Gastro-oesophageal reflux disease in children: NICE guidance

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This is one of a series of BMJ summaries of new guidelines based on the best available evidence; they highlight important recommendations for clinical practice, especially where uncertainty or controversy exists.

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.

**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 given in italic in square brackets.

**Diagnosing and investigating gastro-oesophageal reflux disease**

- Recognise regurgitation of feeds as a common and normal occurrence in infants and that it:
  - 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 ([Based on high, moderate, and low quality evidence from observational studies and on the experience and opinion of the Guideline Development Group (GDG).])
- 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. ([Based on the experience and opinion of the GDG.])
- 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.
Recognise the following as possible complications of gastro-oesophageal reflux:

- Reflux oesophagitis
- A single episode of pneumonia.
- 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.
- Epigastric pain.
- Distressed behaviour
- Epigastric pain.

Common symptoms of gastro-oesophageal reflux disease in children and young people:
- Heartburn
- Retrosternal pain
- Epigastric pain
- Frequent episodic vomiting
- Bile stained vomiting
- Feeding difficulties
- Distressed behaviour
- Unexplained feeding difficulties
- Gagging, or choking

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.

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
- 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 flags" (such as projectile vomiting, bile stained vomiting, haematemesis, blood in stool, abdominal distension, or systemic features) that may suggest more serious conditions, and 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 routinely investigate or treat for gastro-oesophageal reflux in infants, children, and young people.

In infants and children who present with regurgitation or vomiting, actively look out for "red flag" symptoms (such as projectile vomiting, bile stained vomiting, haematemesis, blood in stool, abdominal distension, or systemic features) that may suggest more serious conditions. 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.
- Neurodisability.

[Based on high, moderate, and low quality evidence from observational studies and the experience and opinion of the GDG.]

- 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). [Based on high, moderate, and low quality evidence from observational studies.]

- Consider referring infants and children with persistent back arching or features of Sandifer’s syndrome (episodic torticollis with neck extension and rotation) for specialist assessment. [Based on low quality evidence from observational studies.]

- 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. [Based on high, moderate, and low quality evidence from observational studies and on the experience and opinion of the GDG.]

- 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. [Based on the experience and opinion of the GDG.]

- 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. [Based on the experience and opinion of the GDG.]

- For recommendations relating to the indications for endoscopy and oesophageal pH study or impedance monitoring, see the further information box.

- 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.

[Based on the experience and opinion of the GDG.]

### Initial management of gastro-oesophageal reflux and GORD

- Do not use positional management to treat gastro-oesophageal reflux in sleeping infants. In line with NHS advice, infants should be placed on their backs when sleeping. [Based on moderate and low quality evidence from observational studies and on the experience and opinion of the GDG.]

- 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.

[Based on the experience and opinion of the GDG.]

- 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.

[Based on moderate and low quality evidence from randomised controlled trials (RCTs) and on the experience and opinion of the GDG.]

### Pharmacological treatment of GORD

- Do not offer acid suppressing drugs, such as proton pump inhibitors (PPIs) or H<sub>2</sub> antihistamines to treat overt regurgitation in infants and children occurring as an isolated symptom. [Based on moderate and low quality evidence from RCTs.]

- Consider a four week trial of an H<sub>2</sub> 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.

[Based on the experience and opinion of the GDG.]

- Consider a four week trial of a PPI for children and young people with persistent heartburn, retrosternal pain, or epigastric pain. [Based on moderate and low quality evidence from RCTs and on the experience and opinion of the GDG.]

- Assess the response to PPI or H<sub>2</sub> antihistamine treatment at four weeks and consider referral for specialist assessment and possible endoscopy if the symptoms:
  - Have not resolved or
  - Recur after stopping the treatment.

[Based on the experience and opinion of the GDG.]

- When choosing between PPIs and H<sub>2</sub> 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.
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.

[Based on moderate and low quality evidence from observational studies and RCTs and on the experience and opinion of the GDG.]

- For further recommendations on enteral tube feeding and surgery see the further information box.

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.

The members of the Guideline Development Group were David Bevan, Karen Blythe, Shona Burman-Roy, Jiri Chard, Kate Coles, Sarah Currell, leuan Davies (chair), Hannah Rose Douglas, Charlie Fairhurst, Maryam Gholitabar, Yelan Guo, Rebecca Harrington, Paul Jacklin, Bruce Jaffray, Eleanor Jeans, Dianne Jones, Setor Kunutsor, Rosalind Lai, John Martin, Tom McAnea, Paul Mitchell, Stephen Murphy, Russell Peek, Nitura Prasannan, Mike Thomson, Mark Tigue, and Rowena McCartney (invited expert).

