Gastro-oesophageal reflux disease in children: NICE guidance

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Gastro-oesophageal reflux is a normal physiological event, whereas gastro-oesophageal reflux disease (GORD) occurs when this process causes symptoms severe enough to merit medical treatment or when there are associated complications. In infants and children it is particularly difficult to differentiate between the two conditions because of the wide variety of potential symptoms and the lack of a simple, reliable, and widely available diagnostic test. The true burden of the problem is therefore difficult to quantify, and it is accepted that clinical practice varies greatly.

Children affected by the disease include premature and term neonates, otherwise well infants and children, and those with known risk factors, such as repaired diaphragmatic hernia and other congenital anomalies or severe neurodisabilities. This last group of children may have complex comorbidities and the underlying pathophysiology may have important differences.

This article summarises the most recent guidance from the National Institute for Health and Care Excellence (NICE) on how to recognise, diagnose, and manage gastro-oesophageal reflux disease in infants, children, and young people.1

Recommendations

NICE recommendations are based on systematic reviews of best available evidence and explicit consideration of cost effectiveness. When minimal evidence is available, recommendations are based on the guideline development group’s experience and opinion of what constitutes good practice.

Evidence levels for the recommendations are in the full version of this article on bmj.com.

Diagnosing and investigating gastro-oesophageal reflux disease

• Recognise regurgitation of feeds as a common and normal occurrence in infants and that it:

THE BOTTOM LINE

• Frequent, effortless regurgitation of feeds is common during early infancy. Although worrying for parents, it usually resolves by the age of 1 year and usually does not need investigation or specific treatment. Effective management requires detailed, repeated, and confident reassurance
• For infants and children who present with regurgitation or vomiting, actively look out for “red flags” (such as projectile vomiting, bile stained vomiting, haematemesis, blood in stool, abdominal distension, or systemic features) that may suggest more serious conditions
• Consider simple cheap interventions, such as minor feed modifications or thickening agents, when possible and avoid acid suppressing drugs in isolated overt regurgitation
• Do not use upper gastrointestinal contrast radiology to diagnose or assess the severity of gastro-oesophageal reflux disease. This test is indicated for other reasons such as dysphagia or unexplained bile stained vomiting

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DEFINITIONS USED IN THE GUIDELINE

Gastro-oesophageal reflux: The passage of gastric contents into the oesophagus. It is a common physiological event that can happen at all ages from infancy to old age and is often asymptomatic. It is more common after feeds or meals. In many infants it is associated with a tendency to “overt regurgitation”—the visible regurgitation of feeds.

Gastro-oesophageal reflux disease: Gastro-oesophageal reflux that causes symptoms (for example, discomfort or pain) severe enough to merit medical treatment or that has associated complications (such as oesophagitis or pulmonary aspiration). In adults, the term is often used more narrowly, referring specifically to reflux oesophagitis.

Marked distress: There is limited evidence, and no objective or widely accepted clinical definition, for what constitutes marked distress in infants and children who cannot adequately communicate their sensory emotions.

In this guideline, marked distress refers to an outward demonstration of pain or unhappiness outside of that considered to be the normal range by an appropriately trained competent healthcare professional on the basis of a thorough assessment. This assessment should include a careful analysis of the description offered by the parents or carers of the individual child.

– Is caused by gastro-oesophageal reflux—a normal physiological process in infancy (the box outlines the definitions of gastro-oesophageal reflux and GORD used in this guideline)
– Does not usually need any investigation or treatment
– Is managed by advising and reassuring parents and carers.

– Be aware that in a small proportion of infants, gastro-oesophageal reflux may be associated with signs of distress or may lead to certain recognised complications that need clinical management. This is known as gastro-oesophageal reflux disease.
– Give advice about gastro-oesophageal reflux, and reassure parents and carers that in well infants effortless regurgitation of feeds:
  – Is common (affects at least 40% of infants)
  – Usually begins before the infant is 8 weeks old
  – May be frequent (5% of those affected have six or more episodes a day)
  – Usually becomes less frequent with time (it resolves in 90% of affected infants before age 1 year)
  – Does not usually need further investigation or treatment.
– When reassuring parents and carers about regurgitation, advise them that they should return for review if any of the following occur:
  – Regurgitation becomes persistently projectile
In infants, children, and young people with vomiting or regurgitation, look out for “red flag” symptoms (table) that may suggest disorders other than gastro-oesophageal reflux. Investigate or refer, using clinical judgment.

