>14 15</sup> but they contain a high sodium load that may be inappropriate in preterm babies. Antacids may be used in the older child as a tablet or liquid, to be taken before meals, before bed, or as symptoms arise.

#### (3) MILK THICKENERS

Thickening agents may be added to feeds to increase feed viscosity and decrease the symptoms of regurgitation and vomiting. They may be based on carob seed flour such as Carobel (Cow and Gate) or Nestargel (Nestlé), or on modified maize starch (Thixo-D; Cirrus). Although such thickeners may reduce the number of reflux episodes,<sup>16 17</sup> they may prolong the duration of remaining episodes, and therefore may be inappropriate in patients with known or suspected oesophagitis.

#### (4) DIETARY REGIMENS

Our usual dietary advice in infants is to give smaller feeds of increased frequency, although periods of postprandial reflux may thereby increase, and to give solids at a different time from liquids. Severe failure to thrive may arise if significant calories are lost through vomiting, and ensuring adequate energy intake is of vital importance. In older children we advise the avoidance of spicy foods, coffee, tea, cola and other fizzy drinks, and late evening meals.

#### (5) PROKINETIC AGENTS

If the general measures outlined above have failed to improve symptoms after 4–6 weeks, and secondary causes of GOR have been excluded, it is reasonable to start cisapride, one of the prokinetic drugs, without performing oesophageal pH monitoring.<sup>18</sup> Cisapride is a non-dopamine receptor blocking agent, which acts by enhancing acetylcholine release in the gut, thereby increasing gastrointestinal motility and improving antroduodenal coordination.<sup>19–21</sup> Reported side effects are usually minor and transient: colic, diarrhoea, headache, and occasional drowsiness. The usual dose is 0.8 mg/kg/day (0.4–1.2 mg/kg/day), given in 3–4 divided doses before meals and before bed.

#### Indications for oesophageal pH monitoring

If the above regimen fails to show any benefit after a further 4–6 weeks, lower oesophageal

pH monitoring studies are indicated to document and quantify GOR.

If pH monitoring results suggest no significant GOR, the diagnosis should be reconsidered. A full clinical reassessment is necessary, and further investigations to exclude an underlying cause of the vomiting or other symptoms should be considered (see table 1).

If GOR is confirmed by pH monitoring, we base any modifications to treatment on the severity of GOR confirmed, and on the presence of complications.

#### MILD-MODERATE GOR

In patients in whom pH monitoring confirms mild (5–10%) or moderate (10–20%) GOR, we continue treatment with general measures and cisapride for a further period of up to three months.

#### SEVERE GOR

If pH monitoring indicates severe GOR (over 20%), we add an H<sub>2</sub> antagonist (cimetidine at a dose of 30 mg/kg/day or ranitidine at 4–8 mg/kg/day) to prevent oesophagitis,<sup>21–23</sup> while continuing the regimen of cisapride and general measures as outlined above. We would also proceed to early endoscopy before starting H<sub>2</sub> blockers if there were clinical indicators of oesophagitis.

#### OESOPHAGITIS

We investigate patients presenting with symptoms suggestive of oesophagitis (chest pain, melaena, haematemesis, positive faecal occult blood in the stool, etc) with pH monitoring and endoscopy. Barium studies to exclude hiatus hernia and malrotation, and scintigraphy to exclude alkaline reflux or abnormal gastric emptying, may be appropriate in some cases. We treat the GOR with a prokinetic agent and the general measures outlined above. If oesophagitis is minimal (grade 1–3, mucosal redness), healing may occur with a prokinetic agent and general antireflux measures alone, continued for 4–12 weeks, but it is our practice to add H<sub>2</sub> antagonists to prevent worsening ulceration. More severe oesophagitis (above grade 3 with mucosal ulceration), however, is a definite indication for H<sub>2</sub> antagonists to be used<sup>21–23</sup> in combination with a prokinetic agent and general measures. Omeprazole, a proton pump inhibitor, is also effective in treating GOR related oesophagitis,<sup>24–26</sup> although experience of its use in children is limited. We have used omeprazole in 20 children with severe oesophagitis in whom H<sub>2</sub> antagonists had failed.<sup>26</sup> An optimal dose regimen is yet to be established, and our centre is contributing to a multicentre trial to evaluate an effective dose regimen for children. We currently use a dose of 5 mg daily for children under 5 years of age, 10 mg for 5–10 year olds, and 15 mg above 10 years of age.

We aim to perform a follow up endoscopy at

2–3 months after starting treatment. If the mucosa has healed, H<sub>2</sub> blockers or omeprazole may be discontinued, but prokinetic agents, antacids, and general antireflux measures should be continued for a prolonged period, certainly over six months. If there is no evidence of healing, we continue to treat medically for a further three months, ensuring once again that anatomical or other problems have been excluded.