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Further information on the guidance

A gastro-oesophageal reflux disease (GORD) pathway that visually represents all of the recommendations is available on the National Institute for Health and Care Excellence (NICE) pathways website (http://pathways.nice.org.uk/pathways/dyspepsia-and-gastro-oesophageal-reflux-disease). NICE guidelines are for health and social care professionals, public health experts, commissioners or providers of health and social care services, and members of the public. Audit and costing tools to support implementation are also available (www.nice.org.uk/guidance/NG1/resources). Parents, children, and young people can also be directed to corresponding NICE information for the public (www.nice.org.uk/guidance/NG1/informationforpublic).

Methods

This guidance was developed by the National Collaborating Centre for Women’s and Children’s Health in accordance with NICE guideline development methods (www.nice.org.uk/guidelinemanual). The Guideline Development Group (GDG) comprised two paediatric gastroenterologists (including the chair); a paediatrician; a neonatologist; a consultant in paediatric neurodisability; a paediatric surgeon; two general practitioners; an advanced paediatric nurse practitioner; a paediatric dietitian; a health visitor; lay members with experience of caring for such infants, children, or young people; and experts in guideline methodology. There was also a pharmacist as an “invited expert.” The GDG identified relevant clinical questions, collected and appraised clinical evidence, and where possible evaluated the cost effectiveness of proposed interventions. The draft guideline underwent a public consultation and a validation process in which stakeholder organisations were invited to comment; all comments were considered when producing the final version of the guideline.

NICE has produced four different versions of the guideline: a full version containing all the evidence, the process undertaken to develop the recommendations, and all the recommendations; a version containing a list of all the recommendations, known as the “NICE guideline”; a version for patients and the public (www.nice.org.uk/guidance/NG1/informationforpublic); and a web version of the care pathway (the “NICE pathway”). All these versions are available from the NICE website (www.nice.org.uk/guidance/NG1). Implementation tools will also be available from the NICE website. The guideline will be reviewed for update in two years’ time as part of the NICE guideline development programme.

Future research

A prospective cohort study to evaluate the diagnostic accuracy of symptoms associated with GORD in infants, children, and young people with complex severe neurodisability to detect GORD (diagnosed as reflux oesophagitis identified by endoscopy and oesophageal pH monitoring).

A randomised controlled trial in formula fed infants with suspected GORD that compares the effects of an extensively hydrolysed formula feed versus a placebo milk substitute on clinical symptoms and the results of objective measurements (endoscopy and oesophageal pH monitoring).

A prospective evaluation of objective symptom profiles, oesophageal pH monitoring, and upper gastrointestinal endoscopy before and after fundoplication surgery in children with GORD.

Further recommendations

Gastrointestinal contrast study

- Do not offer an upper gastrointestinal contrast study to diagnose or assess the severity of GORD in infants, children, and young people. [Based on the experience and opinion of the GDG.]
- Perform an urgent (same day) upper gastrointestinal contrast study for infants with unexplained bile stained vomiting. Explain to the parents and carers that this is needed to rule out serious disorders such as intestinal obstruction caused by midgut volvulus. [Based on the experience and opinion of the GDG.]
- Consider an upper gastrointestinal contrast study for children and young people with a history of bile stained vomiting, particularly if it is persistent or recurrent. [Based on the experience and opinion of the GDG.]
- Offer an upper gastrointestinal contrast study for children and young people with a history of GORD who present with dysphagia. [Based on the experience and opinion of the GDG.]

Endoscopy and oesophageal pH or impedance monitoring

- Refer infants, children, and young people to a specialist for a possible upper gastrointestinal endoscopy with biopsies if there is:
  - Haematemesis (blood stained vomit) not caused by swallowed blood (assessment to take place on the same day if clinically indicated; also see table 1)
  - Melaena (black, foul smelling stool) (assessment to take place on the same day if clinically indicated; also see table 1)
  - Dysphagia (assessment to take place on the same day if clinically indicated)
  - No improvement in regurgitation after age 1 year
  - Persistent faltering growth associated with overt regurgitation
  - Unexplained distress in children and young people with communication difficulties
  - Retrosternal, epigastric, or upper abdominal pain that needs ongoing medical treatment or is refractory to medical treatment
  - Feeding aversion and a history of regurgitation
  - Unexplained iron deficiency anaemia
  - A referral for fundoplication
  - A possible need for fundoplication (see second point under “Investigations for surgery”)
  - Back arching or features of Sandifer’s syndrome.
  - A suspected diagnosis of Sandifer’s syndrome.
  - Consider performing an oesophageal pH study (or combined oesophageal pH and impedance monitoring if available) in infants, children, and young people with:
    - Suspected recurrent aspiration pneumonia
    - Unexplained apnoeas
    - Unexplained non-epileptic seizure-like events
    - Unexplained upper airway inflammation
    - Dental erosion associated with a neurodisability
    - Frequent otitis media
    - A possible need for fundoplication (see second point under “Investigations for surgery”)
  - Consider performing an oesophageal pH study without impedance monitoring in infants, children, and young people if, using clinical judgment, this is thought necessary to ensure effective acid suppression. [Based on the experience and opinion of the GDG.]