<table>
<thead>
<tr>
<th>“Red flag” symptoms suggesting conditions other than gastro-oesophageal reflux in infants and children</th>
<th>Possible diagnostic implication</th>
<th>Suggested action*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequent, forcible (projectile) vomiting</td>
<td>May suggest hypertrophic pyloric stenosis in infants up to 2 months old</td>
<td>Paediatric surgery referral</td>
</tr>
<tr>
<td>Bile stained (green or yellow-green) vomit</td>
<td>May suggest intestinal obstruction</td>
<td>Paediatric surgery referral</td>
</tr>
<tr>
<td>Haematemesis (blood in vomit) with the exception of obviously swallowed blood (for example, after a nose bleed or ingested blood from a cracked nipple in breastfed infants)</td>
<td>May suggest an important and potentially serious bleed from the oesophagus, stomach, or upper gut</td>
<td>Specialist referral for investigation</td>
</tr>
<tr>
<td>Onset of regurgitation or vomiting (or both) after age 6 months or persisting after age 1 year</td>
<td>Late onset suggests a cause other than reflux, such as a urinary tract infection (also see National Institute for Health and Care Excellence (NICE) clinical guideline on urinary tract infection in children). Persistence suggests an alternative diagnosis</td>
<td>Urine microbiology investigation</td>
</tr>
<tr>
<td>Blood in stool</td>
<td>May suggest a variety of conditions, including bacterial gastroenteritis, infant cows’ milk protein allergy (also see NICE clinical guideline on food allergy in children and young people), or an acute surgical condition</td>
<td>Stool microbiological investigation and specialist referral</td>
</tr>
<tr>
<td>Abdominal distension, tenderness, or palpable mass</td>
<td>May suggest intestinal obstruction or another acute surgical condition</td>
<td>Paediatric surgical referral</td>
</tr>
<tr>
<td>Chronic diarrhoea</td>
<td>May suggest cows’ milk protein allergy (also see NICE clinical guideline on food allergy in children and young people)</td>
<td>Specialist referral</td>
</tr>
<tr>
<td>Systemic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Appearing unwell, fever</td>
<td>May suggest infection (also see NICE clinical guideline on feverish illness in children)</td>
<td>Clinical assessment and urine microbiology investigation and specialist referral</td>
</tr>
<tr>
<td>Dysuria</td>
<td>May suggest urinary tract infection (also see NICE clinical guideline on urinary tract infection in children)</td>
<td>Clinical assessment and urine microbiology investigation and specialist referral</td>
</tr>
<tr>
<td>Bulging fontanelle</td>
<td>May suggest raised intracranial pressure—for example, owing to meningitis (also see NICE clinical guideline on bacterial meningitis and meningococcal septicaemia)</td>
<td>Specialist referral</td>
</tr>
<tr>
<td>Rapidly increasing head circumference (more than 1 cm/week); persistent morning headache and vomiting worse in the morning</td>
<td>May suggest raised intracranial pressure—for example, owing to hydrocephalus or a brain tumour</td>
<td>Specialist referral</td>
</tr>
<tr>
<td>Altered responsiveness—for example, lethargy or irritability</td>
<td>May suggest raised intracranial pressure—for example, owing to meningitis (also see NICE clinical guideline on bacterial meningitis and meningococcal septicaemia)</td>
<td>Specialist referral</td>
</tr>
<tr>
<td>Infants and children with, or at high risk of, atopy</td>
<td>May suggest cows’ milk protein allergy (also see NICE clinical guideline on food allergy in children and young people)</td>
<td>Trial of cows’ milk exclusion and specialist referral</td>
</tr>
</tbody>
</table>

*Specialist refers to a paediatrician with the skills, experience, and competency necessary to deal with the particular clinical concern that has been identified by the referring healthcare professional, usually a consultant general paediatrician. Depending on the clinical circumstances, specialist may also refer to a paediatric surgeon, paediatric gastroenterologist, or a doctor with the equivalent skills and competency.

- There is bile stained (green or yellow-green) vomiting or haematemesis (blood in vomit)
- There are new concerns, such as signs of marked distress (box), feeding difficulties, or faltering growth
- There is persistent frequent regurgitation beyond the first year of life.