### Surgery

Surgical treatment of GOR (usually a Nissen fundoplication) may be inevitable if full medical treatment has failed, or if there is an oesophageal stricture or Barrett's oesophagus at initial diagnosis. We assess such patients in a joint gastroenterological medical/surgical clinic at an early stage to consider each child's problems individually. Surgery should be preceded by a full functional and anatomical assessment including review of barium studies, repeat oesophageal pH monitoring, motility and gastric emptying studies to enable appropriate surgical procedures to be selected after consultation with the parents.<sup>27 28</sup> These may, for example, include a pyloroplasty or insertion of a feeding gastrostomy. Complications of surgical treatment include dumping, retching, intestinal obstruction, 'gas bloat', and recurrence of GOR.<sup>29 30</sup>

### GOR in neurologically abnormal children

Children with neurological disability often suffer from feeding difficulties, vomiting, failure to thrive, recurrent chest infections and irritability, and such symptoms are often accepted as part of the disability. The association between GOR and cerebral palsy was first reported by Abrahams and Burkitt in 1970,<sup>31</sup> who found reflux in 75% of cases, and extended lower oesophageal pH monitoring has confirmed this association.<sup>32</sup> GORD remains undiagnosed in many of these patients, but even when recognised, this group is difficult to manage effectively. Spontaneous resolution of GOR is less common in such children, as the neurological deficit itself causes delayed oesophageal clearance, delayed gastric emptying, etc. Our experience with a small number of children with Cornelia de Lange syndrome, for example, has been that the reflux index is as high as 50%, and most have needed early surgery for failure of medical treatment.

In the neurologically abnormal child, we always use pH monitoring at an early stage to establish the severity of GOR. We use a prokinetic agent with central nervous system activity such as domperidone (1 mg/kg/day) or metoclopramide (0.5 mg/kg/day)<sup>33 34</sup> because cisapride has been found to be poorly effective in this group of patients compared with its effects in neurologically normal children,<sup>35</sup> although this finding needs further evaluation. We endoscope those children found to have severe GOR on pH monitoring or those with symptoms of oesophagitis. We

treat oesophagitis with an H<sub>2</sub> antagonist, using omeprazole as second line treatment if healing has not occurred. Fundoplication is frequently needed in this group,<sup>30 36</sup> however, and is preceded by full assessment in joint medical/surgical setting.

### Children with 'silent' GOR and respiratory manifestations

Since the advent of oesophageal pH monitoring, it has become apparent that GOR may be clinically 'silent', that is, may present only with complications in the absence of regurgitation or vomiting.<sup>37</sup> Many respiratory complications have been linked to GOR on the basis of presumed aspiration or via oesophageal-respiratory tree reflexes. Up to three quarters of children with apparent life threatening events may have pathological GOR,<sup>38 39</sup> and it is our practice to investigate these children with pH monitoring combined with overnight sleep studies in conjunction with the respiratory team. The duration of reflux episodes during sleep may be an important determinant of reflux associated respiratory disease and sudden infant death syndrome,<sup>40</sup> and pH monitoring is directed at determining the duration of the reflux episodes and their correlation with clinical events such as apnoea, bradycardia, and drops in oxygen saturation rather than relying on the reflux index alone. If GOR is confirmed, energetic medical treatment is instituted in such infants and our own practice is to treat with cisapride in full dosage and H<sub>2</sub> antagonists, with early consideration of surgery if medical treatment is ineffective.

Silent reflux may be a contributing factor in intractable asthma and chronic lung disease such as cystic fibrosis, although its precise role in pathophysiology is unclear.<sup>37</sup> If clinically suspected, we carry out 24 hour oesophageal pH monitoring before starting any treatment.

### Conclusion

We recommend that children with typical symptoms of GOR without complications can be treated with simple measures and prokinetic agents such as cisapride without extensive investigations. However, oesophageal pH

Table 4 Summary of treatment of primary GOR

(1) <i>Uncomplicated GOR</i>
Antacids
Positioning
Head raised to 30 degrees
Nurse in lateral position
Dietary advice
+/- Prokinetic agents – cisapride 0.2 mg/kg four times a day before meals
If treatment fails – perform oesophageal pH monitoring
(2) <i>Mild-moderate GOR (reflux index &lt;20%)</i>
Continue as for (1), including prokinetics for up to 3 months
(3) <i>Severe GOR (reflux index &gt;20%)</i>
Add H <sub>2</sub> antagonist
Ranitidine 2–4 mg/kg/twice a day (or)
Cimetidine 5–10 mg/kg four times a day
(4) <i>Oesophagitis</i>
Use H <sub>2</sub> antagonist +/- omeprazole*
If medical treatment fails – surgical treatment, for example Nissen fundoplication

\*Dosage schedule yet to be established.

monitoring should be carried out if simple measures fail or if silent GOR is suspected (see table 4). Oesophageal pH monitoring should be available in a district hospital setting, but data need evaluation by an experienced clinician. If complications are present, the patient should be referred for further assessment to the regional paediatric unit equipped with full gastroenterological and surgical services.

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