Enteral tube feeding for GORD

- Consider enteral tube feeding to promote weight gain in infants and children with overt regurgitation and faltering growth only if:
  - Other explanations for poor weight gain have been explored or
  - Recommended feeding and medical management of overt regurgitation is unsuccessful.
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 enteral tube feeding as soon as possible
- An exit strategy, if appropriate, to stop enteral tube feeding as soon as possible.

In infants and children receiving enteral tube feeding for faltering growth associated with overt regurgitation:
- Provide oral stimulation, continuing oral feeding as tolerated
- Follow the nutrition plan, ensuring that the intended target weight is achieved and that appropriate weight gain is sustained
- Reduce and stop enteral tube feeding as soon as possible.

Consider jejunal feeding for infants, children, and young people:
- Who need enteral tube feeding but who cannot tolerate intragastric feeds because of regurgitation or
- If reflux related pulmonary aspiration is a concern.

Investigations before surgery
- Offer an upper gastrointestinal endoscopy with oesophageal biopsies for infants, children, and young people before deciding whether to offer fundoplication for presumed GORD.
- Consider performing other investigations such as an oesophageal pH study (or combined oesophageal pH and impedance monitoring if available) and an upper gastrointestinal contrast study in infants, children, and young people before deciding whether to offer fundoplication.

Table 1 | “Red flag” symptoms suggesting conditions other than gastro-oesophageal reflux in infants and children

| Symptom or sign | Possible diagnostic implication | Suggested action* |
|-----------------|---------------------------------|-------------------|
| **Gastrointestinal** | | |
| Frequent, forceful (projectile) vomiting | May suggest hypertrophic pyloric stenosis in infants up to 2 months old | Paediatric surgery referral |
| Bile stained (green or yellow-green) vomit | May suggest intestinal obstruction | Paediatric surgery referral |
| Haematemeses (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) | May suggest an important and potentially serious bleed from the oesophagus, stomach, or upper gut | Specialist referral for investigation |
| Onset of regurgitation or vomiting (or both) after age 6 months or persisting after age 1 year | 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 | Urine microbiology investigation⁷ |
| Blood in stool | 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 people⁵), or an acute surgical condition | Stool microbiological investigation and specialist referral⁶ |
| Abdominal distension, tenderness, or palpable mass | May suggest intestinal obstruction or another acute surgical condition | Paediatric surgical referral |
| Chronic diarrhoea | May suggest cows’ milk protein allergy also see NICE clinical guideline on food allergy in children and young people⁵ | Specialist referral³ |
| **Systemic** | | |
| Appearing unwell, fever | May suggest infection (also see NICE clinical guideline on feverish illness in children⁴) | Clinical assessment and urine microbiology investigation and specialist referral⁵ |
| Dysuria | May suggest urinary tract infection (also see NICE clinical guideline on urinary tract infection in children⁶) | Clinical assessment and urine microbiology investigation and specialist referral³ |
| Bulging fontanelle | May suggest raised intracranial pressure—for example, owing to meningitis (also see NICE clinical guideline on bacterial meningitis and meningococcal septicaemia⁴) | Specialist referral³ |
| Symptom or sign                                      | Possible diagnostic implication                                                                 | Suggested action                        |
|-----------------------------------------------------|--------------------------------------------------------------------------------------------------|----------------------------------------|
| Rapidly increasing head circumference (more than 1 cm/week); persistent morning headache and vomiting worse in the morning | May suggest raised intracranial pressure—for example, owing to hydrocephalus or a brain tumour | Specialist referral                     |
| Altered responsiveness—for example, lethargy or irritability | May suggest raised intracranial pressure—for example, owing to meningitis (also see NICE clinical guideline on bacterial meningitis and meningococcal septicaemia) | Specialist referral                     |
| Infants and children with, or at high risk of, atopy | May suggest cows’ milk protein allergy (also see NICE clinical guideline on food allergy in children and young people) | Trial of cows’ milk exclusion and specialist referral |

*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.*