- In infants, children, and young people with vomiting or regurgitation, look out for “red flag” symptoms (table) that may suggest disorders other than gastro-oesophageal reflux. Investigate or refer, using clinical judgment.

- Do not routinely investigate or treat for gastro-oesophageal reflux disease if an infant or child without overt regurgitation presents with only one of the following:
  - Unexplained feeding difficulties (such as refusing to feed, gagging, or choking)
  - Distressed behaviour
  - Faltering growth
  - Chronic cough
  - Hoarseness
  - A single episode of pneumonia.

- Recognise the following as possible complications of gastro-oesophageal reflux in infants, children, and young people:
  - Reflux oesophagitis
  - Recurrent aspiration pneumonia
  - Frequent otitis media (for example, more than three episodes in six months)
  - Dental erosion in the presence of a neurodisability, in particular cerebral palsy.

- Recognise the following as possible symptoms of gastro-oesophageal reflux in children and young people:
  - Heartburn
  - Retrosternal pain
  - Epigastric pain.

- Be aware that gastro-oesophageal reflux is more common in children and young people with asthma but has not been shown to cause or worsen it.

- Be aware that some symptoms of a non-IgE mediated cows’ milk protein allergy can be similar to the symptoms of GORD, especially in infants with atopic symptoms, signs, or a family history (or a combination thereof). If a non-IgE mediated cows’
milk protein allergy is suspected, see the NICE guideline on food allergy in children and young people.

- When deciding whether to investigate or treat, take into account that the following are associated with an increased prevalence of GORD:
  - Premature birth
  - Parental history of heartburn or acid regurgitation
  - Obesity
  - Hiatus hernia
  - History of congenital diaphragmatic hernia (repaired)
  - History of congenital oesophageal atresia (repaired)
  - Neuromuscular disease
  - For children and young people who are obese and have heartburn or acid regurgitation, advise them and their parents or carers (as appropriate) that losing weight may improve their symptoms (also see the NICE guidelines on obesity).

- Consider referring infants and children with persistent back arching or features of Sanderfer’s syndrome (episodic torticollis with neck extension and rotation) for specialist assessment.

- Gastro-oesophageal reflux causes episodes of apnoea or apparent life threatening events only rarely, but consider referral for specialist investigations if reflux is suspected as a possible factor after a general paediatric assessment.

- Do not offer upper gastrointestinal contrast studies to diagnose or assess the severity of GORD in infants or children. This should be used to investigate unexplained bile stained vomiting (very urgently in infants) or dysphagia. It is used to diagnose and demonstrate structural or anatomical upper gastrointestinal problems and is usually arranged through secondary care.

- Arrange an urgent specialist hospital assessment to take place on the same day for infants younger than 2 months with progressively worsening or forceful vomiting of feeds to assess them for possible hypertrophic pyloric stenosis.

- For recommendations relating to the indications for endoscopy and oesophageal pH monitoring, see the further information box in the full version of this article on thebmj.com.

- Investigate the possibility of a urinary tract infection in infants with regurgitation if there is:
  - Faltering growth
  - Late onset of regurgitation (after age 8 weeks)
  - Frequent regurgitation and marked distress.

Initial management of gastro-oesophageal reflux and GORD

- Do not offer positional management to treat gastro-oesophageal reflux in sleeping infants. In line with NHS advice, infants should be placed on their backs when sleeping.

- In breastfed infants with frequent regurgitation associated with marked distress:
  - Ensure that a person with appropriate expertise and training carries out a breastfeeding assessment
  - If marked distress continues despite breastfeeding assessment and advice, consider treatment with alginate for a trial period of one to two weeks. If successful continue with the treatment, but try stopping it at intervals to see if the infant has recovered.

- In formula fed infants with frequent regurgitation associated with marked distress use the following stepped care approach:
  - Review the feeding history, then
  - Reduce the feed volumes only if excessive for the infant’s weight, then
  - Offer a trial of smaller more frequent feeds (while maintaining an appropriate total daily amount of milk), unless the feeds are already small and frequent, then
  - Offer a trial of thickened formula (for example, containing rice starch, cornstarch, locust bean gum, or carob bean gum)

- If the stepped care approach is unsuccessful, stop the thickened formula and offer treatment with alginate for a trial period of one to two weeks. If successful, continue with the treatment, but try stopping it at intervals to see if the infant has recovered.

Pharmacological treatment of GORD

- Do not offer acid suppressing drugs, such as proton pump inhibitors (PPIs) or H2 antihistamines to treat overt regurgitation in infants and children occurring as an isolated symptom.

- Consider a four week trial of an H2 antihistamine or a PPI for those who are unable to tell you about their symptoms (such as infants and young children, and those with a neurodisability associated with expressive communication difficulties) who have overt regurgitation with one or more of the following:
  - Unexplained feeding difficulties (such as refusing feeds, gagging, or choking)
  - Distressed behaviour
  - Faltering growth.

- Consider a four week trial of a PPI for children and young people with persistent heartburn, retrosternal pain, or epigastric pain.

- Assess the response to PPI or H2 antihistamine treatment at four weeks and consider referral for specialist assessment and possible endoscopy if the symptoms:
  - Have not resolved
  - Recur after stopping the treatment.

- When choosing between PPIs and H2 antihistamines take into account:
  - The availability of age appropriate preparations
  - The preference of the parent (or carer), child, or young person (as appropriate)
  - Local procurement costs.

- Offer PPI or H2 antihistamine treatment to infants, children, and young people with endoscopy confirmed reflux oesophagitis and consider repeat endoscopic examinations as necessary to guide subsequent treatment.

- Do not offer metoclopramide, domperidone, or erythromycin to treat gastro-oesophageal reflux or
Overcoming barriers
It can be difficult to persuade families that distressing and disabling symptoms (such as frequent and severe vomiting in thriving infants) will almost certainly improve with time but can be helped by relatively minor interventions, rather than referral for unnecessary tests or the use of drugs with no confirmed effect. This guideline offers clear direction as to when and how families can be appropriately reassured and provides links to downloadable information for parents. However, for different clinical presentations or evolving symptoms, especially potentially serious red flag presentations, the guideline recommends actions that are clearly necessary by way of investigation, treatment, and referral.

Surgery for GORD
• Consider fundoplication in infants, children, and young people 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.
• For further recommendations on surgery and enteral tube feeding, see the further information box in the full version of this article on thebmj.com.

ALL THINGS CONSIDERED
Failed phlebotomy? Think William Harvey

Why do health professionals take blood in the wrong direction? Shortly before his death in 1657, William Harvey told the young Robert Boyle that the main thing that convinced him of the circulation of the blood was that the valves in arm veins prevent flow down the arm. This is a truth universally acknowledged, but ignored, given that it is the retrograde direction in which all hopeful phlebotomists expect blood to flow into their needles. We sometimes get away with it, when the blood, travelling headwards up a vein, struggles past the occluding needle, does an about turn, and ends up in the right place. Sometimes. The headwards approach will generally work in large veins. But the smaller the vein the more guaranteed we are of a mere dribble, loss of self-esteem, and another bruise in a disheartened patient.

When the needle is in a large vein in the arm, flow may be improved by invoking the phenomenon of vis a tergo. This Latin term (literally “force from behind”) entered English at the start of the 19th century and generally refers to the force exerted by the heart in pushing the blood around the circulation. Contracting the nearby muscles increases this, for example by asking the patient to clench and unclench the fist, but when a sample is sought from smaller vessels, such as those in the hand, this manoeuvre is less helpful. Other ways of increasing flow or inducing distension in a vein include tapping it, lowering the limb, and using a tourniquet.

Another solution is to remember Harvey. When asked to see a patient from whom others have failed to obtain blood, find that tiny vein in the arm or hand and gently insert a needle or cannula facing down the arm. Harvey’s method is to empty a segment of vein by stroking along it with a finger, moving away from the heart, and noting the point beyond which a valve prevents the retrograde refilling of the vein from the proximal end of the segment, the distal segment still being occluded by the finger. A cannula may be useful if repeated samples are needed; it can sit there for a while without spearing the wall of the vein and springing a leak that heralds another failure. However, there is evidence that using a cannula may be associated with a higher risk of haemolysis than using a butterfly needle. Even if the flow is sluggish, a needle or cannula facing fingerwards in a small vein will always serve up the required sample (see figure). In this case, don’t use an aggressive vacuumed sample tube—it may be too impatient to cope.

In 125 pages of WHO guidelines on best practices in phlebotomy there is no concession to Harvey. Needles are shown dutifully pointing headwards. This is perhaps because we are used to delivering fluids and medications in the direction of flow. But a little physiology shows how to solve a very common problem in difficult cases.

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References and Competing interests are on thebmj.com.

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